

Bureau International des Poids et Mesures

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

Report of the 22nd meeting  
(21-22 April 2016)  
to the International Committee for Weights and Measures



Comité international des poids et mesures

Note:

Following a decision of the International Committee for Weights and Measures at its 92nd meeting (October 2003), reports of meetings of the Consultative Committees are now published only on the BIPM website and in the form presented here.

Full bilingual versions in French and English are no longer published.

M. Milton  
Director BIPM

**LIST OF MEMBERS OF THE  
CONSULTATIVE COMMITTEE FOR AMOUNT OF SUBSTANCE:  
METROLOGY IN CHEMISTRY AND BIOLOGY**

as of 21 April 2016

**President**

Dr W.E. May, member of the International Committee for Weights and Measures also  
National Institute of Standards and Technology, NIST, Gaithersburg

**Executive Secretary**

Dr R. Wielgosz, International Bureau of Weights and Measures [BIPM], Sèvres.

**Members**

Centro Nacional de Metrología [CENAM], Querétaro.  
D.I. Mendeleev Institute for Metrology, Rosstandart [VNIIM], St Petersburg.  
Danish Fundamental Metrology Ltd [DFM], Lyngby.  
Dutch National Metrology Institute [VSL], Delft.  
Federal Institute for Materials Research and Testing/Bundesanstalt für Material-forschung und -prüfung [BAM] Berlin.  
Federal Office of Metrology [METAS], Bern-Wabern.  
Health Sciences Authority [HSA], Singapore.  
Institute for Reference Materials and Measurements [IRMM].  
Instituto Nacional de Metrologia, Qualidade e Tecnologia [INMETRO], Rio de Janeiro.  
International Atomic Energy Agency [IAEA].  
International Federation of Clinical Chemistry and Laboratory Medicine [IFCC].  
International Organization for Standardization, Committee on Reference Materials [ISO REMCO].  
International Union of Pure and Applied Chemistry [IUPAC].  
Istituto Nazionale di Ricerca Metrologica [INRIM], Turin.  
Korea Research Institute of Standards and Science [KRISS], Daejeon.  
Laboratoire National de Métrologie et d'Essais [LNE], Paris.  
Laboratory of the Government Chemist [LGC Ltd], Teddington.  
National Institute of Metrology [NIM], Beijing.  
National Institute of Metrology [NIMT], Pathumthani.  
National Institute of Standards and Technology [NIST], Gaithersburg.

National Measurement Institute, Australia [NMIA], Lindfield.

National Metrology Institute of Japan, National Institute of Advanced Industrial Science and Technology [NMIJ/AIST], Tsukuba.

National Metrology Institute of South Africa [NMISA], Pretoria.

National Metrology Institute of Turkey/Ulusal Metroloji Enstitüsü [UME], Gebze-Kocaeli.

National Physical Laboratory [NPL], Teddington.

National Research Council of Canada [NRC], Ottawa.

Physikalisch-Technische Bundesanstalt [PTB], Braunschweig.

Slovak Institute of Metrology/Slovenský Metrologický Ústav [SMU], Bratislava.

SP Technical Research Institute of Sweden [SP], Borås.

State Laboratory [SL], Co. Kildare.

The Director of the International Bureau of Weights and Measures [BIPM], Sèvres.

### **Observers**

Agency for Science, Technology and Research [A\*STAR], Singapore.

Bulgarian Institute of Metrology, General Directorate “National Centre of Metrology” [BIM], Sofia.

Central Office of Measures/Główny Urząd Miar [GUM], Warsaw.

Centro Español de Metrología [CEM], Madrid.

Cooperation on International Traceability in Analytical Chemistry [CITAC], Trappes.

Hong Kong Government Laboratory [GLHK], Kowloon.

Hungarian Trade Licensing Office [MKEH], Budapest.

Instituto Português da Qualidade [IPQ], Caparica.

National Physical Laboratory of India [NPLI], New Delhi.

National Physical Laboratory of Israel [INPL], Jerusalem.

## 1. OPENING OF THE MEETING

The Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) held its twenty second meeting at the International Bureau of Weights of Measures (BIPM), at Sèvres on 21-22 April 2016.

The following were present: M. Akgöz (UME), H. Andres (METAS), M. Bilsel (UME), C. Boonyakong (NIMT), A. Botha (NMISA), P. Brewer (NPL), R.J.C. Brown (NPL), G. Carroll (SL), S. Choquette (NIST), V.S. da Cunha (INMETRO), B. J. de Vos (NMISA), S. Ellison (LGC Ltd), H. Emons (IRMM and ISO REMCO), A. Fajgelj (IAEA), P. Fisicaro (LNE), T. Fujimoto (NMIJ/AIST), C. Gonzalez (NIST), A.C. Gören (UME), B. Güttler (PTB), C. Haraldsson (SP), P.T. Jakobsen, (DFM), J.S. Kim (KRISS), S.K Kim (KRISS), Y. Kustikov (VNIIM), T.K. Lee (HSA), H. Li (NIM), L. Locascio (NIST), L. Ma (NIM), L. Mackay (NMIA), M. Máriássy (SMU), W.E. May (President of the CCQM), M. McNamee (SP), J. Melanson (NRC), Z. Mester (NRC), S.R. Park (KRISS), H. Parkes (LGC Ltd), M. Pérez-Urquiza (CENAM), A.M. Rossi (INRIM), M. Sargent (LGC Ltd), M.P. Sassi (INRIM), S. Scapin (INMETRO), M. Sega (INRIM), P. Silva (NIMT), A. Takatsu (NMIJ/AIST), T.L. Teo (HSA), W. Unger (BAM), A. van der Veen (VSL), S. Vaslin-Reimann (LNE).

Observers: F. Dias (IPQ), J. Dumanska (GUM), W. Kozłowski (GUM), F.W. Lee (GLHK), Z.N. Nagyné Szilágyi (MKEH), L. Samuel (CITAC), D.W.M. Sin (GLHK).

Invited: M. Buzoianu (INM and CIPM), P.A. Gatti (INTI), H. Klich (INRAP), D. K. Koech (KEBS), J. Morrow (NIST), D. Moturi (KEBS), J.K. Olthoff (NIST and JCRB), R. Parris (NIST), A. Plant (NIST), O. Zakaria (NML-SIRIM).

Also present: A. Daireaux (BIPM), R. Josephs (BIPM), S. Maniguet (BIPM / KCDB / JCTLM-DB), M.J.T. Milton (Director of the BIPM), S. Picard (BIPM / KCDB Coordinator), S. Westwood (BIPM), R. Wielgosz (BIPM / Executive Secretary of the CCQM).

Sent regrets: M. Adeogun (NPL), G. Beastall (IFCC), T. Fernández Vicente (CEM), J. Meija (NRC), H.K. Rotich (KEBS), L. Siekmann (Universitätsklinikum – Bonn).

Dr May, President of the CCQM, officially opened the meeting at 9:00 am on 21 April 2016. He thanked the CCQM members for their work over the last year and remarked that attendance at the CCQM continued to be large and had surpassed that of last year's meeting.

He then paid tribute to Prof. Paul De Bièvre, a founder member of the CCQM, who had died on 14 April 2016 in Leuven (Belgium) at the age of 82. Paul De Bièvre was born in Blankenberge (Belgium) on 7 July 1933. He obtained his PhD from Ghent University in 1959 where he continued to work as a lecturer until 1961. In 1961 he joined the Central Bureau for Nuclear Measurements of the European Commission (renamed "Institute for Reference Materials and Reference Measurements", in 1994) where he stayed for 37 years. He was co-founder (1989) and President (1993-1995) of EURACHEM, and co-founder (1992) of CITAC ("Co-operation on International Traceability in Analytical Chemistry"). He had a penchant for philosophy of science and he believed that great measurements start with great thinking. His writings on metrology in chemistry appeared frequently in the journal *Accreditation and Quality Assurance* of which he was the founding Editor-in-Chief (in 1995).

Prof Emons led the tributes, noting that Prof. De Bièvre was a true ambassador for metrology in chemistry and had a passion for the global comparability of measurement results. He continued to be

very active after his official retirement and Prof. Emons noted that it was only recently that he and Prof. De Bièvre had an intensive discussion about one of his planned columns in *Accreditation and Quality Assurance* on purity. Dr Milton remarked that he had first met Paul De Bièvre at the first CCQM meeting and that he had a deep understanding of why the extra decimal places mattered for chemical measurement and had enjoyed long and detailed discussions with him on the definition of the mole and amount of substance. Dr Milton noted that Prof. De Bièvre was last at the BIPM in December 2015 for a meeting on the International Vocabulary of Metrology – another topic on which he was passionate. Dr Kaarls added (by correspondence) that Prof. De Bièvre had been a global contributor to the acceptance of chemical measurement and of the requirement to improve the quality of chemical measurement results via traceability to the SI. Ms Parkes added that he had helped her introduce a structure for formalizing enumeration in the bioanalysis area. Dr May concluded the tributes by stating that Paul De Bièvre was a straightforward, cheerful person and his colleagues fondly remember his passion for science. He believed in his principles and stuck to them: his passion for the highest quality measurements and accuracy in communication was always clear for all to see. Dr May said that Paul had been an inspiration to generations of analytical chemists and this would be his lasting legacy.

The introduction to the meeting concluded with Dr May initiating a round table self-introduction by all participants and observers.

## **2. APPOINTMENT OF A RAPPORTEUR**

Dr May proposed Dr Brown as the rapporteur for the meeting; Dr Brown agreed.

## **3. APPROVAL OF THE AGENDA**

The agenda was approved. Dr May commented that his opening presentation would cover items 5 to 8 on the original agenda.

## **4. REPORT OF THE 21ST MEETING OF THE CCQM**

Dr May thanked Dr Brown, rapporteur for the 21st meeting of the CCQM, for producing the report. Progress with decisions and actions arising from the 21st meeting of the CCQM would be taken as part of Dr May's opening presentation.

## 5. UPDATE FROM THE CCQM PRESIDENT

Dr May provided an overview of the status of the CCQM. He noted that the meetings in 2016 had been attended by over 240 delegates with about 70 at the plenary meeting and that this was starting to test the resources of the BIPM. Dr May commented that this continual expansion in attendance was not sustainable in the long term. Dr May went on to observe that the CCQM was responsible for over 6 000 calibration and measurement certificates (CMCs) for 840 different analytes that are currently published in the BIPM key comparison database (KCDB) with a total of 3 050 different analyte-matrix combinations. The number of analyte-matrix combinations is increasing at a rate of about 350 per year. Dr May noted that the CCQM has performed over 380 comparisons (204 key comparisons and 176 pilot studies). Whilst these were impressive statistics showing the enormous output of the CC, it was Dr May's opinion that the current rate of growth in this output was not sustainable. Dr May took the opportunity to remind participants of the CCQM's Terms of Reference and responsibilities, namely: 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's scientific programme. The responsibilities of the CCQM are:

- 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;
- to contribute to the establishment of a globally recognized system of national measurement standards, methods and facilities for chemical and biological measurements;
- to contribute to the implementation and maintenance of the CIPM MRA with respect to chemical and biological measurements;
- to review and advise the CIPM on the uncertainties of the BIPM's calibration and measurement services as published on the BIPM website;
- to act as a forum for the exchange of information about the research and measurement service delivery programmes and other technical activities of the CC members and observers, thereby creating new opportunities for collaboration.

Dr May continued by reviewing the current organizational structure of the CCQM, noting in particular the creation of the new working groups in the bioanalysis area and the change in name of the CC to incorporate biology. Dr May considered the decisions and actions from the 21st meeting of the CCQM, observing that some progress had already been made in unifying the nomenclature for core comparison approaches and for the terminology used for key comparisons (KCs) and pilot studies, although more effort was still required. Noting the agreement to continue to hold the WG meetings at the BIPM in association with the CCQM plenary meeting, Dr May stated that this would mean having to continue to use nearby hotel facilities external to the BIPM in order to cope with the number of delegates. Dr May reminded members of the need to observe the rules for publishing data from CCQM studies. For pilot studies, the coordinating laboratory had the first option to publish data, and required agreement from participating laboratories that their data could be published.

