Bureau International des Poids et Mesures

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

Report of the 24th meeting
(19-20 April 2018)
to the International Committee for Weights and Measures

Comité international des poids et mesures

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

as of 19 April 2018

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. Mendeleyev Institute for Metrology, Rosstandart [VNIIM], St Petersburg.

Danish Fundamental Metrology Ltd [DFM], Lyngby.

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.

Instituto Nacional de Metrologia, Qualidade e Tecnologia [INMETRO], Rio de Janeiro.

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.

RISE Research Institute of Sweden AB [RISE], Borås.

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

VSL B.V. [VSL], Delft.

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

Observers

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

All-Russian Scientific Research Institute of Physical Technical Measurements, Rosstandart [VNIIFTRI], Moscow

Bulgarian Institute of Metrology [BIM], Sofia.

Central Office of Measures/Glówny Urzad Miar [GUM], Warsaw.

Centro Español de Metrología [CEM], Madrid.

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

Government Office of the Capital City Budapest [BFKH], Budapest.

Hong Kong Government Laboratory [GLHK], Kowloon.

Instituto Português da Qualidade [IPQ], Caparica

Kenya Bureau of Standards [KEBS], Nairobi

National Physical Laboratory of Israel [INPL], Jerusalem.

Liaisons

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

European Commission – Joint Research Centre [JRC-Geel], Geel

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].

1. OPENING OF THE MEETING

The Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) held its twenty fourth meeting at the International Bureau of Weights of Measures (BIPM), at Sèvres on 19-20 April 2018.

The following were present: H. Andres (METAS), M. Arce Osuna (CENAM), O. Bottauscio (INRIM), P. Brewer (NPL), R.J.C. Brown (NPL), S.Z. Can (UME), B.J. de Vos (NMISA), L. Deleebeeck (DFM), S. Ellison (LGC Ltd), P. Fisicaro (LNE), T. Fujimoto (NMIJ/AIST), B. Garrido (INMETO), C. Gonzalez (NIST), B. Güttler (PTB), C. Haraldsson (RISE), J.S. Kim (KRISS), S.K. Kim (KRISS), J. Koelliker Delgado (CENAM), Y. Kustikov (VNIIM), T.K. Lee (HSA), H. Li (NIM), L. Ma (NIM), L. Mackay (NMIA), M. Máriássy (SMU), W.E. May (President of the CCQM), J. Melanson (NRC), Z. Mester (NRC and IUPAC), J. Nammoonnoy (NIMT), S.R. Park (KRISS), H. Parkes (LGC Ltd), J. Pillay (NMISA), M. Sargent (LGC Ltd), M. Sega (INRIM, also CITAC), A. Takatsu (NMIJ/AIST), M. Tarlov (NIST), T.L. Teo (HSA), W. Unger (BAM), A. van der Veen (VSL), S. Vaslin-Reimann (LNE), J. Wang (NIM), C. Yafa (NIMT).

Observers: F. Dias (IPQ), V. Dobrovolskiy (VNIIFTRI), W. Kozlowski (GUM), D. Moturi (KEBS), A. Stakheev (VNIIFTRI), Z.N. Nagyné Szilágyi (BFKH).

Liaison: A. Fajgelj (IAEA).

Representatives from Member State invited to attend as Observer: A.R. Alaskar (SASO-NMCC), G. Carroll (SL), P.A. Gatti (INTI), S. Gonzalez -Monico (INM Colombia), A.I. Silva (LATU).

Invited: R. Kaarls (CIPM honorary member), H. Klich (INRAP), E. Lin (NIST MML), J. Morrow (NIST).

Also present: S. Maniguet, M.J.T Milton (Director of the BIPM), S. Picard (BIPM / KCDB Coordinator), R. Wielgosz (BIPM / Executive Secretary of the CCQM), N. Zviagin (JCRB Executive Secretary).

Sent regrets: M. Adeogun (NPL), M. Akgöz (UME), S. Choquette (NIST)

Dr May, President of the CCQM, officially opened the meeting at 9:00 am on 19 April 2018. He thanked the CCQM members for their efforts over the last year and noted the unique nature of the CCQM meetings as the only forum world-wide dedicated to measurement science in chemistry and biology. 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 Melanson as the rapporteur for the meeting; Dr Melanson agreed, fulfilling the second year of his two-year term in this capacity.

3. APPROVAL OF THE AGENDA

The agenda was approved. Dr May noted that RMO reports had been submitted prior to the meeting so their reports in the meeting should be two-minute discussions, as opposed to presentations. Dr Wielgosz suggested that agenda item 8.2 "Use of evidence other than comparisons for supporting CMCs" be incorporated into the KCWG report.

4. OPENING REMARKS FROM THE CCQM PRESIDENT AND ACTIONS FROM THE 23RD MEETING OF THE CCQM

Dr May began by providing a brief history of CCQM, noting its establishment by the CIPM in 1993. He noted figures of merit of CCQM, both in terms of growing numbers of participants and a substantive list of CMCs. Dr May then reviewed general objectives of CCQM:

- Document and improve the world-wide comparability of measurements and measurement standards
- Improve chemical and biological measurement science
- Provide chem/bio metrology-related solutions to address important global/societal issues

Dr May continued by reviewing the current organizational structure of the CCQM, noting that the CCQM operates in a different manner than most other CCs as its scope is much broader. He highlighted the ten permanent working groups (WGs) and the current *ad hoc* group, along with their respective chairs. He noted that a decision had been made to formally identify deputy chairs for each working group, and commented on the merits of having a succession plan in place with a large turnover in working group chairs anticipated over the next year.

The goals of the CIPM MRA were highlighted, and Dr May noted that the CIPM MRA should be a means for 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. He repeated a message that had been sent to all existing and new members of CCQM, reminding them of the spirit of the CIPM MRA:

"NMI/DI's deliver measurement/metrology services and/or products to customers that are internationally recognized within the framework of the CIPM MRA.

- CMCs are peer-reviewed descriptions of the capabilities that NMIs/DI's maintain to support consistent delivery of individual or a class of such services
- Developing and articulating capabilities which do not underpin delivery of measurement/ metrology services available to customers is not consistent with the spirit of the MRA."