Dr Wielgosz stated that the CIPM, via Decision CIPM/104-26, had adopted the traceability exception related to delta value isotope ratio measurements proposed by the CCQM. The text of this traceability exception still needed to be made openly available on the BIPM website.

## 6. OUTCOME OF THE CIPM MRA REVIEW WORKSHOP AND MEETING

Dr May began by outlining the structure of international metrology and the role that the CIPM MRA plays within this. Dr May stated that his interpretation was that the CIPM MRA should be a means for National Metrology Institutes (NMIs) to document and vet the capabilities they maintain to underpin the measurement services they provide to customers and for customers to assess the degree of comparability of a given service across the NMI/DI community. It was Dr May's opinion that CMCs should be a derivative of this process and not a means to an end in their own right. The growth in the number of CMCs produced by the CCQM was described. CMCs in this area continue to increase by about 350 per year and this increase has been relatively constant since the start of 2004. In assessing this output and workload Dr May remarked that no other CC meets every year and no other CC has over 100 delegates at its meetings – the CCQM has closer to 300. Dr May stated that by any measure, the CIPM MRA had been a great success, not least in bringing the metrology community together for discussion. However, the comparison programme, the evaluation of CMC claims and the maintenance of the database have required and continue to require significant resources from the NMIs, the Regional Metrology Organizations (RMOs) and the BIPM. A number of NMI Directors had proposed that the implementation and operation of the CIPM MRA should be reviewed with a view to improving its efficiency and effectiveness. As a result, the CIPM proposed to the 25th CGPM that a review of the implementation and operation of the CIPM MRA should be conducted. Dr May added that the CIPM had established a working group under the chairmanship of its President to conduct the review.

Dr May reviewed the membership of this working group and the matters discussed during the CIPM MRA Review Meeting held on 13-14 October 2015. Nine specific questions to be addressed by the CIPM MRA Review Working Group came out of the meeting. Dr May elaborated on these questions, in particular those that were most relevant to the CCQM. Question 3 was related to constraining the proliferation of CMCs, specifying that the results of KCs and supplementary comparisons (SCs) should be interpreted as widely as reasonably applicable to indicate coverage of CMCs and that the use of CMCs to cover as many services as is technically justified should be encouraged, so that CMCs become representative rather than comprehensive. Dr May emphasized that the goal is for NMIs to develop services and that CMCs are a tool for describing the capabilities maintained to underpin delivery of those services. The NMI quality system should document the relationship between services and CMCs. Dr May noted that this is particularly important to facilitate the submission of CMCs by NMIs that are still developing. Question 4 related to improving the efficiency of the CMC review process, with particular emphasis on adopting a 'risk-based' approach to review and ensuring greater consistency across the entire process. Questions 6 and 7 related to the governance of the MRA by the JCRB and the CIPM, specifying that the Joint Committee of the Regional Metrology Organizations and the BIPM (JCRB) should exercise its authority more fully, as defined in its terms of reference for the implementation of the MRA. Dr May invited Dr Olthoff to comment. He remarked that the JCRB needed to understand better the roles and responsibilities across the different CCs and RMOs in order to best determine how it could be most effective in exercising its authority. Dr May expressed his opinion that, as a major contributor of CMCs and CMC review, the CCQM ought to be represented on the JCRB. Question 8 called upon the CCQM and the Consultative Committee for Ionizing Radiation (CCRI) to review and revise the templates for chemical, biological and ionizing radiation CMCs to ensure they are appropriate. Dr May concluded by stating that the final report of the working group would be produced in August and, when agreed, would be fed through to the CIPM in October 2016 and eventually to the 26th CGPM. Dr Brown

asked whether the CCQM's desire for broad-scope CMC claims was the main solution for reducing CMC proliferation. Dr May replied that it would certainly reduce the numbers, although this was just one technique of many at the CCQM's disposal to address this issue.

## 7. OUTCOME OF THE CCQM BROAD CMC CLAIM WORKSHOP

Dr May introduced the outcomes and associated discussions of the workshop that was held on 20 April 2016 by stating that the driver had been to find a way of registering capabilities more broadly to reduce the workload associated with the CMC process. Dr Wielgosz added that examples of where this system was already being applied, notably in the gas standard and organic purity areas, had started with comparisons that included broad 'how far the light shines' statements, which allow broad claims to be made resulting from these comparisons. Dr Wielgosz continued that the operation of the broad-claim format used by the GAWG and OAWG provides a way of registering much broader CMC claims, but still enables comparisons to map directly onto CMC claims. It was noted that, as an example, the NPL's CMCs in the gas analysis areas could be reduced by up to 25 % by implementing such a format.

Dr May implored the WG chairs to consider their approaches to reduce the proliferation of CMCs and added that it was likely that there would be no single solution appropriate for every WG. Dr Sargent agreed, stating that this was not a trivial task and there would certainly not be a single solution across the CCQM WGs. Dr Wielgosz replied that when setting up schemes for comparisons with broad 'how far the light shines' statements, consideration should be given to the fact that the boundary condition of the problem was quite clear: there are limited resources and therefore a limited number of comparisons available to cover the measurement space in a fixed time period. If measurement space was being defined with respect to analyte characteristics (molecular weight and polarity) as well as measurement challenge (for which the type of matrix was being used as a surrogate), as had been proposed in the organic field, then this would limit the number of matrix types and the complexity of the model that could be developed. Dr May stated that we should not necessarily be constrained by the CCQM strategic plans since these may change over time. Prof. Emons countered that given the resources available, we may not be able to cover the whole chemical measurement space and that we would need to prioritize. He continued by stating that the current requirement to review CMCs on a time-limited basis may not be appropriate since capabilities are much more closely related to staff turnover and changes in equipment. Dr Mackay reminded members that the difficulty of covering all the different matrix systems should not be underestimated and that one model system may not accurately reflect capability across a number of areas.

Dr May stated that broad CMC claims were a new concept and the CCQM was only just starting to explore this: a compromise between the two extremes was required and this was what the CCQM should try to work towards. He added that this would require a different mode of thinking about CMCs: not using them as commodities where 'more is better' but using CMCs to underpin real services that are offered to customers. Ms Parkes agreed, with the caveat that it was not until an area became more mature that it was possible to define broader claims and to use these effectively. Dr Brown asked whether, given that accreditation was a key part of the quality system review process, the CCQM had enough formal contact with accreditation bodies. Dr May replied that peer-review was the alternative to accreditation. Dr Brown countered that peer-reviewers were part of the

NMI and DI community but that accreditors may not be, and this could cause problems in the absence of proper engagement and communication with accreditation bodies.

Dr Mester reminded members that it was not for the CCQM to impose broad claim CMCs, but that the willingness to do this had to come from the NMIs. Dr May encouraged NMIs to think about how to design comparisons to encourage this process, thereby encouraging the formulation of broader scope CMCs. Dr Kustikov proposed that CMCs reflect the degree of equivalence of national standards with those of other countries and where possible they would also reflect the services delivered. In reply Prof. Emons questioned whether national measurement standards really existed in the chemical and biological measurement areas.

Dr May stated that, as a result of the recommendations of the CIPM MRA review and the workshop on broad-scope CMCs, NIST would commit to recraft their CMCs accordingly and align these with the services they provided to customers. In general these were certified reference materials in the chemistry and biology area and calibrations in the physical measurement areas. Ideally these reworked CMCs would be based on broad claims. Dr Sargent proposed that a change to broad-scope claims should take place concurrently with revision of the templates used for submitting CMCs. Dr Jakobsen added that claims must be searchable for everyone, thereby allowing the relevant service to be found quickly and efficiently. Dr May agreed, but made it clear that the CMC claims were just a tool for documenting recognized capabilities and that the services actually provided to customers were the most important information. Dr van der Veen asked whether the database should contain the actual service (which related to accreditation scope in many cases) or the capabilities that underpin them. Dr May replied that the CMC database is a statement of capabilities, which is quality assured by the peer community, and underpins the services provided. Dr van der Veen developed his argument, suggesting that currently in the gas area there was a direct relationship between CMCs and services delivered and that this could probably continue into the future in this technical area. Dr May agreed that, if this was the case, it was acceptable but in general the CCQM could not expect the KCWG to scrutinize CMCs if they are not covering services that an NMI offers to its customers. He reiterated that having CMCs but not delivering services that are based on these CMCs was unsustainable.

Dr Mackay stated that ILAC currently directs users to the KCDB as part of the ILAC Policy on the traceability of measurement results (ILAC P10), and wondered how these users would cope with broad capability claims in the future. Dr May replied that this would require a change in approach and that ILAC had been invited to take part in the process and it would be beneficial to have their involvement. However he cautioned that it was not the job of the CCQM or NMIs exclusively to meet the requirements of accreditation agencies and the CCQM should not use this as a reason not to adopt a broader scope approach to claims. Dr Máriássy mentioned that ILAC documents state the traceability requirement and, in this respect, CMCs are a real driver for providing services since it is to these that accreditation bodies will refer. He continued by stating that this meant the database must be searchable for the service provided and that the CCQM must be very careful and precise about what information is available on the database. Dr Mackay asked how uncertainty would be dealt with under broad-scope claims and whether this would result in larger uncertainties that may not align with specific services. Dr Milton replied that in order to present wider scope claims the uncertainty would clearly need to be larger, perhaps in the form of an uncertainty versus concentration function. However customers will still refer to the product catalogue of the individual institute since this will provide essential practical details such as availability and cost. Dr Brewer added that the broader scope system would work well in the gas analysis area since it would be easiest to display to customers the services provided, both on the database and in the product catalogue. Dr May stated

that these mechanisms proposed in the gas area would not work as well in areas where matrices were a consideration.

Dr May concluded the discussion by deciding that each technical WG was to propose a way forward for broader-claim CMCs to be presented and reviewed at the next plenary meeting of the CCQM.

## **8. REVIEW OF CCQM ACTIVITIES VERSUS THE PUBLISHED STRATEGIC PLAN (2013-2023) AND UPDATE OF THE CCQM STRATEGIC PLANNING DOCUMENT (2017-2027)**

Dr Wielgosz reported that the plans for comparisons were being updated by the WGs on a six monthly basis. When these WG plans were added together they provided the CCQM plan for comparisons. Dr Wielgosz announced that the 4-year review of the CCQM strategy was now due, and that this process would produce the CCQM Strategy for 2017-2027. As part of this, the deadline for individual WGs to update their strategies would be 1 December 2016 and these would then be scrutinized by the CCQM SPWG. It was noted that as well as this bottom-up approach, top-down comments would also be invited on the current strategy document as part of the revisions. This revised strategy would expand on the comparisons proposed by the CCQM over the next ten years. Dr Wielgosz noted that against a background of increasing numbers of CMCs the review would need to consider the CIPM MRA review, in particular: the future plan required to deliver an effective and efficient programme of comparisons to support current capabilities; whether the CCQM community has enough resources to review the growing number of CMCs; and whether all the capabilities described were delivering services. Dr Wielgosz noted that the number of comparisons performed in the period 2013 to 2015 was 18 % fewer than predicted in 2012, based on KCWG data from December 2015. This has been against a background of increased comparison activity in the RMOs and new activities in some areas (such as the GAWG WG on particles). Dr Wielgosz proposed that this decrease could lead to the following questions, which will be answered by the new strategy:

- Can the CCQM support its CMCs with 20 % fewer comparisons than predicted?
- Is the CCQM simply behind with the organization of comparisons and therefore the numbers will increase over the next few years?
- Is the reduced number of stand-alone pilot studies due to the maturing of the CCQM's activities, and therefore a much reduced number of stand-alone pilot studies can be expected in the future?

Dr Milton initiated a discussion of the strategy by stating that following a review of the Chem-Bio CMC submissions by the JCRB Executive Secretary, it had become clear that the increase in CMCs did not occur because of new CMCs from new CCQM members but was instead a result of the major NMIs continuing to submit more CMCs. Dr Milton proposed that this strategy update represented a good opportunity for the major NMIs to address these increases. Dr Ellison asked about the timescale for updating the database software and how would the CCQM be involved in developing this. Dr Milton replied that the project had now been endorsed by the CIPM and JCRB, and a tender document inviting bidders to provide the new service would be produced in the first half of 2017. The CCQM would be involved in drafting the specification and the tender document. Dr May confirmed that he would appoint a task group to review and propose required modifications to templates for chemical and biological CMCs as well as database search engines and functionalities, and report back to the next meeting of the CCQM.

Dr Wielgosz noted that the updated strategy document would contain information about the role of the CCQM and its WGs. He added that this was prompted by a high-level discussion among CC Presidents planned for June 2016 about the roles of CCs and what their membership would be. This would lead to consideration of what the role of individual WGs should be. Dr Wielgosz stated that some generic text (document CCQM/16-45) had been drafted to describe the role of WGs, which in summary is: a) carrying out key comparisons to ensure the comparability of services; b) carrying out pilot studies for the development of reference measurement systems; and c) acting as a forum for the exchange of information between institutes. Dr Wielgosz stated that one would expect the balance of activities to move from b) to a) as an area became more mature. Dr Brown asked whether there was a role for WGs to advise their CC about technical matters in their sub-area in the same way that CCs advise the CIPM. Dr Milton replied that this was indeed their historical role, but that the meeting in June 2016 would consider the full range of activities of the Consultative Committees. Dr May mused over whether the CCQM might split into chemistry and biology parts sometime in the future, although he stated that it was not currently mature enough to consider this. Further, he reassured members that there was no external pressure for this to happen and when and if the time came, this would be a CCQM decision. Dr Locascio stated that the current CCQM format was extremely useful and allowed a lot of cross-fertilization between different disciplines which was probably something that the physical CCs missed out on.

## 9. **BIPM PROGRAMME ON ACTIVITIES IN SUPPORT OF METROLOGY IN CHEMISTRY AND BIOLOGY**

Dr Wielgosz presented the activities of the BIPM in support of metrology in chemistry and biology. These broadly fell into four areas of activity all under the umbrella of the international equivalence of measurement standards: gas analysis for air quality and greenhouse gases; organic purity analysis for health, diagnostics, pharmaceutical, food, environmental and forensics; outreach activities; and capacity building and knowledge transfer. Dr Wielgosz summarized some of the recent outputs of the department. The department has ten FTEs but this is augmented by secondments, which have doubled in recent years. Secondments in this area account for 80 % of all secondments to the BIPM. He thanked CCQM members for their support for the secondment programme and Dr May interjected that this demonstrated the support for metrology in chemistry among NMIs. Dr Milton added that in addition to secondments, support for the BIPM's capacity building programme had increased significantly.

Dr Wielgosz continued, describing the impact of a selected number of activities undertaken by the BIPM and working with the NMIs. The BIPM had measured and published a new value for the ozone adsorption cross section which, when taken together with other new literature values, may result in an update to the ozone adsorption cross section value, and this was being studied by a task group in the CCQM WG on Gas Analysis (GAWG). At this stage Dr Brown requested that regulators be included in the discussions at an early stage regarding any change since the solution may not be as simple as changing the ozone adsorption cross section. Dr Brown stated that this was because the health effect-based legislative limit values may have been set using measurements which rely on the current ozone adsorption cross section. Dr Wielgosz said that they would be included as soon as possible, but that the first priority was to decide on the correct ozone adsorption cross section before opening discussions. Dr Wielgosz explained the positive impact in terms of improving comparability that the

BIPM's work and the relevant CCQM comparisons has had on the WMO scales that underpin greenhouse gas monitoring world-wide. In addition the BIPM programme on organic primary calibrators was promoting the wider adoption of new technologies for purity assignment, notably qNMR, and the increased availability of primary and secondary calibrators. Visiting scientist opportunities to the BIPM in 2017 were highlighted.

Dr Wielgosz detailed the number of comparisons coordinated by the BIPM over the last three years and reported some of the results. [CCQM-K55.d](#) on the purity of folic acid highlighted the comparability between the qNMR and mass balance approaches to organic purity. Dr Wielgosz mentioned the BIPM collaboration with the NMIJ which focuses on characterizing qNMR universal organic calibrators and validating material purity in different solvents. This project had proved to be particularly successful in attracting NMI secondees to the BIPM. Dr Wielgosz reported on the results of [CCQM-K115](#) on C-peptide purity, demonstrating the large number of impurities that had to be identified and quantified as part of the comparison. Dr Wielgosz displayed the results of [CCQM-K90](#) on formaldehyde, which showed good comparability despite being a challenging comparison. Forthcoming comparisons were discussed, starting with [CCQM-K120](#) on ambient level CO<sub>2</sub>, for which the BIPM is establishing a manometric gas measurement system. Due to the fact that this involves a sampling technique rather than a preparative technique, very low uncertainties can be achieved, and the facility would be used to support CO<sub>2</sub> in air comparisons on an ongoing basis in the future. The comparison on CO<sub>2</sub> mole fractions was being carried out at a level of uncertainty for which the isotopic composition of the CO<sub>2</sub> gas would need to be measured to correct for instrument response, and this had led to the development of CO<sub>2</sub> isotope ratio measurement capabilities at the BIPM. There was a discussion on the subsequent work required to extend this into a CO<sub>2</sub> isotope ratio key comparison in 2019, in collaboration with the IAEA.

Dr Wielgosz presented the BIPM's Capacity Building and Knowledge Transfer Programme (CB&KT). There has been growing recognition that recent (and future) BIPM Member States and Associates often have emerging metrology systems and are unable to become members of CCs or to participate in CC key comparisons. Dr Wielgosz explained that action was needed to support their integration into the global metrology system. As a result the CB&KT programme had been established at the BIPM. It includes a number of projects which are all supported by voluntary funding. Training courses on the operation of the CIPM MRA as well as a Summer School on Metrology were being run as part of the programme. In the area of Metrology in Chemistry, a BIPM CB&KT programme is being set up on metrology for safe food and clean air in developing economies – in particular AFRIMETS has identified a regional need for certified reference materials to support its mycotoxin analysis in food.

Dr Wielgosz concluded by highlighting future plans for BIPM coordinated OAWG key comparisons over the next ten years, designed to help cover the new OAWG "3-sector" organic purity model. More long-term plans to support PAWG key comparisons between 2020 and 2023 were also presented. Finally, Dr Wielgosz presented details of a forthcoming NIM-BIPM workshop on Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance and a BIPM-WADA Workshop on Standards and Metrology for Anti-doping Analysis.

Dr Brown started the discussion on the presentation by commending the work of the BIPM CB&KT Programme and noting the clear need for capability building in the technical areas that had been identified. Dr Wielgosz replied that countries with emerging metrology systems had to deal with complex problems and that providing them with reference materials would only help in the short term, but providing them with capability will help in the long term. Dr May noted that the CGPM had wanted to support the capacity building programme but that this was not possible from the BIPM's

dotation, which had remained fixed. However, individual NMIs had been able to find other ways to support these activities. Dr Milton added that this was a new way of working for the BIPM and that it was necessary to interact closely with the funding NMIs to ensure that their priorities were met. In many cases the programmes being offered had been heavily oversubscribed and the BIPM had asked the RMOs to have a role in prioritizing topics. Dr Milton added that it was very encouraging to see organizations such as UNIDO and WADA interacting with the BIPM – something that would have been unthinkable when the CCQM was set up.

Dr Fajgelj asked whether the BIPM was employing more staff to deliver the CB&KT programme. Dr May replied that the money was provided in the form of a grant and that no permanent staff would be employed. Dr Wielgosz added that a number of NMIs had already agreed to send their scientists on secondment to the BIPM to support the programme. Prof. Emons added that he did not think any EU food reference laboratories had been approached about participating in the programme and gave the opinion that they might be interested. Dr Wielgosz replied that so far, contact had been made with sponsors and an initial group of participating organizations, and the start-up meeting had only taken place a few days ago. However, it was foreseen in the programme that expert laboratories from countries with developed food metrology systems could support the programme either by providing funds or seconding their experts to aid in knowledge transfer.

Dr May asked Dr Milton to give a brief introduction to the BIPM strategy, given that there had been so much interest in the CB&KT programme. Dr Milton explained that the BIPM works towards the global comparability of measurements, working with governments and international organizations to achieve this goal. He explained that the BIPM performs both technical coordination and technical operations via its laboratory programmes. The BIPM has a liaison role in presenting metrology as part of the quality infrastructure (that comprises metrology, documentary standards and accreditation). Finally, it has a visitor programme, which has been expanded to encompass the CB&KT programme. Dr Milton noted that even countries with quite well developed economies can have an immature metrology structure. He noted that capacity building was a characteristic of many international organizations, but one which the BIPM had not undertaken until now.

Dr Fajgelj noted at this point that the CCQM has only 40 members whereas the IAEA has 164. Dr Milton responded that formally there are 57 members of the BIPM and 41 associates, however there are 250 institutes that participate in the CIPM MRA. Dr Milton suggested that should lead to a reconsideration of what the objectives of a CC are. Dr Milton proposed to the CCQM that a CC should:

- Examine, debate and support the state-of-the-art in their field of expertise.
- Engage with stakeholders within their field of measurement – CCs can do this better than NMIs alone.
- Be responsible for benchmarking the quality of measurements in the area through the framework of the CIPM MRA.

Dr Milton suggested that the order of these characteristics was so given to suggest that the final activity of a CC should not overwhelm the first two. Dr Milton hypothesized that once these principles are understood and agreed upon that this should lead naturally to a debate about the membership of a CC and how it should operate. Dr Milton proposed that the first two activities could be delivered via a workshop or lectures attended by a large number of people, but the third activity was more of a member-based forum where decisions are taken, perhaps by means of voting. Such a forum would need to have a clear membership. Dr Rossi stressed that metrology has an impact across

different sectors and that in future this may mean that WGs have to think in terms of impact for energy, environment and health, amongst other areas. Dr May replied that the activities of CCs and WGs were driven by stakeholders and the main requirement was that the CCs must continue to drive cutting edge measurement science.

## **10. REPORTS FROM CCQM WORKING GROUPS**

### **10.1. CCQM WG on Key Comparisons and CMC Quality (KCWG)**

Dr Sin provided the CCQM with an update of the WG's activities. The meeting of the KCWG had taken place prior to the CCQM on 16-17 April and Dr Sin noted that this annual face-to-face meeting is one of the key components of the inter-regional review of chemistry CMCs. In 2016 a total of 404 CMCs were submitted, of which 156 CMCs were under re-review. Dr Sin stated that a new approach is being taken in the review of CMC claims – in particular focusing on doing more with less. This would involve:

- Use of core comparisons, competence concepts and benchmarking comparisons.
- Fewer comparisons but with more time spent in the planning, design and organization, especially for core and benchmarking comparisons.
- The use of record or report cards, and competence tables developed by some CCQM WGs to prove long-term competence.

Dr Sin observed that these changes will affect how CMCs are reviewed. She speculated that in future there may be hardly any one-to-one links between CMCs and KCs in some cases. Dr Sin noted that during Cycle XVII there had been an improvement in the efficiency of the review process and some broad-claim CMCs had been submitted (although it was noted that these were not grouped based on similar analytical challenges but on toxicity etc.). Dr Sin expressed the opinion that in future the WG may require further expert input to properly assess some of the broader scope CMC claims – but how to do this without compromising available resources was a challenge. In the future, it was the intention to continue enhancing effectiveness and efficiency and adhering to hard deadlines: a taskforce would identify key factors affecting efficiency and make recommendations for improvements. Dr Sin stated that there was to be a more rigorous review of the intra- and inter-regional review process with data being collected on the percentage of CMCs that were changed or rejected at each stage. Dr Sin noted that working towards a web-based review system would speed up the process, as would more flexibility in the CMC template. It was proposed that in 2017, category 13 or some category 1 CMCs would be re-reviewed but this would depend on the status of current key comparisons and a decision would need to be made on this at a later date. Dr Sin concluded by stating that for broad-claim CMCs, the relationship between CMCs and services needed further consideration.