Dr May continued by reviewing decisions and actions from the 23rd meeting of the CCQM. One outstanding issue was that of overlapping CMCs, and whether an exception should be requested for a DI with neutron activation analysis (NAA) capabilities who provides services internationally. After exploring advantages and disadvantages, the CCQM President's decision was to not request an exception for this case, and suggested the DI must work collaboratively with the NMI. Referring to Decision CIPM/106-18, Dr May noted that the CCQM should not vote on this issue but reach consensus. Dr May thus requested consensus from the CCQM and opened the floor for comments. Dr Mackay remarked on the difficulty of the situation as the NMI and DI offer different services, but the DI is currently unable to underpin these services by participation in key comparisons or with CMCs. Dr Mackay commented that as we move to broader scope key comparisons this becomes more of an issue. Dr May noted that the situation was no different than that of BAM and PTB in Germany. Dr Milton commented that while he is sympathetic to the NMIA, it needs to balance its scope versus that of its DI. Dr Mackay clarified that the NMIA and its DI offers different services but that they may require the same key comparison as support and the measurand of a CMC might look the same even though the service is different Dr Güttler noted the division of work on CRMs by BAM but underpinned by PTB, and conceded that with the trend toward more broadly defined CMCs, this will increasingly become a problem. Dr May concluded the discussion by re-affirming his decision, and noted that while the CIPM has offered a number of exceptions in the past, great care must be taken when requesting such an exception.

5. REPORT FROM THE CCQM *AD HOC* WORKING GROUP ON THE MOLE

Dr Güttler reported on progress of the CCQM *ad hoc* Working Group on the Mole and its role in the revision of the SI. He began by reviewing the timeline of the revision, with the CCU recommendation to the CIPM completed on 5-7 September 2017 followed by the drafting of the CIPM recommendation to the CGPM on 16-20 October 2017, with anticipated approval at the CGPM meeting on 13-16 November 2018, and implementation planned for World Metrology Day on 20 May 2019.

The current status of the determination of the value of the Avogadro constant was then described, and Dr Güttler noted that Kibble balance results had begun to merge, with good agreement of new NMIJ and NRC values in 2017, but subsequent results from IAC, NIST, and LNE appeared to be in less good agreement and complicated the issue. However, meta-analysis by CODATA using $k = 2$ confirmed agreement of the results and the value was fixed by CODATA at $6.022140758(62) \times 10^{23}$ mol^{-1}, noting that any new results would not have any significant effect on the fixed value. Dr Güttler commented on the strong collaboration with Japan, China, and Canada on achieving this goal and noted the contribution of Dr Vocke (NIST), whose methodology was key to the molar mass value assignment.

Dr Güttler continued by discussing the CCQM position on the CCU recommendation and noted that full consultation with CCQM has not been possible on all issues over the past year. He remarked that CCQM does not have the same requirements for the accuracy as the CCM and that while mass determinations are of central importance in quantitative chemistry, continuity conditions imposed on redefinitions of SI base units have ensured that the molar mass constant M_u is effectively still 1 g/mol with a finite, very small relative standard uncertainty ($< 1 \times 10^{-9}$). This is approximately thirty times smaller than the relative uncertainty achievable in the most accurate realization of the mole and several orders of magnitude smaller than the uncertainties in examples of more common realizations of the mole.

Following consideration and discussion of the IUPAC recommendation for the redefinition of the mole, and a recommendation for a revised wording of the definition of the mole to the CCU, Dr Güttler presented the wording for the mole definition:

"The mole, symbol mol, is the SI unit of amount of substance. One mole contains exactly 6.022 140 76×10^{23} elementary entities. This number is the fixed numerical value of the Avogadro constant when expressed in the unit mol^{-1} and is called the Avogadro number.

The amount of substance, symbol n, of a system is a measure of the number of specified elementary entities. An elementary entity may be an atom, a molecule, an ion, an electron, any other particle or specified group of particles."

Dr Güttler noted that the new wording, with the unit defined first followed by the definition of quantity, is in line with other historical definitions. He commented on the positive acceptance of this definition in the community, and the good bridge between redefinition of the mole and the teaching of chemistry. Dr Brown commented that the final definition is an excellent outcome and the fact that the CCU made an exception shows how far chemistry has come within this community. Dr Milton suggested that the 'mise en pratique' for the mole be edited to include: the value of the uncertainty of the Avogadro constant prior to re-definition and the values, after redefinition, of the uncertainty in the molar mass constant and the difference between the molar mass constant and its former value (1 g/mol).

6. REPORT FROM THE CCQM TASK GROUP ON ISOTOPE RATIO MEASUREMENTS AND STANDARDS

Dr Mester began by reviewing the mandate of the task group, which was to study the metrological state of isotope ratio measurements and formulate recommendations to the CCQM regarding potential engagement in this field. He then described the timeline of the task group's activities, with an initial meeting in October 2017 held at VSL in Delft, Netherlands, and a second meeting held earlier in the week at BIPM that attracted 36 participants. A first draft report was circulated to stakeholders in January 2018 with the final report submitted to the CCQM President in February 2018. He briefly summarized the report, which was a comprehensive survey of NMI capabilities in this area, with 25 NMIs responding. The survey confirmed that approximately 75 % of responding NMIs have isotope

ratio measurement capabilities, whilst the majority of the remaining NMIs plan to invest in this area over the next seven years. Major research themes across the NMIs focussed on food, atmospheric monitoring and reference material development.

Dr Mester continued by summarizing the rationale for the creation of a new CCQM working group, noting that uncertainty and traceability of isotope ratio measurements are still actively debated and the delta annotation for light elements has been accepted as the only traceability exception within the CIPM MRA. He also noted the use of high-precision isotope ratios in the realization of several SI units and the determination of fundamental constants. While NMIs have invested heavily in developing isotope ratio capabilities, demonstration of equivalency of capabilities between NMIs has been limited. As a result, Dr Mester confirmed that the recommendation of the task group was to establish a CCQM working group dedicated to isotope ratio measurements.

He then reviewed proposed terms of reference:

i. To progress isotope ratio measurement science and support measurement applications in this field by providing a permanent forum for NMI/DIs to exchange information, advance capabilities and demonstrate comparability;

ii. To carry out Key Comparisons, and where necessary pilot studies, to critically evaluate and benchmark NMI/DI claimed capabilities and competences for isotopic ratio measurements in pure materials and complex samples providing demonstrable evidence of the validity and international equivalence of measurement services offered to customers.

iii. To provide isotope ratio characterization and data treatment support to other WGs of the CCQM.

iv. To act as a focal point for stakeholder engagement with the user community, expert laboratories and other stakeholders;

v. To define calibration hierarchies and promote the use of SI traceable measurements where applicable

vi. To develop and then operate a process which enables the CCQM to review and update the list of reference materials that meet requirements to define or realize isotope ratio delta scales, and to carry this out in close cooperation with stakeholders.