Dr Brown opened the discussion by asking whether the data collected on CMC changes or rejections was available for this year. Dr Sin replied that all CMCs were submitted on time and that 90 % of CMCs had gone straight into the fast track. Dr Wielgosz added that RMOs had been asked to monitor their internal processes as a corrective action in 2015. He further noted that the CCQM should keep

this as a preventative action into the future and publish the data. Dr May thought it would be useful if the KCWG could produce a flow diagram of the CMC production and review process for future presentations. Dr May also stated a preference for the term 'wider' claims rather than 'wide' claims to indicate the direction of travel rather than the absolute destination. He also expressed the opinion that the efficiency drive in this area was not necessarily about reducing the number of key comparisons but was instead about making the ones that were conducted more effective. Dr Brewer was of the opinion that since the majority of CMCs came from mature areas; it might be worth focusing the most effort towards driving efficiency in these WGs first. Dr May thought that whilst this was a good idea in theory, it was probably easier for the GAWG to drive this forward rather than the other WGs that have the potential for producing larger numbers of CMCs.

## 10.2. CCQM Working Group on Protein Analysis (PAWG)

Dr Park reported that the protein analysis WG had met twice; once in autumn 2015 and once earlier in the CCQM week. He noted that there had been many first time attendees at the recent meeting. The focus of the group's activity had been priority setting and discussions on strategy. The work of the group had been split into two parts: core and extended capabilities. Dr Park noted that two focus groups had been set up to prioritize the activities in these areas to define strategy, one working on primary calibrators and solutions and the second looking at matrix materials and measurement methods. He demonstrated how recent and planned comparisons aligned with the PAWG roadmap. It was noted that the core components on the roadmap could be addressed in the short term, whereas some of the more complex, extended capability analyses would need to be addressed in the longer term.

Dr Park gave an update on the studies within the group that were ongoing. He mentioned [CCQM-K115](#) on the purity of synthesized peptide, which Dr Wielgosz had previously talked about. In particular he noted the challenging nature of the study in terms of the requirement to identify and quantify over 60 impurities. The results had generally been good and Dr Park discussed the methods for establishing the reference value that had been discussed in the WG. Dr Park expressed his hope that this landmark study would allow appropriate CMCs with suitable uncertainties to be claimed.

Dr Park continued by describing the new studies proposed within the group on haemoglobin in whole blood, glycated haemoglobin and a sulphur-based quantification of insulin. Approximate timescales for these and other studies through to 2020 were proposed. Dr Park stated his expectation that these new studies would be underpinned by some emerging measurement methods such as isotope dilution Raman, neutron activation analysis, and sulphur-based protein quantification, and also by capability building in ongoing EMPIR projects, which were undertaking large-scale biomedical research and development in relevant areas.

Ms Parkes began the discussion by asking whether participants would need to use a specific method for the insulin study. Dr Park replied that the study was more aimed at investigating the hydrolysis process rather than insulin itself and he hoped it would be good for supporting all future peptide hydrolysis CMC claims. Dr May countered that protein hydrolysis is not a service in itself, but is a capability which supports the service of protein purity. He further stated that the CCQM must always be cautious of specifying a set method for a comparison since this is more like standardization than metrology and that this may lead to the study not fully uncovering sources of bias in the measurement that would be seen if different techniques were used. Dr Wielgosz added that the peptide purity study had allowed the hydrolysis method to be examined for a straight 31 amino acid chain peptide and all

methods were observed to be equivalent within the measurement uncertainty. Dr Josephs added that during a BIPM study of insulin purity no problems with the hydrolysis process were observed. Dr May observed that it should not be assumed that this would be the same for all peptides. Dr Ellison asked whether the glycosylated haemoglobin study would link to IFCC standard methods. Dr Park replied that this was possible but that the differences between the methods needed to be studied in more detail first. Dr Güttler suggested that the study should use several different methods and examine the difference between them.

### 10.3. CCQM Working Group on Nucleic Acid Analysis (NAWG)

Ms Parkes reported that the nucleic acid WG had held its second meeting at the BIPM in the week leading up to the CCQM meeting and that 25 experts had attended from about 20 NMIs and DIs. Ms Parkes added that 14 of these NMIs and DIs claimed to actively deliver services in the nucleic acid area and the others have plans to do so in the future. Ms Parkes highlighted the terms of reference of the WG and highlighted the complex nature of the biological measurement space and the relationship that the group has with the PAWG and CAWG. Ms Parkes elaborated that the main task for the WG currently is to perform a gap analysis in the NAWG measurement space, based on information provided by WG participants on their current and planned services and reference material development programmes. This would provide evidence for planning and prioritization of future studies for the group. Ms Parkes stated that the current requirements for supporting services were in the nucleic acid quantification area for both DNA and mRNA, but in future Ms Parkes saw these requirements increasing to encompass sequence, miRNA, gene editing and synthetic biology requirements.

Ms Parkes then reviewed the group's ongoing studies. [CCQM-K86.b/P113.3](#) on GM rice was presented. The results showed good comparability within the uncertainty of measurement, although the estimated uncertainty showed significant variation between NMIs. A small expert group would consider how to assign a KCRV for the comparison. Ms Parkes reported that a new study in the K86 series had been proposed on oilseed rape (canola). This was a high-oil matrix providing a significantly different technical challenge for extraction. The study was designed to support the GM food measurement space in the high-oil, low-carbohydrate area. Ms Parkes noted that the final report for CCQM-P154 on the absolute quantification on DNA had now been submitted to the KCDB and this would be used to support CMCs. Ms Parkes then reported on CCQM-P155 on multiple cancer cell biomarker measurement. The initial results had shown that there was good agreement between the reported copy number ratios and the WG had discussed during its meeting the CMC claims that this study could support. Ms Parkes concluded by mentioning the proposed pilot study on single nucleotide variant quantification being proposed by the NMIA and LGC and reviewed the workshop sessions held by the WG over the past year on dPCR partition volume measurement and metrology to support massively parallel sequencing.

Following the presentation there was an extensive discussion about the fact that a NMI in [CCQM-K86.b](#) had submitted two values for the key comparison before subsequently choosing which value to use as part of their submission and for calculating the KCRV. Other NMIs had submitted two results, but one of these had been in the pilot study part of the comparison. Dr May was of the opinion that a NMI should use the method that it uses to deliver services. In the case where services are delivered by more than one method, Dr May stated that the method with the lowest uncertainty should be used in the comparison. If other methods are also used to deliver services, this should be

the subject of internal benchmarking which could then be submitted to the KCWG as required. Dr Sargent disagreed, stating that in the IAWG core capability approach it was desirable to submit more than one result from an institute using different methods since this supported scope in different parts of measurement space and helped deliver an efficient approach to key comparisons. Dr Sargent did concede that only one value must be used for the KCRV and that this must be declared when the results are submitted. Dr Brown supported the view that this additional work to support extra areas of the measurement space could still be performed as part of an internal benchmarking study. Dr Sargent said that CMC reviewers wanted to receive less data and this was minimized by including more than one value from each institute in the comparison rather than performing internal benchmarking and then providing this as additional evidence. Dr Mackay added that in the past the OAWG had, on occasion, allowed multiple values to be submitted to a key comparison for well justified reasons and making any change was an important decision that required some consideration. Dr May reiterated that in future he expected only one result per organization in each key comparison and that if multiple methods were used for different services this should be the subject of an internal benchmarking study submitted to the CMC process as additional information.

The discussion then addressed the problem of where two NMIs or DIs in the same country wanted to have CMCs for the same measurand in the same range of concentrations but using different methods. Dr Mackay stated that there had been an example of this in Australia where a DI using INAA had participated in the same comparisons as the NMIA but was unable to claim CMCs. Dr May confirmed that the CIPM MRA did not allow overlapping claims from institutes in the same country. Dr Fajgelj stated that as a signatory to the CIPM MRA the IAEA had previously participated in comparisons with two independent IAEA laboratories, although they had not gone on to claim CMCs as a result. Dr Kim raised the issue of NIST and NOAA participating in studies at the same time but Dr Wielgosz explained that this was because NOAA were designated as part of the WMO's participation in the CIPM MRA and that NOAA were not representing the USA in this context. Dr Wielgosz explained that [CIPM MRA-G-03](#) '*Guidelines for the review of Quality Systems operated by IGO institutes and/or designated institutes, and the review of their calibration and measurement capabilities (CMCs)*' deals with all the issues raised in this discussion and is based on the premise of one NMI providing traceability per measurand. He added that this was a high-level document and that the CCQM would need to think very carefully before asking for an exception for the chemistry community. Dr May concluded the discussion by stating that he would discuss these issues with the SPWG and if there was reason to do something differently for the chemistry community he would take this to the CIPM, although he warned against the CCQM appearing to ask for too many exceptions for its work. Dr May proposed that many of the difficulties covered in the discussion could be resolved by a more rigorous programme of accreditation and on-site peer review at NMIs and DIs. In particular, Dr May asked Dr Mackay to draft a note on previous practices in the OAWG and the WG chairs more generally to provide data on the number of times there has been more than one result per NMI in a key comparison.

#### 10.4. CCQM Working Group on Cell Analysis (CAWG)

Dr Plant reported on the activities of the CAWG. She noted that the responsibilities of the CAWG are to carry out key comparisons and where necessary pilot studies, to critically evaluate and benchmark NMI/DI claimed competences for measurement standards and capabilities for cell analysis (where the target species (analyte) is a characteristic of cells) and included, but were not limited to, the identification and quantification of cells in complex matrices and mixtures relevant for functional

activity. Furthermore, the WG has been tasked to identify and establish inter-laboratory work and pilot studies to enable the global comparability of cell analytical measurement results through reference measurement systems of the highest possible metrological order with traceability to the SI, where feasible, or to other internationally agreed units, in response to the demands of end users. The WG aimed to establish global comparability of cell measurements through bioanalytical reference measurement systems of the highest possible metrological order comprising: traceability to the SI when possible or to other agreed units, reference methods, CRMs and uncertainty estimates.

Dr Plant noted that unlike other WGs, the CAWG also dealt with issues relating to identity, noting that emergent properties of cells and measures of biological response and function were unique to this WG and this distinguished much of the group's work from what might be considered as traditional chemical and biochemical measurements. Dr Plant stated that new therapies based on the use of cells are driving the requirement for measurements in this area since these treatments need urgent characterization for regulatory purposes. It was noted that the shipping of samples for comparison studies is a significant challenge for this WG.

Dr Plant continued by explaining that a lot of mutual education between NMIs and stakeholders is required to understand and address the measurement challenges in the area and to define where quality control measurements and materials would be useful. This is particularly challenging since: the measurand may not be easily defined, there is often no ground truth, and reference materials may be difficult to devise and prepare. Furthermore, Dr Plant stated that quantifying uncertainty in this area is very challenging, not least because living systems are dynamic in nature.

Dr Plant reported that the WG is at the stage of defining the measurement services currently provided by members, where there might be future interest for measurement services and determining the requirements of stakeholders. This would be used to formulate the strategy of the WG and its roadmap for future work. Clear measurement capabilities of interest were cell counting and identifying and counting cells of particular characteristics in a background of other cells. These key requirements had driven the current and recent pilot studies: CCQM-P102 on Quantification of cells expressing CD4 in the presence of non-expressing PBMC, which had recently been completed; CCQM-P123 Number and geometric property of cells adhered to a solid substrate; and CCQM-P165 Quantification of CD34+ cell counts.

Prof. Emons started the discussion by encouraging Dr Plant and the WG not to be concerned that at this stage there were more questions than answers as this was a difficult area and he sympathized with the difficulties in transporting samples. However, Prof. Emons disagreed that the community needed robust reference materials but was of the opinion that instead they needed reproducible reference materials. He cautioned the group against confusing what is most easily measured with what is most relevant to measure. Prof. Emons stated that this was an area where one had to accept that measurands would be operationally defined. Dr Plant agreed that it was difficult to define what should be measured and that this must be led by end-user requirements. Dr May commented that the robustness of cell line might make a good study but agreed that the area was so nascent that the studies proposed must be led by user requirements. Dr Locascio asked at what point does the sequencing of proteins become cell related, or whether the two relevant WGs would work together on this. Dr Plant thought that the tipping point came when it was too difficult to examine individual components although she expected some cross-WG collaboration as well, not least to define the boundaries of the WGs.

Concluding the discussion, and recognizing the emerging science in this area, Dr May asked whether seminars about cutting edge measurement science at NMIs would be a good addition to the CCQM

meetings, perhaps in place of the current mid-week workshops. Dr Brewer felt that this was a good idea provided it could be fitted into the meeting schedule.

#### 10.5. *ad hoc* Steering Group on Microbial Measurements (MBSG)

Dr Morrow reported on the history of the steering group, which was established in 2011. It has three tasks, to:

- Investigate, in close cooperation with the food community, two relevant but “simple” measurement cases, of which the measurand can be clearly defined and for which a metrologically sound validated method can be developed;
- Execute the two case studies, including the organization of global comparisons, and reporting back to the CCQM and the microbial stakeholders/participants;
- Discuss and propose what can be achieved on the basis of the results, what should be planned and prioritized next, and how future cooperation can be best organized.

The group used a questionnaire to define the measurement priorities in the area and followed this up by performing a microbial quantification study. The study showed that results were comparable between participants but that uncertainty estimates were not comprehensive. A follow-up study has been recommended for the CAWG to conduct. The steering groups also conducted a microbial identity investigative study with results indicating that estimated variant copy ratios at biologically variable positions were only reproducible for high-throughput sequencing methods. A further microbial sequencing study has been recommended for the NAWG to conduct. Bacterial shape and arrangement was highlighted as an important future measurand.

Dr Morrow went on to highlight the additional services being developed by MBSG members and how these mapped onto the work in the CAWG and the NAWG, highlighting that anti-microbial resistance is a big issue where metrology support will be of great importance in the near future. It was stated that bio-informatics is a related area that the WGs in the bio-measurement space will need to consider.

Dr Morrow concluded by asking the CCQM to discuss whether the MBSG had fulfilled its original 2011 charter, considering the completion of the two preliminary studies and successful transfer of studies to the newly formed Nucleic Acid Analysis and Cell Analysis Working Groups. In addition Dr Morrow stated that in light of the challenges of defining the measurand for microbiology, further discussion of the value of broad-claim CMCs for microbiological measurements will be essential to advance measurement capabilities.

Ms Parkes opened the discussion by stating that most culture-based work could not currently be done at NMIs and this limited the scope of studies in this area. Ms Parkes agreed that bio-informatics was an area of increasing importance for the community. Dr May asked the CCQM specifically about the future of the MBSG and whether it had now completed its job. Prof. Emons thought that with respect to exploring the technical field it had completed its job and its outputs were now feeding into the newly created WGs in the biology area. Dr Locascio stated that the MBSG had done a tremendous job and now was the right time to focus its outcomes into other groups. Dr Wielgosz agreed and pointed out that, referring back to the terms of reference of the group, these had all been completed. Dr May agreed that the MBSG had completed its work and should be disbanded, but that the CCQM should ensure its outputs were captured by the existing WGs. Dr May thanked Dr Morrow for her

leadership of the MBSG over the last five years. Dr Morrow thanked the members for the opportunity given to the MBSG to contribute to the work of the CCQM.

At the end of the first day of the CCQM meeting Dr May took the opportunity to pay tribute to the BIPM's excellent organization of the CCQM meetings and the outstanding service and hospitality provided by the BIPM to the CCQM during the week and a half of meetings. In particular the efforts of Mrs Johanne Flament and Mrs Céline Fellag Ariouet were praised very highly, as were the catering services provided by Mrs Maria José Fernandes.

## 10.6. CCQM Working Group on Surface Analysis (SAWG)

Day two of the CCQM meeting began with Prof. Unger describing the recent work of the Surface Analysis WG. It was noted that the recent meeting of the WG had included two new institutes, one from Canada and one from Turkey. Prof. Unger highlighted that most of the drivers for the work in the SAWG came from the advanced manufacturing sector.

Prof. Unger updated the CCQM on the comparison studies performed by the WG. [CCQM-K129](#) was on CIGS alloy composition. It was noted that traceability in this study was provided either from a thin film CRM from KRISS distributed to all participants or from the standard free XRF measurements made by PTB. The results for the four elements Cu, In, Ga and Se had all been good, showing comparability in most cases within the measurement uncertainty of the measurement. Prof. Unger presented the proposal that the WG had produced in terms of the range of CMCs that the comparison could support. Both a range of composition and film thickness was included in the proposal.

Prof. Unger then presented the results of [CCQM-K136](#) on measurements of specific surface area, specific pore volume and pore diameter on a nanoporous aluminium oxide powder using the BET method. He explained that the BET method is an important and standardized conventional method based on a value assigned to the area that physically adsorbed N<sub>2</sub> molecules occupy on a solid surface at low temperature, operationally defined by documentary standard ISO 9277. The results showed some spread, with not all measurements agreeing within the stated uncertainty. As a result there was still some debate as to the preferred method to assign the KCRV. Prof. Unger explained that there was an ongoing debate about the statement of scope within the report of the comparison: for instance, should CMCs be limited to the scope of the ISO 9277 standard or should even wider claims be accepted, based on the expert judgement of the WG.

Prof. Unger concluded his presentation by sharing some of the SAWG's proposed future comparisons. The first was Raman surface analysis under ambient conditions – Prof. Unger speculated that this may provide label-free, ambient and fast measurement of chemical species with sub- $\mu\text{m}$  spatial resolution. Second was a proposed study on the amount of substance in buried organic layers – this was prompted by new measurement capabilities amongst NMIs, providing quantitative depth profiling of nanoscale chemistry by SIMS and XPS using argon cluster sputtering. Similarly there was a plan for a study on the chemical identity and amount of substance on the surface of a nanoparticle. The final idea, which was still at early stages of development, related to measuring the number concentration of nanoparticles in a solution, although Prof. Unger questioned whether or not this fitted within the scope of the CCQM.

Dr Brown started a lengthy discussion of Prof. Unger's presentation by asking whether the measurements of surface area, pore volume and pore diameter were all correlated. Prof. Unger

confirmed that they were all calculated from one set of experimental data. Prof. Emons was concerned that if one was not able to independently calibrate the measurement and express the results in SI units then it is not relevant to metrology and the CCQM. Dr Wielgosz thanked Prof. Unger for a very detailed presentation but observed that the BAM submitted a very small uncertainty compared to the spread of results for the BET comparison, but that if the median was to be used for the KCRV then this would not be taken into account properly. Prof. Unger agreed that the calculation of the KCRV needed further discussion. Dr Milton moved the discussion onto the subject of traceability. He observed that the reason the SAWG was created was to provide traceability in areas where the current WGs were unable to do so and a good example of this was for silicon oxide layers on silicon which has made an important contribution to the Avogadro project. However, Dr Milton suggested that the CCQM would want to see more examples of the SAWG using techniques that provide independent traceability: and asked specifically what would be put in the column for 'traceability' when CMCs were claimed for these studies. Prof. Unger replied that there were already many CMCs for BET measurement on the KCDB and the study aimed to support these claims. Dr Wielgosz replied that the measurement of enzyme activity was expressed in katal, and it was possible to do this in these SI units because the measurement method had been standardized. He went on to state that the JCTLM database had many similar examples. Dr Ellison added that the Eurachem guide on traceability in chemical measurement suggested that the conventional method defined the measurands and that if all inputs are in SI traceable quantities then the output should be accepted as SI traceable. Dr May suggested that because BET was an operationally defined measurand, what was presented as a key comparison was in fact a proficiency testing scheme for NMIs. Dr Brown did not entirely agree with this position, stating that whilst BET was operationally defined, if the NMI provided the highest level of reference for this measurement in their country then the comparison was justified, in the same way that the KCDB contains many CMCs for Rockwell hardness measurement, which, as an ordinal quantity, is even further from the SI system. Dr Brown noted that any CMC claim relating to an operationally-defined measurand must be specific in the method used, for instance by mentioning the ISO standard method in the BET case. Dr May replied that this was a suitable time to consider all CMCs on the KCDB and why they are there.

The discussion then moved onto [CCQM-K129](#) on CIGS alloy composition. Dr May expressed concern that any NMI that took part would be traceable to the CRM provided by KRISS. He asked what would happen if, when they delivered the service for customers, they used a different material. Prof. Unger replied that KRISS has guaranteed to continue supplying the material and also that the uncertainty associated with the material was very low. Dr May pressed the case that people should be allowed to choose their route for traceability. Prof. Unger conceded that this was often a problem in the SAWG where routes to traceability were limited. Dr Milton asked how the independent data from PTB was used in the KCRV – currently it seemed as though it was not involved and that this meant the KCRV was heavily weighted toward the values established using the CRM provided by KRISS. Dr Milton questioned whether this approach was really adding value to the measurement space and suggested that the added value might be in the comparison of the two independent methods. Dr May added that ideally there would have been other routes to traceability and this would have allowed the full uncertainty of the comparison to be realized. Dr Brown agreed that this was a fair criticism and that the way the comparison was currently conducted, with traceability to the KRISS CRM, made this seem like a secondary level comparison – the primary comparison would have been of NMIs performing acid digestion ICP-MS analysis of an unknown CIGS material. Dr Brown contrasted this with the BET measurement which, whilst operationally defined, was still the highest order of measurement that could be conducted for this analysis. He added that it was up to CCQM to decide whether either of these had a place in the work programme. Prof. Emons concluded the discussion by

suggesting that the CMC scope statement for the comparison could be broader and not include any thickness constraints. Dr May made clear his view that similar studies in future should not require the use of a single CRM and should make participants aware of all traceability options. If only one route to traceability was available for a comparison then the relevant WG should consider whether or not the study was appropriate.

#### **10.7. CCQM Working Group on Electrochemical Analysis (EAWG)**

Dr Máriássy presented recent progress within the EAWG. He stated that the presentation would be relatively short since there were no new results to show since last year. The EAWG meeting had seen two new members participate, one from Tunisia and one from Saudi Arabia.

Dr Máriássy described discussions in the EAWG about CCQM-P143 – a preparative study of CRMs. There was a remaining question about whether using a calibrant, prepared according to a recipe, could be considered as a valid route of traceability for electrolytic conductivity. The results of CCQM-P143 did not indicate that NMIs that use calibrants prepared according to a recipe are performing differently from NMIs using routes of traceability leading directly to their own or another institute's primary cell. The recommendation of the EAWG was to draft a guidance document detailing acceptable sources of conductivity values for solutions according to recipes and to provide guidance on how to estimate the uncertainty of these conductivity values. The discussion on CCQM-P152, on phthalate buffer in a water/ethanol mix, centred on the conclusion by the EAWG that the sample had been unstable due to an esterification in solution. Dr Máriássy reported that whilst the measurements of individual NMIs had been satisfactory, the instability had caused most of the disagreement in the measurement results. Dr Máriássy reported that the data would be corrected to the same measurement date for each participant in an effort to remove the effects of the esterification reaction.

Dr Máriássy noted that a number of interesting technical presentations had been given at the EAWG including a description of applying controlled-potential coulometry, a comparison of solution bulk resistance calculation and complex data evaluation to extract the bulk resistance and impedance spectrum shape. It was hoped the technical advances presented would help improve the comparability of pH and conductivity measurements in future. Furthermore, an extra pilot study on impedance spectroscopy was needed to understand more of the subtleties of conductivity measurement.

Dr Máriássy mentioned the request by Dr Wielgosz for the group to provide input into the JCTLM database. Dr Wielgosz had noted that whilst 21 NMIs have CMCs for pH in the KCDB there are no entries for pH and blood gases in the JCTLM database. Dr Máriássy raised the issue of a CMC for electrical conductivity of aviation fuel, approved by the CCEM, which covered 11 orders of magnitude with one conductivity cell. Dr Máriássy said that it was necessary to clarify which of the CCs have the responsibility for these CMCs, and that he could contact the chair of the relevant WG in the Consultative Committee for Electricity and Magnetism (CCEM) to discuss this. Dr Máriássy concluded by showing the forward plan for the group to 2020 which was now to include preparative comparisons as well as analytical comparisons.

Dr May asked what the rationale is for repeat comparisons in the pH area, given that it is a rather limited measurement space, and wondered whether it related to turnover of staff. Dr Máriássy replied that most of the pH systems were of similar difficulty except for carbonate and phthalate. In general these difficult comparisons needed to be repeated every ten years, and from time-to-time there needed

to be a repeat of the easier buffers because a) uncertainties that are obtained improve over time and b) to assist new institutes joining the group to assess their capabilities.