Dr May opened the discussion by reminding members that CCQM has been performing isotope ratio measurements for years, but spread out across different WGs. He stated that the CCQM can continue to do that or we could have a dedicated group not just focusing on compatibility but advancing isotope measurement science, and welcomed comments from the floor. Dr Fajgelj commented that this area has historically been linked to IUPAC, so care should be taken to avoid duplication between these two groups. Dr May responded that the CCQM will differentiate itself with a focus on metrological aspects of isotope ratio measurements. Dr Mester added that IUPAC's role is a CODATA-type role, where our group will focus on metrological aspects. Dr Wielgosz noted that MoUs are typically established with other organizations in this type of situation, but we are lacking an MoU in this area with IUPAC. Dr Sargent commented that the proposed terms of reference relating to promoting the use of SI traceable measurements is a key issue and that more prominence should be given to it with more specific goals. Dr May agreed and noted that since an SI traceability exception had been requested, eliminating the need for it as soon as possible will be major step forward. Dr May then raised the question of whether to defer the decision on the creation of a new

WG for the next CCQM President, or to present a case at the next CIPM meeting in June 2018, which would require quick action. Dr Ellison commented that the report was very comprehensive, and suggested to move this forward now, making slight changes to the terms of reference if needed. Dr Güttler added that if there is no disagreement, then we should proceed now, and confirmed his support for emphasis on SI traceability. Dr Li also pledged her support for moving forward now with the creation of the working group. Dr May confirmed Dr Mester's willingness to serve as the working group Chair, and they agreed to work together to seek approval for the new working group from the CIPM in its June 2018 meeting.

7. REPORT FROM THE CCQM TASK GROUP ON METHOD DEFINED MEASURANDS

Dr Andres provided an update on the task group and began by reviewing its membership, which consists of himself, R. Brown, S. Ellison, H. Emons, B. Güttler, H. Li, Z. Mester, J. Morrow, and R. Wielgosz. He then reminded attendees of the goal of the group, which was to develop a position paper describing the criteria used to decide which method-defined measurands and measurement services were in the scope of activities covered by the CCQM. Dr Anders referred to clause 3.7 of ISO 17034:2016 that defined an operationally defined measurand as "a measurand that is defined by reference to a documented and widely accepted measurement procedure to which only results obtained by the same procedure can be compared". Dr Andres then presented the proposed criteria developed by the Task Group for decision making:

a. Realization of the method-defined measurand requires traceability for a quantity within the remit of the CCQM.

b. The method-defined measurand must be internationally agreed.

c. The method-defined measurand must be a stable reference point in time.

d. The method, as applied at the relevant NMI or DI, is considered as the highest metrological reference within a calibration hierarchy.

e. No higher level calibration hierarchy or method-independent definition for the measurand is already in existence.

He then assessed the practicality of the criteria by applying them to a series of example measurands. Measurands such as pH, particle number concentration in air and catalytic activity of enzymes fulfilled all criteria, suggesting they were clearly within the scope of the CCQM. By contrast, measurands such as protein content by ELISA, amount of TOC, total protein content in food/feed as measured by Kjeldhal method had more than three criteria that were not met, so would be out of scope of the CCQM according to these criteria. More challenging cases would be a measurands such as specific surface area defined by the Brunauer Emmett Teller (BET) method and mass fraction of moisture in grain, where one or two criteria are not met. Specifically, the BET method is not the highest metrological reference, while moisture in grain is not a stable reference point in time and not the highest metrological reference. Dr Andres noted that in these cases it is not clear whether they fall within the scope of CCQM or not.

Dr May thanked the Task Group for their efforts and opened the floor to comments on the proposed criteria. Dr Brown commented that the criteria are quite robust and that there is distinction between

SI-traceability and expressing results in SI units. So if the criteria are met, ordinal quantities such as octane level or dead/live cells will not be ruled out. Dr Brown then remarked that for BET, it is not clear whether the method as implemented at NMIs is higher level than those providing services. Dr Andres responded that in some areas it is mandatory that certified materials need to be used to calibrate the BET method. Dr Brown responded that that is a local and legal requirement but not part of the ISO procedure.

Dr May then commented that since some method defined measurands fall under other organizations' scope, such as ISO, should CCQM be duplicating effort. Dr Mester noted that there would be only value in engaging in BET comparisons if we are feeding information back to ISO to improve the method. Dr May added that value would be derived if ISO came to CCQM and asked us to provide traceability, but that these initiatives usually come from the bottom up. Dr Fajgelj commented that for moisture content in grain, the measurand is not well defined and should be based on constant mass. Dr Brown added that even defining moisture as water is problematic, as different temperatures can be used for drying, with the measurand changing at the different temperatures.

Dr May concluded the discussion by inquiring if any criteria should be eliminated. Dr Máriássy remarked that we have to be careful with our wording as the measurand is what we intend to measure not what we measure. Dr Ellison proposed adopting the criteria as defined now and review in a few years to determine if they were successful. Dr Andres responded that the criteria are not yet finalized and should be thoroughly tested for other measurands. Dr May asked if next year's meeting would be reasonable timeframe for a final report and Dr Andres agreed.

8. OUTCOMES OF THE CIPM MRA REVIEW

8.1. Update on the MRA review

Mr Henson provided an update on the CIPM MRA review. He noted that relative to other CCs, the CCQM has no significant gaps in addressing major recommendations from the CIPM MRA *ad Hoc* WG on Implementation. In addition, the CCQM is ahead of the wave as the CCQM's most recent strategic plan already reflects new objectives defined by the CIPM for the CCs. Mr Henson commented that the broad scope claims are one of the most complex issues facing the CIPM MRA review, in trying to decide what is covered and striking the right balance. He added that the MRA revision did not redefine CMCs and the original definition remains. He commented on the risk-based approach of reviewing CMCs, where the effort in reviewing should reflect the measurement challenge covered in the CMC. Mr Henson concluded his presentation by noting that MRA processes could be more transparent, and that if possible, it would be beneficial to have any CCQM-specific MRA documentation available for stakeholders.

Dr Wielgosz opened the discussion by noting that the CCQM will soon have a large turn-over in its WG Chairs, and asked how plans are proceeding for capacity building and training of new Chairs. Mr Henson responded that there is potential support from NIST on MRA training, and courses offered by RMOs. Dr Milton commented that training has been successful for candidate RMO TC Chairs, but we need to consider training for WG Chairs. Dr May noted that NIST's decision to fund the CBKT programme was for people to get exposure to the MRA in developing NMIs, and

suggested that it should remain that way. He added that other mechanisms of funding should be sought for established NMIs to receive training.

8.2. Plans for BIPM KCDB 2.0

Dr Picard presented an update on the revision of KCDB 2.0. She began by reviewing the background of the project, which was driven by recommendations from the Working Group on the Implementation and Operation of the CIPM MRA. Dr Picard highlighted the main objectives of the project: web-based CMC submission and review, better search capabilities, the ability to track comparisons, and user-friendly web support. She then described details of the web platform to be accessible via user accounts, with sequential access for the RMO, JCRB, and KCDB, supporting both intra- and inter-RMO reviews. Other improvements to the CMC review procedure were then described, such as the elimination of CMC "batches", direct links to degrees of equivalence (DoE) of comparisons, and the possibility for risk-based evaluation. Dr Picard then discussed statistical tools within KCDB 2.0 with customized data with pre-programmed graphs. She commented that the issue of how to deal with broad-scope CMCs is still under discussion and that there will be no harmonization of units such that service providers can decide based on client needs. In addition, the "CMC Analyte Group" will be removed and there will be the possibility to add a table that can sort, filter, or list an equation, but will not be searchable. Dr Picard concluded by reviewing the timeline for implementation, with partial delivery planned for November 2018 and full implementation proposed for 2019.