#### 10.8. CCQM Working Group on Organic Analysis (OAWG)

Progress in the OAWG was presented by Dr Mackay who began by reviewing the analysis space currently covered within the 'Track A' core competency organic purity comparisons. It was noted that the results from [CCQM-K55.d](#) on folic acid purity were all within about 1 % except for a couple of outliers – the spread of results was marginally larger for qNMR than for the mass balance approach. Dr Mackay reported that stability assessment had also been an important part of this comparison. There had been significant work within the WG to identify and quantify as many of the impurities present in the sample as possible as this reduces the uncertainty of the mass balance approach, although Dr Mackay said that this was difficult because of the lack of available standards for most of the impurities observed. The NMIJ had subsequently proposed a follow-on comparison to the previous pilot study, CCQM-P150, for qNMR which would aim to evaluate the importance of the experimental set-up and selection of a solvent and internal standard.

Dr Mackay presented progress with current matrix comparisons. In the Track A area, [CCQM-K102](#) on brominated flame retardants in sediment had shown a positive bias among many participants because they had not separated all the impurities successfully, but now additional work had been done to solve these problems at most of the NMIs in question. Another Track A comparison, [CCQM-K109](#) on urea and uric acid in serum, was under way with results expected in late 2016. CCQM-K141 on enrofloxacin and sulfadiazine in bovine tissue was planned with reporting due in 2017. The results from the Track C comparison [CCQM-K126](#) on pharmaceuticals in surface water were presented. Dr Mackay explained that this was an international measurement issue but that a limited number of NMIs offered services in this area. The results were very promising but Dr Mackay stated that there had been much discussion in the WG about the two results from one institute and the incorporation of this into the study report. The WG had also more generally been examining uncertainty estimates and the WG had decided to cover this in more detail at a subsequent workshop. The results from the Track C comparison [CCQM-K132](#) on vitamin D metabolites in human serum were presented and showed good comparability. A proposal for the KCRV in this comparison was calculated using the DerSimonian-Laird method and more sophisticated KCRV estimators were being discussed by the WG. A Track C comparison [CCQM-K138](#) on aflatoxins in dried fig has commenced recently and would be challenging because of the multiple analytes and very low amount fractions being considered.

Dr Mackay concluded by reviewing the plan for the WG over that next ten years. The main strategic development had been to revise the high-purity organics measurement space and define X (low polarity, small size), Y (high polarity, large size) and Z (all polarities, large size) spaces going forward. Dr Mackay outlined a number of Track A key comparisons planned for the next ten years that would work towards covering this measurement space. Following a survey of its members, the highest priority among OAWG participants was services related to food safety. As a result Dr Mackay mapped out proposed comparisons to cover competencies related to food matrices based on the AOAC food matrix triangle.

Ms Parkes initiated the discussion by asking about the clinical biomarkers space and 'how far the light shines' with respect to the matrix in these comparisons since some were very complex. Dr Mackay said that there had been a lot of discussion about this in the WG and that matrix systems

are always more complex and need careful consideration. Dr Ellison reminded the OAWG that many matrices had a biological origin but were not clinical; he gave meat as an example. Dr Sargent thought that matrix issues cause most difficulties in the organic area and as a result CMCs claimed needed a tighter scope. Dr Mackay replied that this was the case for Track C comparisons, but that in Track A the OAWG had decided to keep broader scopes.

#### 10.9. CCQM Working Group on Inorganic Analysis (IAWG)

Dr Sargent briefly summarized the recent work of the IAWG and gave an update on the progress of the key comparisons and pilot studies being undertaken by the group. The IAWG has presented the results of seven key comparisons in the last year. It was noted that the results of these studies had all been good, except for a stability issue with Hg and Mo in [CCQM-K124](#) on elements in drinking water. Dr Sargent reiterated that no IAWG key comparisons were compulsory but members were strongly encouraged to participate in the benchmarking studies, of which [CCQM-K125](#) on Cu, K and I in infant formula was an example from the past year.

Dr Sargent noted that the results of CCQM-K124 had shown the instability of mercury in drinking water had been as expected, but the observed instability of Mo had come as a surprise and more investigation was required to understand this. It was stated that the results of the chromium speciation measurement associated with this comparison had been extremely good. The repeat of [CCQM-K108](#), [CCQM-K108.2014](#) on arsenic species and total arsenic in brown rice flour was an enormous improvement on the previous results obtained. More spread in the results was observed in [CCQM-K127](#) on contaminants and other elements in soil. It was observed that two samples, one with high-contamination and one with low-contamination were provided, and the difference in the matrix between these two samples might have made the comparison more challenging. CCQM-P167 on nitrogen mass fraction in milk powder had produced very good results and it was proposed that a key comparison study be organized in the near future. Dr Sargent reported that [CCQM-K140](#) on carbon-stable isotope ratio delta values in honey had produced very good results despite the range of techniques used. It was noted that the results from the universities and forensic laboratories that participated in the pilot study were also extremely good, showing a spread that was only about half as big again as that shown by the NMIs.

Dr Sargent went on to report that the IAWG had had a discussion about the applicability of CCQM-P149 on the determination of impurities in zinc in supporting CMC claims. This discussion developed a detailed ‘how far the light shines’ list of what is not supported. The conclusion was that the study was primarily for CMCs where the service is not a pure material or calibrant (except where additional evidence is provided). It recommended more comparisons on salts and non-metals and also for pure metals with non-metallic impurities and occluded gases. A final draft of the summary of these discussions has been circulated for comment. Dr Sargent reviewed the current status of CMCs in the inorganic area and then proposed the IAWG’s work programme up to 2020, noting that this was dominated by food and biomaterial matrices, indicating what services were planned to be delivered in these areas by NMIs in the future. New comparisons agreed for 2016-2017 included preparation of primary copper solution, a successor to [CCQM-K49](#) on essential and toxic elements in bovine liver, and the analysis of elemental impurities in alumina powder. Dr Sargent concluded by summarizing the 12 IAWG technical presentations that had been given during the year, highlighting state-of-the-art metrology in the inorganic area.

Dr Wielgosz opened the discussion by asking about [CCQM-K122](#) on anionic impurities and lead in salt solutions. In particular he commented that the uncertainties of participants were in some cases very small and not overlapping and that it appeared that the KCRV, which had a much larger uncertainty, had been chosen on the basis of the spread of the results. Dr Wielgosz asked what the implication of this was for participants: was there a problem with the study material or had the participants underestimated their uncertainties. Dr Sargent replied that it was up to the NMIs to choose the uncertainty to claim during the CMC process. He added that some of the smallest uncertainties came from electrochemical methods. Dr Ellison stated that there was a clear underestimate of the uncertainty by participants and it was sensible to ask why, perhaps because there were some processes going on that were not possible to model, but that the full story about uncertainty was unlikely to always be clear. He went on to say that the degree of equivalence was the difference between the NMIs added to the uncertainty in that difference, and the customer would be able to see this. There was general disagreement on this final point, which was summed up by Dr Wielgosz who stated that this lack of comparability between NMIs, which had been allowed because of a reference value whose uncertainty was too large, would be invisible to customers. He added that the NMIs could not be allowed to quote the low uncertainties they used during the comparison when claiming CMCs as this would mislead customers as to the quality of the services provided, unless it could be clearly shown that the excess variance observed was due to problems with the comparison material rather than lack of compatibility of measurement methods. Dr Milton agreed that there must be a solution to this issue.

#### 10.10. CCQM Working Group on Gas Analysis (GAWG)

Dr Kim summarized the work of the GAWG. The meeting earlier in the CCQM week had been attended by 47 participants from 21 economies and the BIPM, NOAA and IAEA. Dr Kim reported that there had been 12 comparisons in 2015-2016 but that only eight were expected in 2017-2019. The [CCQM-K111](#) study on propane in nitrogen was presented as a good example of a CC key comparison with a number of RMO supplementary comparisons following it. In general, good agreement had been found in the GAWG and the RMOs.

Dr Kim reported that [CCQM-K90](#) on formaldehyde in nitrogen, to support air quality regulations, was a difficult comparison because of the low concentrations involved, but that the results have been good and mostly agreed with the reference value within the uncertainty of the measurement. The results of two complex multi-component fuel gas studies, [CCQM-K112](#) on biogas and [CCQM-K119](#) on LPG (stored as liquid in the cylinder but measured as a gas) were presented. The results had shown good comparability across the full range of components and between NMIs. The spread of results in [CCQM-K121](#) on terpenes was larger because of the challenging nature of the analysis and the low nmol/mol concentration at which these compounds were present. In some cases uncertainties of up to 5 % were quoted, which is much higher than is usually associated with gas analysis.

Dr Kim then highlighted the comparisons that were due to have their measurement phase during 2016. This included [CCQM-K116](#) on water in nitrogen, [CCQM-K117](#) on ammonia in nitrogen, [CCQM-K118](#) on hydrogen enriched natural gas and [CCQM-K120](#) on ambient level CO<sub>2</sub>. It was noted that GAWG participants were encountering problems with the transport of cylinders because of changes in international agreements about cylinder type testing. This problem could be circumvented by purchasing cylinders with UN certification. However the cost of these cylinders was significant and in order to continue with [CCQM-K117](#) each participant will have to pay €2000 for their cylinder

which they will then own at the end of the comparison. Dr Kim summarized the planned key comparisons from 2017 to 2019, noting in particular the core comparisons, the first of which on NO in nitrogen would take place in 2017.

Dr Kim stated that the GAWG strategy document had been approved by participants at the GAWG meeting. The document sets out:

- Strategy for selecting comparison studies for the GAWG work programme
- Strategy for CMC claims
- Implementation of the flexible scheme to support CMCs
- Guidance for CMC claims for purity analysis
- Guidance for linking RMO comparisons to Track A key comparisons.

Dr Kim said that during CMC cycle XVIII there would be an optional re-review of Track A components based on evidence from previous core comparisons.

The GAWG meeting included an update on the status of the task group on particle and particulate composition. The task group has produced a roadmap to provide traceability for some of the key particulate metrics over the next ten years. The first step in this would be a pilot study on particle number concentration and particle charge concentration in 2017. Dr Kim mentioned the progress with the task group on ozone cross-section measurements, previously mentioned by Dr Wielgosz, which had a large component of GAWG members. Their first task will be to perform a critical assessment of the uncertainty budgets of data in the literature for the ozone cross-section.

Dr Sin started the discussion by thanking the GAWG for its efforts in adopting a broader scope approach to CMCs. Dr Wielgosz reiterated the statement made by Dr Kim that comparisons were becoming more difficult because of the changes in international agreements over the type testing of cylinders.

Prompted by the comparison on particle number concentration Prof. Unger asked whether particle number concentration in liquids was a topic for the CCQM. Dr Milton replied that particle number concentration in air is clearly within the scope of the GAWG because of the gas matrix, but the situation for particle number concentration in liquids is less clear and more discussion is needed.

## **11. CCQM APPROACH TO CALIBRATION AND MEASUREMENT CAPABILITIES AND KEY COMPARISONS**

Dr May introduced an extra item that had not been on the agenda about the CCQM approach to calibration and measurement capabilities and key comparisons, which was prompted by some of the discussions earlier in the meeting. Dr May stated that the objective of CMCs was to document the peer-reviewed and accepted statements of the measurement capabilities that a NMI maintains to underpin the measurement services it provides to customers. He added that following peer-review and acceptance of both the technical aspects of the claim and the NMI's quality system covering the

capability(s), the CMC is published in a publicly available website maintained by the BIPM – the KCDB.

In the context of the recent CIPM MRA review it had been observed that:

- The planning of key comparisons should be strategic, not opportunistic.
- As stated in the text of the CIPM MRA, key comparisons test the principal techniques and methods in the field. For chemistry and biology it was noted that key comparisons validate a NMIs' ability to develop and use higher order methods for delivering SI-traceable services to customers. Not all NMI services can be directly underpinned by a key comparison.
- Reducing the numbers of CIPM key, RMO key and supplementary comparisons should not be objectives in their own right, but rather they should be used more efficiently to achieve the goal articulated above.
- The progress of CIPM key, RMO key and supplementary comparisons at each stage through to completion should be monitored actively, with appropriate interventions when necessary.

Dr May observed that key comparison studies should assess and document the degree of equivalence of chemical measurement capabilities used by NMIs and DIs to provide measurement services, but that they are not for assessing specific techniques and methods for the determination of chemical measurands. He reiterated that not all services provided by a NMI are expected to be directly underpinned by a key comparison, but that only NMIs, NMI-designated laboratories and other MRA signatories can participate in a key comparison. Dr May urged all WGs to consider the following for all non-core key comparisons:

- Why is this key comparison needed?
- How many NMIs provide services in this area?
- How many are planning to begin delivering services over the next 3 years or so?

Dr May explained that pilot comparison studies are intended to:

- Demonstrate or define the state-of-the-art for measurements in high-priority areas.
- Assess suitability of various methods for addressing a given measurement problem.
- Provide an opportunity for NMIs/DIs to participate in studies in an area new to them.
- Pilot studies are not intended to provide evidence for equivalence or to underpin CMCs.

Two types of pilot study could be considered. First, a parallel pilot study – a study in which the same study material is being used in a parallel key comparison. Second, a stand-alone pilot study – a study where no key comparison is being conducted at the same time and thus the study is unique with regard to the measurands, matrices and objectives. Dr May stated that the same questions mentioned above, which must be asked before considering a key comparison, must also be considered before initiating a pilot study.

Dr May elaborated on the presentation he had just given by saying that in the CCQM, partly because of its size, the individual WGs were on occasions acting more like sub-CCs and he reminded members that it was for the CCQM plenary meeting to approve proposed comparisons. Dr May noted that the CCQM had fallen out of the habit of doing this but that this would start again in some form, starting at the next CCQM plenary meeting. Dr Ma added that many of the RMO comparisons were not particularly visible to the CCQM and that it would help with planning and collaboration if the details of these comparisons were more widely shared with other RMOs and with the CCQM.

## 12. REPORT FROM THE CCQM AD HOC WORKING GROUP ON THE MOLE

Dr Güttler reported on progress in the CCQM *ad hoc* working group on the mole, reiterating that its tasks were: preparation of a CCQM draft for a *mise-en-pratique* of the mole; providing a response to the CCU draft of the 9th SI Brochure; providing a response to IUPAC activities; and disseminating information for the external community. The 5th meeting of the WG had taken place earlier in the week of CCQM meetings. An opening presentation had been given by Dr Bettin on the status of the redefinition of the Avogadro constant, in particular on the progress with reducing the uncertainty of results from the Avogadro project and the various Watt balance projects over time. It was noted that the latest Watt balance and Avogadro project results are in good agreement. Dr Rienitz had given an opening presentation that highlighted progress on CCQM-P160 on isotope ratios and molar mass of highly enriched silicon. The importance of the study in reducing the uncertainty of one of the dominant components of the overall Avogadro constant uncertainty was explained. The deadline for reporting results for this comparison is the end of September 2016.

Dr Güttler gave a brief update on the status of the IUPAC project on the mole and in particular a survey it had carried out among national science and chemistry academies. It was notable that the response to the survey had been poor and that no clear pattern had emerged. Equal numbers of responders had either liked or did not like the old definition of the mole. The same was true for the new definition. It was agreed that the lack of response to the survey was disappointing. Dr Güttler recalled the ACS symposium on the mole which had taken place in Boston (USA) in August 2015 and noted that the presentations from this meeting should be publicly available soon. He mentioned that the draft *mise-en-pratique* for the mole was now available on the BIPM website and that comments were still welcome.

Following the presentation Dr Brown asked if the CCQM should re-double its efforts to communicate with the wider chemical community about the mole following the poor response to the IUPAC survey. Dr Güttler agreed that all additional engagement was welcome, and added that the CCU has established a sub-group to look at publicity surrounding the new SI. Furthermore, Dr Güttler said that stakeholders must understand that the redefinition of the mole is not a standalone event but is associated with the other changes to the SI. Dr Mester added that the draft IUPAC report would be published in the summer and agreed that there was still a lack of engagement within the community. Dr Wielgosz advised that an action was needed to make the ACS meeting presentations available as soon as possible. Dr Milton concluded the discussion by adding that the meeting of the *ad hoc* group had been very interesting and had demonstrated significant added value. He continued that the redefinition is not just a big opportunity for the SI but is an opportunity to promote the whole of metrology. Dr Milton said that he had recently written to NMI directors to ask them what their plans are for publicising the redefinition, so that the CCU sub-group looking at the publicity aspects of the re-definition could be informed and co-ordinate appropriately.

## 13. MEMBERSHIP OF THE CCQM – APPLICATION PROCESS

Ms Parris presented some of the general criteria for membership of CCs. It was noted, that the current criteria for membership of a Consultative Committee ([CIPM-D-01](#)) state that it is open to institutions

of Member States of the BIPM that are recognized internationally as being the most expert in the field. This normally requires that they:

- be national laboratories charged with establishing national standards in the field;
- be active in research and have a record of recent publications in research journals of international repute;
- have demonstrated competence by a record of participation in international comparisons organized either by the Consultative Committee, the BIPM or a RMO.

Observer status on a CC may be granted to those institutes:

- of Member States and to intergovernmental organizations and international bodies, and scientific unions that actively participate in the activities organized under the auspices of the CC and its working groups but do not yet fulfil all the criteria for membership.
- of an Associate of the CGPM that is not eligible to become a State Party to the Metre Convention when these institutes actively participate in the activities organized under the auspices of the CC and its working groups.

Ms Parris then reviewed the proposed process for applying for CCQM membership (document CCQM/15-39, presented at the 21st meeting of the CCQM).

Dr May cautioned that whilst the CCQM had developed documents on membership, a higher level process was going on to revise CIPM-D-01 (an updated document is expected in October) and that this would have an impact on the CCQM documents. Dr Milton concurred that the CIPM had decided (CIPM/104-46) to review the policy for approving and reviewing membership and observership of the Consultative Committees at a meeting of CC Presidents to be held in June 2016. The decisions on observer and member status presented at Session II of the 104th meeting of the CIPM have been postponed until after this review. Dr Wielgosz confirmed that the CCQM's existing documentation has not yet appeared on the open-access BIPM website. Dr May added that HSA (Singapore) and NIMT (Thailand) were recent additions to the membership of the CCQM. Dr Brown added that some documentation existed at the RMO level, especially in EURAMET, that might be useful to consider during revision of the CCQM process.

## **14. REPORTS FROM RMOs**

### **14.1. COOMET**

Dr Kustikov presented the current membership of COOMET and highlighted the active role that COOMET has in CCQM comparisons, especially in the gas analysis area. It was noted that this year had seen new CMCs from Russia, Belarus, and Kazakhstan (which had submitted its first ever CMC). Dr Kustikov then listed the large number of ongoing COOMET intraregional comparisons in the chemistry area. Dr Kustikov concluded by noting that the next meeting of COOMET TC 1.8 "Physical chemistry" would be in St Petersburg in May 2016.

Dr Milton observed that it was encouraging to see participation from Moldova within COOMET and asked Dr Kustikov to provide him with the relevant contact person so that Moldova could be encouraged to participate more widely in CIPM MRA activities. Dr May asked how many of the COOMET CMCs are linked to services provided by the NMIs. Dr Kustikov replied that all of the CMCs underpinned services. Dr May encouraged Dr Kustikov to show some results from recent COOMET comparisons during his next presentation.

#### 14.2. APMP

Dr Ma, the new chair of APMP TCQM, presented a summary of CMCs from the region. This indicated that APMP was particularly active in the chemistry area. Dr Ma noted that 101 CMCs had been received and reviewed by APMP TCQM and 86 of these were subsequently submitted to the KCWG. Dr Ma presented the ongoing key comparisons and supplementary comparisons that are in progress within the region and the peer-review visits that had taken place within the region in the last year. Dr Ma stated the intention of TCQM to implement a new strategy which would mirror that of the CCQM, in particular in order to strengthen intra-RMO review to increase CMC quality, increase the number of peer-review visits and decrease the number of APMP key comparisons and supplementary comparisons. Dr Ma concluded by noting that the next TCQM meeting would take place in Viet Nam in November 2016.

Dr May suggested that NMIs should not need to participate in both CCQM key comparisons and RMO supplementary comparisons as this was asking them to do the same job twice. He suggested to Dr Ma that a member from outside the APMP region should be included in peer-review visits.

#### 14.3. EURAMET

Dr Andres reported that EURAMET TC-MC consisted currently of 28 member countries and the associate member JRC-IRMM. National standards were held at 22 National Metrology Institutes and 22 Designated Institutes, and the TC comprised four technical subcommittees (gas analysis, inorganic analysis, organic analysis, and electroanalysis) and an *ad hoc* working group on perspective on European Metrology Centres. Dr Andres listed a number of ongoing EURAMET comparisons, mostly in the gas analysis area, and highlighted other joint research activities that were taking place under the EMPIR programme. Dr Andres mentioned a number of other activities within EURAMET such as the recent EURAMET “Workshop on Designated Institutes”, the draft EURAMET guide on comparisons (final version expected in June 2016) and general discussions on further integration of the EURAMET metrology infrastructure from a chemistry and biology perspective. He summarized a joint project with TC-T on moisture content in materials. Dr Andres concluded by stating that the next TC-MC meeting would take place in Warsaw (Poland) in February 2017.

Following the presentation Dr Brown asked whether the OIML would be involved in the project on moisture content. Dr Andres replied that the project group was still being formed. Dr Morrow was interested in more information on the EMPIR projects, especially the contact details for coordinators; Dr Andres replied that this information was available on the EURAMET website.

#### 14.4. AFRIMETS

Dr Botha gave an update on AFRIMETS stating that there were 44 members at the end of 2015. Dr Botha highlighted the increase in the number of Members of the BIPM and Associates of the CGPM across the continent over the last 10 years and there had also been an improvement in the scientific metrology categorization of many countries during this period. Dr Botha noted that the new AFRIMETS Chair for 2015-2017 was Mr Dennis Moturi from KEBS (Kenya). In 2016 the RMO had submitted a total of 24 CMCs for review, one from KEBS and the remainder from NMISA. Dr Botha updated members on the progress being made towards accepting the quality systems of more countries within the region. Dr Botha concluded by summarizing the recent proficiency testing scheme operated in the region by NMISA and the NMISA African Food and Feed Reference Material Programme which was launched in 2015 and involved the training of analysts from less developed countries.

Following a question from Dr Morrow, Dr Botha confirmed that there were still a few countries within the region that were classified as has having no activity in scientific metrology. Dr Fajgelj wondered if the strong development in the region over the last decade reflected recent international investment. Dr Botha replied that a large proportion of the scientific metrology development had been in the physical measurement area and that in the chemistry area more emphasis had been on chemical testing capability.

#### 14.5. SIM

Dr da Cunha reported on recent activities in the SIM region. He noted that there had been 23 participants from 12 countries at the SIM chemical metrology WG meeting in Argentina in May 2015. Dr da Cunha said that a workshop on the CMC review process was planned as part on the SIM General Assembly in the Dominican Republic in November 2016. Dr da Cunha proceeded to highlight the ongoing comparisons in the region. He then presented the new CMC claims from the region – there were 150 in total with the majority coming for the USA (95) and Canada (32). Dr da Cunha concluded by highlighting an upcoming “hands-on” training course being provided in SIM on Clinical Chemistry and on Statistical Models and Methods Supporting the Production of CMCs. The next SIM Chemical Metrology WG meeting will be in Costa Rica in May 2016.

In response to the presentation, Dr May reminded members that there were only two reasons for participation in RMO comparison exercises: 1) as evidence for CMC claims or 2) as a pivot laboratory to link with CCQM key comparisons. He stated that these reasons must be considered when planning comparison exercises.

#### 15. REPORT FROM THE JCTLM

Dr Wielgosz gave a brief update on the JCTLM. He reminded members that the JCTLM database was developed to help the IVD industry meet metrological traceability requirements of the EU IVD Directive. Currently, the BIPM provides the Secretariat for the JCTLM, maintains the JCTLM IVD

Reference Measurement Systems Database, coordinates the nomination and review process for database entries and contributes to ISO TC 212 WG2: revisions of ISO 17511 and ISO 15195. The database contains 295 CRMs, 170 Reference Methods and 130 Reference Measurement Services.