Dr May noted that the release of an early version of KCDB 2.0 coincided with timing of the General Conference on Weights and Measures (CGPM). He then inquired if migrating of data would occur in blocks as previously mentioned. Dr Picard responded that it has yet be decided if data will be migrated in blocks or gradually. Dr Brown asked for clarification of Dr Picard's statement in her presentation that "we are continuing to use our own units". Dr Wielgosz replied that during the last meeting the CCQM debated whether all units should be harmonized, but it was decided that this should be user-defined.

9. CONSULTATIVE COMMITTEE GOVERNANCE AND OPERATIONAL ISSUES

9.1 Member and Observer Status in CCs, Privileges and Obligations of Liaison Status, and CCQM process for reviewing applications for Members and Observers

Dr Wielgosz and Dr Milton guided a discussion that was focused on proposed revisions to the CIPM-D-01 document that governs CCs. Dr Milton noted several potential improvements that better reflect the current state of CCs. He summarized three objectives that CIPM had developed for CCs, noting that CCQM is very well-positioned to meet these objectives:

- to progress the state-of-the art by providing a global forum for NMIs to exchange information about the state of the art and best practices,
- to define new possibilities for metrology to have impact on global measurement challenges by facilitating dialogue between the NMIs and new and established stakeholders, and
- to demonstrate and improve the global comparability of measurements. Particularly by working with the RMOs in the context of the CIPM MRA to:
    - plan, execute and monitor KCs, and to
    - support the process of CMC review.

Dr Milton continued by reviewing CIPM terms governing member, observer, liaison, and guest status, and noted that the CIPM wishes to promote participation in meetings and that all types of attendees should be able to speak in CC meetings. Dr Milton also noted that the CIPM reaffirmed that CCs should operate by consensus, and that document CIPM-D-01 should be updated so as not to make any reference to voting taking place in CCs.

Dr May noted that CC Presidents can invite a limited number of guests as individuals from Member State institutes for one year, but these are not open invitations. Dr Kaarls commented that we have voted in the CCQM in the past, but it was not always productive and agreed with the CIPM's decision that CCs should operate on a consensus basis. Dr Klich asked what the difference is between observer and member status. Dr Milton responded that it only defines how you are invited to the meeting and there should be no difference during the meeting.

9.2 CCQM Working Group contact persons

Dr Wielgosz led a brief discussion on the initiative to renew the working group contact lists as current lists are not fully up to date. Due to turnover of staff and reorganization within NMIs, it has been determined that simply adding the last person that attended a particular WG meeting to contact lists is not the most appropriate approach. Dr Wielgosz confirmed that each WG website now has a list of contacts with up to two representatives from each NMI. The WG websites also contain a link for NMI Directors to nominate WG contact persons. Dr May offered his support for this initiative and encouraged NMIs to keep these lists up-to-date.

9.3 Open access CCQM and CCQM WG documents

Dr Wielgosz presented a draft policy for CCQM open access and documentation. This issue came to the forefront as the CCQM has the smallest number and percentage of open access documents of any of the Consultative Committees. Dr Wielgosz noted that while many of the CCQM documents refer to studies that are ongoing, with information not to be made publicly available, there are other documents which could be made available and would raise the profile and understanding of CCQM activities. The following policy on open access documents was proposed:

> From and including the 24th meeting of the CCQM and its WGs onwards, it is proposed that the following categories of documents shall be open access when posted on the BIPM website:
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> 1. Meeting agendas
>
> 2. Workshop and Symposium presentations
>
> 3. Policy and guidance documents (for example related to CMCs, uncertainties, WG guidelines etc.)
>
> 4. Decisions and Actions from CCQM Plenary Meetings
>
> Documents falling into the categories above will be made open access unless there is a request from the WG Chair, approved by the President, not to do so.

Dr Brown noted that this is a good first step and asked whether this now brings us in line with other CCs in terms of amount of open access information available. Dr Milton responded that it still falls short of most other CCs. Dr Ellison commented that is seems onerous to require Presidential approval to exclude documents from open access, and should consider adding "unless commercially sensitive" to the policy statement, which should be made clear by presenters before they present. Dr May reaffirmed that the default position will be open access. Ms Parkes commented that it is not clear whether it only applies to CCQM workshops. Dr Wielgosz confirmed that it also applies to WG documents such as agendas, policy documents and workshops. Ms Parkes added that sometimes the NAWG has unpublished results or information about studies that might not be appropriate in NAWG agendas. Dr May responded to request an exemption in these cases, but that agendas should typically be free of sensitive information. Dr van der Veen expressed strong support for this policy, as public funds are supporting CCQM activities, so there is an expectation for a reasonable number of documents to be open access. Dr Kaarls commented that we are working with many stakeholders that sometimes have expectations of confidentiality. Dr Güttler commented that in the cases of workshops such as with WADA, there will be information that cannot be shared. Dr Wielgosz confirmed that all BIPM-WADA documents are restricted access and this was agreed with WADA before the organization of the workshop. Dr Mester remarked that if the meeting agendas are posted then why not the meeting outcomes. Dr Wielgosz responded that we could, but we do not have a system in place in the WGs to provide clean reports suitable for posting. Dr Ellison asked for confirmation that only "agreed upon" policy and guidance documents will be posted; Dr Wielgosz confirmed this. Dr Mester commented that there is no clear distinction between the open and closed working areas. Dr Wielgosz confirmed that it exists but the open area is minimal so can go unnoticed.

Dr Wielgosz suggested that the CCQM agree on the four types of open access documents, have a Presidential decision now, and evaluate compliance of the WGs at the next meeting, and reassess at that point whether further authorizations from the President are necessary to ensure that documents are posted as open access. Dr May responded that he will only support it if there is a consensus between WG chairs on sharing this information. Dr Sargent suggested the addition of a column to the regular BIPM web submission form to differentiate whether a document will be open access. Dr Ellison commented that doing this retrospectively will be difficult as the permission of all presenters should be sought. Dr May agreed in principle, and confirmed that all new presenters will be notified of our policy in the future.

9.4 Terminology for Comparisons in CCQM

Dr Wielgosz described the harmonized nomenclature that has been proposed by the CCQM to describe types of studies: Core Key Comparisons (Track A); Specialized Key Comparisons (Track C); and Pilot Studies (Track D). In addition, comparisons can be carried out with samples sent from coordinating laboratory to participants (Model 1) or samples sent from participants to coordinating laboratory (Model 2).