Dr Wielgosz reported that the main change in the past year had been a reorganization of the JCTLM into two WGs, one on the JCTLM database and one to concentrate on JCTLM Traceability: Education and Promotion. The database WG was further broken down into analyte categories each of which had a separate review team. Dr Wielgosz mentioned the activities in ISO TC212 and in particular the revisions of ISO 15195 'Laboratory medicine - Requirements for reference measurement laboratories', a standard which supplements ISO/IEC 17025. Dr Wielgosz commented that the review had become more complicated because of the review of ISO/IEC 17025 which was now in progress. Dr Botha commented that until the review of ISO/IEC 17025 was complete it would not be clear what the full implications in terms of metrological traceability were for the revision of ISO 15195.

Dr Wielgosz commented that a gap analysis of JCTLM coverage of clinical laboratory tests had recently been performed and this had highlighted pH and dissolved blood gases as areas where input from NMIs was required, especially since in excess of 95 % of reference materials currently listed on the database come from NMIs.

Dr Wielgosz concluded by highlighting the activities that the new JCTLM Working Group on Traceability: Education and Promotion would be undertaking in the near future.

## **16. COMMENTS ON WRITTEN REPORTS FROM INTERNATIONAL ORGANIZATIONS IN LIAISON WITH THE CCQM**

Dr Wielgosz raised the current revision of ISO Guide 34 'General requirements for the competence of reference material producers', soon to become ISO 17034, as an important item. Dr Botha stated that there was an ISO CASCO meeting in May 2016 to discuss comments received on the draft standard and that it was hoped that the ISO 17034 standard would be published by the end of 2016. Dr Botha added that the revised ISO/IEC 17025 draft would be out for first ballot in May and if members had additional comments on the document they should return these through their national standardization organizations.

## **17. FUTURE CCQM WORKSHOPS**

Dr May mentioned that a reduction in the length of future CCQM meetings could allow time in the afternoon of the final day for some presentations on cutting edge metrology topics and proposed this for discussion amongst the WG chairs. Dr Milton recommended attendance at the upcoming 2016 Varenna Metrology School in June/July 2016 which was to give equal prominence to chemical and physical metrology in its programme.

**18. CCQM RESOLUTIONS**

There were no resolutions made during the meeting. Dr May suggested that, given the upcoming CGPM meeting in 2018, the CCQM should give consideration over the coming year as to whether it wished to propose any resolutions following the 2017 CCQM meeting.

**19. DATE(S) FOR THE NEXT MEETING OF THE CCQM PLENARY AND WG MEETINGS**

The next meetings of the CCQM Working Groups at the BIPM were proposed for 22-28 April 2017, with the 23rd meeting of the CCQM taking place on the 27-28 April 2017.

**20. CLOSURE**

In the absence of any other business, the President of the CCQM, Dr May, closed the meeting at 15:30 hrs and thanked participants for their contributions, reports and participation in the discussions. Dr May thanked the staff of the BIPM for their support in hosting the meeting and wished all attendees a safe journey home.

Dr R. J. C. Brown

Rapporteur, 28 April 2016

**DECISIONS AND ACTIONS FROM THE 22ND MEETING OF THE CCQM**

1. As rapporteur, Dr R.J.C. Brown to draft “Decisions and Actions” document and “Report of 22nd Meeting of the CCQM”.
2. CCQM approved the report of the 21st Meeting of the CCQM.
3. Outstanding actions from the 21st Meeting of the CCQM to be progressed as discussed in the report of the 22nd Meeting of the CCQM.
4. KCWG to continue to work to implement a unified nomenclature for the core comparison approaches being undertaken by different WGs to avoid confusion when communicating outside the CCQM.
5. Agreement to continue to hold WG meetings at the BIPM in association with the CCQM plenary meeting next April.
6. CCQM reiterated that for pilot studies, the coordinating laboratory had the first option on publishing data and that a participant wishing to publish pilot study results prior to the coordinating laboratory in any way needed to seek agreement from the coordinating laboratory. In the case that a coordinating laboratory chooses not to publish the results but a participant does wish to do so, both this decision and the request of the participant must be relayed to the relevant WG Chair. For any publication of pilot study results, the agreement from each participating laboratory that its data can be published is required.
7. The text of the traceability exception accepted by the CIPM (Decision CIPM/104-26) to be made clearly available on the BIPM website.
8. The CCQM voiced its concerns on the lack of representation of the Chemistry and Biology community amongst the JCRB membership. The CCQM President will raise the issue with the CIPM to ensure that the opinions of the Chemistry and Biology community are represented and taken into account at JCRB meetings.
9. CCQM WGs to update their strategy documents by 1 December 2016, and submit for review by the CCQM President.
10. SPWG members to comment on the current CCQM strategy document by 30 September 2016. The comments will be collated by the CCQM Executive Secretary, and used in drafting the updated strategy document.
11. CCQM President to appoint a task group to review and propose required modifications to current templates used for proposing, reviewing and approving chemical and biological CMCs as well as KCDB search engines and functionalities, and report back to the next meeting of the CCQM.
12. Each technical WG to propose a way-forward for broader-claim CMCs to be presented and reviewed at the 23rd meeting of the CCQM in 2017.
13. KCWG to decide on which CMC service categories will undergo re-review in Cycle XVIII and report to the relevant RMO Chemical Technical Group Chairs.
14. RMOs to continue to monitor their internal process for intra-regional CMC review and provide relevant statistics to the KCWG.

15. KCWG to generate a flow diagram describing the CMC production and review process in the CCQM for use in presentations and other documentation.
16. Following CIPM MRA rules, only one result per institute per Key Comparison shall be submitted.
17. WG chairs to report to the CCQM President, by 1 October 2016, the Key Comparisons that have been conducted in their WGs where more than one result has been included from one institute.
18. SPWG to consider whether an exception to the CIPM MRA rule of one result per institute per Key Comparison should be sought. Dr L. Mackay to draft a background note on OAWG practices to support the discussion.
19. The work of the MBSG is complete and the group will be disbanded. A decision to be made by the President as to where the work of the group, should reside after consulting with the Chairs of the NAWG and the CAWG.
20. SAWG to reconsider the HFTLS statement for CCQM-K136; in particular whether this needs to be constrained to match the scope of the ISO 9277 standard method and report back to the President by 1 October 2016.
21. SAWG to reconsider the KCRV for CCQM-K129; in particular, on how the independent XRF value from PTB should be included in its calculation. Report back to CCQM President by 1 October 2016.
22. SAWG to make clear in the report of CCQM-K129 that the KRISS CRM used in the study is not a requirement for the measurement, but is one source of available traceability.
23. Going forward, CCQM Key Comparison protocols can make potential participants aware of any relevant CRMs, but no recommendation or requirement for their use may be included in the protocol.
24. SPWG to consider whether the measurement of number concentration of nanoparticles in liquids should be within the remit of the CCQM, and if so within which WG, and if not, which other Consultative Committee could cover this area.
25. Going forward, CCQM to resume approving or disapproving Key Comparison proposals during the CCQM plenary session.
26. NIST to make available online the presentations from the ACS symposium on the mole by 15 June 2016 and provide a link for use on the BIPM (and other NMI) websites.
27. SPWG to discuss the format of future workshops and CCQM meetings to allow extra time for technical presentations during the plenary.
28. At 2017 Plenary Session, CCQM to propose/consider/discuss possible CCQM resolution prior to the 2018 CGPM meeting.

## APPENDIX 1

## WORKING DOCUMENTS SUBMITTED TO THE CCQM AT ITS 22ND MEETING

Working documents submitted to the CCQM at its 22nd meeting are on restricted access.

Documents restricted to Committee members can be accessed on the [restricted website](#).

## Document

## CCQM/

- 16-01 Draft agenda of the 22nd meeting of the CCQM, 1pp
- 16-02 Agenda of the CCQM Workshop on Broad Claim CMCs, 1pp
- 16-03 Timetable of CCQM meetings April 2016, 1pp
- 16-04 Draft *mise en pratique* for the definition of the mole, 6pp
- 16-05 Visiting scientist secondment opportunities to the BIPM Chemistry Dept 2017, 4pp
- 16-06 REMCO Report for CCQM April 2016, 2pp
- 16-07 COOMET report to the CCQM
- 16-08 21st meeting of the CCQM: Agenda, Willie E. May, 40pp
- 16-09 Report of the 21st meeting of CCQM, BIPM, 37pp
- 16-10 CCQM SPWG meeting, Willie E. May, 28pp
- 16-11 CCQM Workshop on Broad Claim CMCs, Willie E. May, 14pp
- 16-12 CMCs KCs PCs, Reenie Parris, 4pp
- 16-13 Core Capabilities and Broad CMC claims in Inorganic Analysis, Paola Fiscaro, 23pp
- 16-14 From Core Comparisons to Broad CMC Claims in Gas Analysis, Paul Brewer, 24pp
- 16-15 Further development of the strategy for core mixtures, Paul Brewer, 12pp
- 16-16 From Core Comparisons to Broad CMC Claims in Organic Analysis, Lindsey Mackay, 30pp
- 16-17 OAWG Update for KCWG re Core Competence Approach, Reenie Parris, 49pp
- 16-18 Overview of Chem-Bio CMCs and opportunities for increasing the efficiency of the review process, Della SIN, 20pp
- 16-19 Broader scopes of CMC claims: CCQM PAWG's Perspective, Sang-Ryoul Park, 13pp
- 16-20 CCQM Strategy Document (2017-2027), R.I. Wielgosz, 12pp
- 16-21 BIPM activities in support of metrology in chemistry and biology, R.I. Wielgosz
- 16-22 CCQM Key Comparison and CMC Quality Working Group Update, Della SIN, 16pp
- 16-23 Protein Analysis Working Group: Report on 2015-2016 activities, Sang-Ryoul Park, 30pp

- 16-24 CCQM Nucleic Acid Analysis WG: Report to CCQM plenary BIPM 21-22 April 2016, Helen Parkes, 21pp
- 16-25 Cell Analysis Working Group April 2016, Anne Plant, 18pp
- 16-26 *ad hoc* Steering Group on Microbial Measurements (MBSG) Report to CCQM Plenary April 2016 BIPM, Sevres France, Jayne Morrow, 35pp
- 16-27 Surface Analysis Working Group (SAWG) Report for 14th meeting (2015/16), Wolfgang Unger, 34pp
- 16-28 CCQM 2016 Report of the WG on Electrochemical Analysis, Michal Mariassy, 24pp
- 16-29 CCQM Organic Analysis Working Group, Lindsey Mackay, 36pp
- 16-30 CCQM April 2016 Report of the CCQM Inorganic Analysis Working Group, Mike Sargent, 18pp
- 16-31 CCQM Gas Analysis Working Group Presentation to CCQM April 2016, Jin Seog Kim, 24pp
- 16-32 CCQM *ad hoc* WG on the mole (17 April), B. Guttler, 16pp
- 16-33 the redefinition of the Avogadro constant, Horst Bettin, 16pp
- 16-34 1st update on CCQM-P160 “Isotope ratios and molar mass of highly enriched silicon”, Olaf Rienitz, 28pp
- 16-35 CC membership, Reenie Parris, 2pp
- 16-36 Attendees of/Participants in CCQM Plenary meetings, Willie E. May, 8pp
- 16-37 Overview of APMP TCQM Activities and Considerations, Ma Liandi, 13pp
- 16-38 SIM Chemical Metrology Working Group, Valnei Smarçaro da Cunha, 12pp
- 16-39 Activities of COOMET TC 1.8 “Physical Chemistry” 2015-2016, Yuri Kustikov, 11pp
- 16-40 Technical Committee in Metrology in Chemistry (TC-MC) annual report 2015/2016, Hanspeter Andres, 6pp
- 16-41 TC Chair Annual Report 2015-2016, Hanspeter Andres, 5pp
- 16-42 AFRIMETS Update April 2016, Angeliqe Botha, 11pp
- 16-43 JCTLM database: Reference materials, methods, and measurement services for IVD industry, R.I. Wielgosz and S. Maniguet, 22pp
- 16-44 The Measurement Methods Matrix used in CCRI, 4pp
- 16-45 Draft generic terms of reference for CCQM technical WGs, 4pp