Dr Ellison noted that some WGs make Track A studies mandatory while others do not, so this should be clarified. Dr Wielgosz responded that different Working Groups had developed different practices. This was described in the 'implementation section' of the document on nomenclature he had presented (CCQM/18-19), and a further reason why it was important that all policy documents were open access, so that it was clear to NMIs what is considered mandatory. Dr May suggested that the "Track" nomenclature be removed since it is redundant with the study type also listed (for example core, specialized, etc.). Dr Brewer expressed support for the Track nomenclature since it is embedded into various documents within many WGs. Dr Mester commented that the Track nomenclature will facilitate internal communication but will not be appropriate for outside communication. Dr Ma added that CCQM document D-05 makes it clear what a key and pilot study are, so we do not need the Track nomenclature. Dr Brown suggested that both naming schemes could be used in parallel until people are comfortable with it, then the Track nomenclature will likely fade away with time.

9.5 Revisiting the publication of results in KCs and PSs

Dr May led a brief discussion on the publication of results in KCs and PSs, centred on the occasional practice that had arisen in some WGs of allowing NMIs to publish results from different methods in the same comparison. Dr May reiterated his concerns regarding this practice, commenting that it should be no different than developing a CRM, where you report a single value and not different values for each method. Dr May thus confirmed the one result per NMI rule for key comparisons.

10. CCQM STRATEGIC PLANNING DOCUMENT AND PROCESS (2017-2026)

Dr Wielgosz presented a summary of the CCQM strategy document for the period 2017-2026 that had been finalized and published on 18 January 2018. The document had been restructured to fit the three objectives established for Consultative Committees by the CIPM, notably; to progress the state of the art of measurement science; to reach out to new and established stakeholders; and to demonstrate the global comparability of measurements.

Sixteen workshops had been organized by the CCQM WGs in the period 2012-2017, covering a wide range of subjects and providing a forum for exchange of information on technical activities, and this was set to continue. In addition the CCQM members had listed twenty five papers published in peer review journals related to twenty one CCQM comparisons as examples of the research and development activities stimulated by the comparison work in the same period.

The strategy document described the CCQM's continuing efforts to streamline the comparison and CMC process, and detailed the strategies developed by the various working groups to develop core comparison models, which would allow a limited set of comparisons to support a broad range of CMC claims. The current models allowed the CCQM to predict that it would be running 16 to 17 comparisons a year, which was a 25 % reduction on the estimated numbers from the previous strategy document, attesting to the progress and impact of the core comparison approach.

Dr Wielgosz went on to explain that the current document described in greater detail RMO activities and future plans, and that the relationship between activities in the CCQM and the RMOs was expected to have even greater emphasis in the years to come.

He concluded by highlighting the eleven case studies that had been developed by CCQM WGs, which describe the impact and long-term outcomes of selected key comparisons in the following sectors: health care; environment; food safety; energy; advanced materials; and fundamental metrology and the SI.

11. REPORTS FROM THE CCQM WORKING GROUPS

11.1 CCQM WG on Key Comparisons and CMC Quality (KCWG)

Dr Andres provided an update on the KCWG activities, noting that he was presenting on behalf of Dr Sin who could not attend and sent her regrets. Dr Andres began by highlighting the growth rate for the chemical and biological CMCs, noting that CCQM activities support over 6000 CMCs. Dr Andres then stated that the meeting of the KCWG had taken place prior to the CCQM on 14-15 April, and he noted that this annual face-to-face meeting is one of the key components of the inter-regional review of chemistry CMCs. In 2018 a total of 361 CMCs were submitted, of which 299 CMCs were new claims. He then reviewed the membership of the KCWG and thanked all members

for their efforts over the last year. He listed CCQM CMC metrics relative to other CCs, noting that the CCQM boasted the best CMC/KC ratio at 23 for the conventional CCs (excluding the CCTF).

Dr Andres continued by commenting that while specific claims continue to dominate, a small but growing number of broad claims are being submitted. He highlighted a broad scope claim that LGC submitted for organics in soil and sediment that was sent back to OAWG for further clarification. The OAWG recommended that it be split from two to three unique CMCs and have compound classes (PAHs, pesticides, etc.) listed, as opposed to simply polarity and molecular weight ranges. Dr Andres commented that this could be considered as a model going forward for broad claims for organics.

Dr Andres concluded his presentation by reviewing two KCWG recommendations to the SPWG and CCQM:

1. All CCQM WG guidelines on CMC review and comparisons to be made available as open access and referenced in KCWG guidance document.
2. Only KCDB published reports to be used for CMC review.

Dr Wielgosz opened the discussion by commenting that the system of peer review is well taken care of within RMOs, as reported during the KCWG meeting, and peer review evidence can be used in CMC review. Dr May reminded members that Draft B reports can be used to support CMC claims, where numbers should be finalized and be identical to those published in the final report. Dr Wielgosz noted frustration within the KCWG that comparisons were being reported as ready for supporting CMC claims, but with no Draft B report available. Dr May suggested that the KCWG's recommendation 2 (above) should be modified to specify only KCDB published reports and official Draft B reports. Dr van der Veen commented that if we allow Draft B reports for review, we need a process in all WGs to generate official Draft B reports and make them available to the KCWG. Dr May added that we need quality control to ensure what we are calling Draft B reports are uniform across all WGs. Dr Mester followed that according to the CIPM MRA, a Draft B report is an official document, so is no longer confidential, and therefore we need a depository to make Draft B reports available. Dr Wielgosz responded that the CIPM MRA states that Draft B reports can be made public with the exception of the KCRV values, which therefore presents a problem. He noted that often when a problem arose this was because the Draft A reports were not completed before the initial discussion of results, and that WGs should be vigilant to avoid this.

Following a request from the President, Dr Wielgosz summarized the discussion by describing two possible ways forward for the CCQM: either, (a) make Draft B reports available as open access WG documents, noting that these would include the agreed KCRV values; or, (b) reduce the time between Draft B and Final reports to a minimum, which would require Draft A reports to be ready in a timely fashion. Dr May confirmed the CCQM practice of continuing to use Draft B key comparison reports to underpin CMC claims, noting that only properly completed reports could be used (following the CIPM MRA guidelines), which contained the agreed KCRV and calculated degrees of equivalence. The reports would need to be accessible on the BIPM website to enable CMC review, and a written policy for this would be established and included in the KCWG and other WG guidelines.

11.2 CCQM WG on Gas Analysis (GAWG)

Dr Kim provided an update on the GAWG's activities and began by summarizing all current and planned studies. Dr Kim then went on to describe the cascading CCQM-K111 study on propane in nitrogen involving a number of RMO regional key comparisons, and noted that results have been published in the KCDB. The results of CCQM-K112 on biogas were also presented. Dr Kim then summarized CCQM-K116 results on water vapour in nitrogen coordinated by NPL, currently at the Draft B stage. Finally, Dr Kim showed results for CCQM-K121 on terpenes in air coordinated by NIST, and also at the Draft B stage.

Regarding comparisons with measurements currently under way, Dr Kim provided an update on CCQM-K117 on ammonia in nitrogen coordinated by VSL with preliminary results planned for December 2018. Similarly, CCQM-K118 on hydrogen enriched natural gas coordinated by BAM is in progress with the Draft A report planned for December 2018. The timetable for completion of CCQM-K120.a&b coordinated by the BIPM, on ambient level CO_2 was then presented, with the Draft B report planned for July 2018. Coordinated by KRISS, CCQM-K41.2017 on H_2S in nitrogen has been delayed, with a Draft A report now planned for after April 2019. Dr Kim described CCQM-K137 on NO in nitrogen, coordinated by BIPM, stating that a Draft A report was planned for June 2018. He then provided a report on CCQM-K150/P189 on particle number and charge concentration, noting that Draft A was due for August 2018 and the Draft B report was planned for February 2019. Dr Kim then reviewed CCQM-K74.2018 on NO_2 in nitrogen, with cylinders to be shipped in May 2018, and CCQM-K10.2018 on BTEX with cylinder shipment in May to June, 2018.

Planned KCs for 2019 include: a Track A (CCQM-K3.2019) on automotive exhaust gases CO, CO_2, C_3H_8, and O_2 in nitrogen coordinated by VSL; CCQM K68.2019 on Ambient N_2O coordinated by BIPM and KRISS; and CCQM K26b.2019 on SO_2 300 nmol/mol in nitrogen coordinated by NPL. Dr Kim concluded his presentation by noting that the next GAWG meeting will take place 8-9 October 2018, at CENAM, with a workshop to be held at CENAM on 10 October 2018.

Dr May commented that in some of the KCRV graphs, more than one value was provided for each NMI. Dr Kim clarified that the BIPM performed multiple methods to determine candidate KCRVs for Model II comparisons, to demonstrate that the results were method independent, but in the final report only one method is used for KCRV determination.

11.3 CCQM WG on Inorganic Analysis (IAWG)

Dr Sargent provided a spirited update on the progress of activities within the IAWG, and began by reviewing the meetings that occurred over the year, including the WG meeting in Turin (Italy) in September/October, and a joint meeting with the PAWG earlier in the week at the BIPM. Dr Sargent noted significant progress in the development of the IAWG strategy, by completely revamping core capability descriptions and better defining broad-scope CMCs. He remarked that activities were now more closely aligned with stakeholder needs.

Dr Sargent continued by reviewing key comparisons published since April 2017, namely CCQM-K108.2014 and P171 on arsenic in brown rice flour and CCQM-K139 and P173 on elements in human serum. He provided a graphical overview of all key comparisons and pilot studies in progress, and noted that all studies are optional to NMIs, but a compulsory benchmarking comparison is held every two years. At the Draft B report stage, Dr Sargent commented on CCQM-K128 Heavy Metals and Organo-Tin in Leather Powder. He also reviewed several comparisons at the Draft A stage, including CCQM-K143 and P181 on the preparation of copper calibration solutions. This was a Model 2 comparison, where copper calibration solutions were prepared by NMIs and analysed by NIST with a high performance ICP-OES method, with further confirmation analysis to be performed at PTB. Dr Sargent noted the results were satisfactory as they confirmed the claim that NMIs were able to prepare calibration solutions within the measurement uncertainties they were being provided at. Dr Sargent then described new comparisons proposed, namely seleno-proteins in serum by NIST and elements and Sr isotopes in rice by NMIJ and KRISS. He also reviewed results from CCQM-P160 derived from methodology developed in the Avogadro project, including application of the PTB "virtual element" technique.

Dr Wielgosz commented that for CCQM-K149 on nitrogen mass fraction in dry milk powder, good agreement was achieved only because a large uncertainty was placed on the KCRV, and it should be explained how this is derived. Dr Haraldsson commented that the y-axis scale is very small so the results actually are in reasonable agreement. Dr van der Veen disagreed, noting that many combinations of results are inconsistent and the uncertainties submitted are too small to explain the dispersion in the data. Dr Sargent responded that it was agreed long ago that we would not calculate pairwise DoEs. Dr Wielgosz replied that further thought should be given to how the comparison results would be used to underpin CMCs, and whether the KCRV uncertainty now defined the smallest uncertainty that could be claimed in CMCs, as stating smaller uncertainties would not achieve compatibility of measurement results. Dr May asked whether the comparison was included in the strategic plan of the working group, and the justification for this with the finite resources available. Dr Sargent responded that the IAWG's approach for selecting future key comparisons is based on a core capability approach and a survey has identified where main interests are. He added that core capabilities only apply to the elements, and other measurements such as isotope ratio are considered specialized. The aim is to have three comparisons per year, split between core and specialized.

11.4 CCQM WG on Organic Analysis (OAWG)

Dr Mackay gave a presentation on progress within the OAWG and began by reviewing comparisons that had been published in the KCDB since the April 2017 meeting, which included CCQM-K102 on PBDEs in sediment and CCQM-K55.d on folic acid purity. She noted that CCQM-K55.d completed the Track A core competency series for organic purity. Dr Mackay then described a revised high-purity organics measurement space, where the high molecular weight quadrants for low- and high-polarity were combined, citing that the effects of the much larger molecules outweighs any effects of polarity in terms of the complexity of the measurements. Comparisons at the Draft B stage were then reviewed, such as the Track A CCQM-K78.a and CCQM-P121.a on the mass fraction of

amino acids in solution and CCQM-K131 and P168 on PAHs in acetonitrile. Also at the Draft B stage was CCQM-K141 and P178 on enrofloxacin and sulfadiazine in bovine tissue, where a series of follow-up experiments by NRC and NMIA failed to determine a key method parameter that explained the variability in the results and instead indicated a complex mixture of issues such as calibration standard stability versus extraction efficiency. Dr Mackay then commented on the Track C CCQM-K138 comparison on measuring aflatoxins in dried fig, and noted that these were very challenging measurands given the low mass fractions of (0.08 – 9.0) µg/kg. She expressed concerns regarding some of the aflatoxin calibration solutions used for this study in that they did not meet traceability requirements of the CIPM. For example, the BCR materials were assigned by consensus and not directly by NMIs and the capability to do this was not supported by CMCs. Dr Mackay also noted that large uncertainties in the DoEs for this study (with relative uncertainties of 50 % in some cases) need to considered when evaluating CMCs in this space.

Dr Mackay continued by describing the OAWG's model to assess core competencies through a 10-year plan, with CCQM-K148.a on bisphenol-A mass fraction and CCQM-K146 on PAHs in olive oil planned for 2018. She then reviewed a broad-scope CMC claim that was recently approved, citing it as an excellent example of what type of evidence is needed, and thanked LGC for their presentation on this topic in the WG meeting. She commented that in 2019 all pure organic CMCs will be reviewed and encouraged NMIs to move to broader claims, noting that the OAWG was preparing guidelines on evidence required for different breadths of CMCs to achieve greater consistency in formats of broad CMCs. Dr Mackay then concluded her presentation by reviewing a comprehensive suite of OAWG guidance documents and templates, and thanked Dr Katrice Lippa of NIST for leading the development of these documents.

Dr May began by commenting that Dr Mackay's presentation was a good model for use of our new presentation template, as it put work into context and provided instruction to KCWG on the review of OAWG CMCs. Dr Milton commented that broad-scope CMCs are of great interest, making this guidance document available to other CCs can let us be very influential. He then inquired if there were narrow-scope CMCs withdrawn by LGC and replaced by the broad-scope CMC presented and Dr Mackay confirmed this was indeed the case.

11.5 CCQM WG on Electrochemical Analysis and Classical Chemical Methods (EAWG)

Dr Máriássy presented a report on the EAWG and noted that their WG meeting earlier in the week attracted 21 participants from 15 institutes. The WG was established in 1998, then underwent name changes in 1999 and 2017. He then provided an overview of completed studies since 1999, subdivided into three main categories: pH, electrolytic conductivity, and coulometric assays. Completed and published since the last meeting was CCQM-K36.2016 on the determination of electrolytic conductivity in aqueous solutions coordinated by PTB. Dr Máriássy then discussed comparisons at the Draft A stage, including CCQM-K18.2016 coordinated by NIST on the determination of pH of a carbonate buffer at a nominal value of 10. One outlier was observed and the DerSimonian-Laird (DSL) random effects model was used for calculation of the KCRV. Also at the Draft A stage was CCQM-K34.2016 on amount content of acid in solid potassium hydrogen phthalate. There were a series of low-level impurities found, namely Na, Ca, Rb, and Fe (all

<40 mg/kg). Reasonable agreement was achieved, although INM who are in early stages of building capabilities in this area was removed as an outlier; the KCRV in this case was based on the median.

Dr Máriássy continued by reviewing planned comparisons for 2018 to 2021, highlighting CCQM-K152 and P192 on potassium iodate with samples due for dispatch and results due in February 2019. Also planned for this year is CCQM-K73.2018 on amount of H^+ in hydrochloric acid, with samples to be dispatched in mid-November and results due in February 2019.

Dr Máriássy then reviewed stakeholder engagement activities within the EAWG, consisting of participation in the Joint Committee on Seawater. He also mentioned a proposal to create a task group to deal with establishing traceability for pH measurements in seawater, with currently six members interested. Dr Máriássy then covered issues arising from the WG to be raised with CCQM, noting the update of the EAWG guidance document and the advantage of having E_n and U_r in same graph of the report cards. He also noted that pH should perhaps be included in discussions of method defined measurands.

Dr Wielgosz commented on the discussion point raised in the presentation of whether to organize a EURAMET SC versus a CCQM key comparison for conductivity, stating that if other RMOs are going to want to link to this comparison at a future date then is should be performed within the CCQM, but if it remains self-contained then it can be coordinated by EURAMET. Dr Máriássy confirmed that in the short term there will be no link to other RMOs. Dr May commented that when we agreed to change the WG name, new terms of reference were to be developed. Dr Máriássy responded that the terms of reference have already been changed in the strategy document. Dr Wielgosz commented that similar to the GAWG, EAWG is completing several repeat studies, and asked whether there were any general trends observed for how the repeat KCs compare to the originals. Dr Máriássy responded that results tend to be similar as there are new participants, with up to 50 % in some cases, and the repeat period is up to 10 years so NMIs can have new staff performing the comparisons. Dr May noted his concern that NMIs' needed to pay more attention to their quality systems if we can clearly see changes in performance due to changes in staff, and further emphasis should be given to continuity of good performance.

11.6 CCQM WG on Surface Analysis (SAWG)

Dr Unger provided an update on the activities of the SAWG and opened with a review of NMI and DI participation, noting new participation from the Danish Fundamental Metrology (DFM) Institute. He then reminded attendees of the scope of the SAWG, which is largely dedicated to measurements for advanced manufacturing. Dr Unger noted that three comparisons had been approved since the last meeting: CCQM-K153 Measurement of Specific Adsorption A (mol/kg) of N_2 and Kr on non-porous SiO_2 at LN temperature (BET), CCQM-P190 Thickness Measurement of nm HfO_2 Films, and a pilot study on measuring the amount of substance in a thin organic layer. He reviewed progress of CCQM-K153 by showing preliminary results and noting that results from INMETRO and NIST were delayed due to technical challenges. He also commented that APMP wishes to perform a supplementary comparison based on this study.

Dr Unger continued by reviewing WG activities that have progressed the state-of-the-art of measurements science. He highlighted a EURAMET project JRP InnaaPart – Metrology for

Innovative Nanoparticles led by NPL and the creation of an *ad hoc* Study Group on quantitative Raman spectroscopy led by NRC. Dr Unger also stated the WG's pilot studies are addressing new and challenging areas and he reviewed development of CCQM-P190, noting that calibration of XPS (IMFP parameter) by traceable XRR works as well as in CCQM-K32.

Dr Unger concluded his presentation by reviewing issues arising from the WG to be raised with CCQM, noting that if CCQM decides to remove the method defined gas adsorption method (BET) from its scope, then a proper exit strategy needs to be developed to satisfy stakeholders. He added that at the given time the specific surface area as measured by the BET method represents the "highest metrological level within the respective calibration hierarchy", a criteria proposed by the Task Group on method defined measurands.

Dr Máriássy commented that for CCQM-K153 it was stated that APMP wants to hold a supplemental comparison, but presumably this would be a linked comparison. Dr Máriássy also noted that for CCQM-K153 there were results shown but it was mentioned that the comparison is still running, in which case results should not be shown. Dr Unger confirmed that the slide will be removed. Dr Wielgosz inquired if a Terms of Reference document has been established for the *ad hoc* focus group on Quantitative Measurements with Raman Microscopy and asked if it should be a task group with a defined task and timeframe instead. Dr Unger agreed and committed to establish Terms of Reference for approval by the CCQM.

11.7 CCQM WG on Cell Analysis (CAWG)

Dr Morrow presented a report on the activities of the CAWG and began by reviewing their charge. She specified that the CAWG was focused on the identification and quantification of cells and cell properties indicative of function as a result of emergent behaviour in complex matrices and mixtures. It was also dedicated to global comparability of cell analytical measurement results through reference measurement systems of the highest possible metrological order with traceability to the SI, where appropriate and feasible.

Dr Morrow continued by defining "emergent behaviour" as novel properties of cells that arise from a collection of constituents that do not themselves exhibit such properties. She followed by stating that cell analysis includes measurements of quantity of intact cells and cell properties indicative of function that are the result of emergent behaviour, and noted that relevant studies will include quantification of cell number or cell components and measures of biological response or function in the context of cell emergent behaviour. Dr Morrow then described the challenges in counting cells due to biological complexity of cells that can differ in size, shape, function, and role in a broader system. She listed a wide range of cell counting needs and methods as proposed by ISO TC 276 with contributions from Dr Sumona Sarkar and Dr Sheng Lin-Gibson of NIST, noting potential synergy between CAWG and ISO TC 276 activities.

Dr Morrow then described the CAWG's Evolving Conceptual Framework for cell measurements, based on a three-dimensional graph with "Property" on the x-axis, "Count" on the y-axis, and "Activity/Function Viability" on the z-axis. She noted that most current work is planned within the x-y quadrant. Outcomes of the fall meeting of the CAWG in Ottawa (Canada) were then reviewed, highlighted by five potential Track D comparison proposals, a final presentation for CCQM-P165,

and a brainstorming session on bioactivity/viability determination. She thanked NRC for providing webinar capabilities for the meeting.

Progress on completed and current pilot studies was presented, and Dr Morrow began by reviewing results of the completed CCQM-P165 study on the quantification of CD34+ cell counts, coordinated by NIBSC, NIST, and PTB. Reasonable agreement was achieved between participants, and it was noted that the volumetric method produces systematically lower CD34 cell concentrations than the Trucount™ values. Dr Morrow also described preliminary results from CCQM-P123 on the number and geometric property of cells adhered to a solid substrate, coordinated by INRIM, NIST and LGC. She noted challenges with uncertainty assessment, for which INRIM has provided a statistician for advice. She then covered an approved pilot study proposal for proliferative stem cell number per unit area proposed by NPL, noting the material has already been characterized through a VAMAS study. Dr Morrow concluded her presentation by describing two proposed papers for the *Metrologia* special issue and she thanked the CCQM and BIPM for their continued support.

Dr May commented on the CAWG's stakeholder engagement and involvement of industrial participants in pilot studies, noting that the CCQM needs to be careful to not be seen as improving market share of any commercial participants. Dr Brown inquired whether one of the topics was chosen for submission to the special *Metrologia* issue. Dr Morrow confirmed they want to submit both. Dr Wielgosz asked if CAWG was ready to update its strategy document and Dr Morrow confirmed that it would be updated soon. Dr Milton commended the CAWG for using the Guest Laboratory Request Form for the approval of commercial participants in pilot studies, noting this is likely to occur more frequently in the CCQM but this should not be interpreted as an advertisement for encouraging commercial engagement. Dr May commented that the biological field is so broad, that perhaps the scope could be reduced to something consistent with measurable characteristics of cells. Dr Milton added that the phrase "but not limited to" suggests you can do anything, and noted than an increase in scope can be requested through this committee. Ms Parkes expressed support for leaving the scope broad, and suggested the focus should be on what the community needs.

11.8 CCQM WG on Nucleic Acid Analysis (NAWG)

Ms Parkes provided an update on NAWG activities and began by thanking NRC for hosting the September 2017 meeting in Ottawa. She described a graphical depiction of the NAWG's measurement space ranging from the chromosome, epigenome, genome, transcriptome, and regulome, highlighting the boundaries in scope with the CAWG and PAWG. Ms Parkes then discussed the strategy for prioritizing studies based on a NAWG member survey, and highlighted the consideration of stakeholder requirements and a broad range of CMCs to support measurement services.

Ms Parkes went on to review completed and ongoing studies, including CCQM-K86.c and P123.4, on measuring copy number ratio of modifications in two rapeseed materials, where the high oil content presents a significant technical challenge for the extraction. The *Brassica napus* L. materials included a genetically modified DG-073496-4 rapeseed powder from JRC, and a GT73/RT73 modified material from NRC Canada. The KCRV was agreed upon at the fall meeting and the Draft B report is in preparation. In addition, she noted agreement on the following measurement statement for the study: "Quantification of the ratio of the number of copies of specified intact sequence fragments of a

length up to 150 nucleotides following extraction from a high oil/fat matrix with a copy number ratio from 0.001 to 1.0". Ms Parkes noted that as extraction from plant material is more challenging than for other food matrices, the study provided support for ratio determination in a broad range of high oil/fat materials.

Ms Parkes then reviewed the CCQM-P184 study coordinated by LGC and NMIA, designed to support SI-traceable measurement of copy number concentration and fractional abundance of a biologically-relevant mutation (SNV or INDEL) in a buffered solution. Excellent agreement for the BRAF material (intact DNA) was achieved, while much poorer agreement was observed for EGFR (sonicated DNA). Therefore, this study demonstrated the strong effect of DNA integrity. Ms Parkes then presented a proposal for a pilot study on RNA copy number in HIV-1, where the aim is to evaluate candidate primary reference measurement procedures for value assignment of RNA reference materials without calibration by RNA reference materials, to be coordinated by LGC with contribution by NIBSC.

Engagement activities for NAWG were then described, including a workshop coordinated by NAWG on Digital PCR as a Reference Measurement Procedure, and a webinar with an instrument vendor (Thermo). She also discussed linkages with ISO/TC276: Biotechnology. Ms Parkes then discussed issues arising within the NAWG and she commented on the resource implications of study coordination and encouraged greater load sharing from NMIs. She also described an incident where a study participant appeared to have submitted results obtained through a contract laboratory, noting that CIPM MRA requirements are such that NMIs and DIs must submit their own results. Ms Parkes concluded her presentation by confirming the next meeting of the NAWG is to be held in Chengdu (China) on 8-9 October 2018.

Dr May asked how long will it take to complete the CCQM-K86.c report such that CMC claims can be submitted. Ms Parkes responded that the report would be completed by the next meeting. Dr May commented that he will contact the study participant who submitted study results contracted to another laboratory, which was not in the working practices of the CCQM. Dr Wielgosz noted that this was for a pilot study. Dr Mester suggested that before sending a letter, proper consideration should be taken of the practices stated for sub-contracting within the CIPM MRA. Dr May responded that nevertheless, in order to ensure transparency, disclosure and discussion prior to the study, would have been the appropriate route to take. Dr Kaarls commented that JRC has been active in NAWG and asked if they are continuing. Ms Parkes confirmed that the NAWG was one of two groups that she believed the JRC would continue to participate in. Dr May commented that he will consult with JRC Directors to enquire on their continued participation in CCQM activities. Ms Parkes commented that the reporting schedule for CCQM-K86.c would continue as planned and would be completed by the NRC. Dr Wielgosz commented that for the HIV-1 study, a key comparison would require a "how far the light shines" statement and protocol, so it should be considered a pilot study for time being. Ms Parkes agreed that a pilot study might be more appropriate and a final decision will be made at the next meeting. Dr Wielgosz asked since this is the first time of using an infectious disease agent for a study, do all laboratories have appropriate safety requirements in place. Ms Parkes responded that it was each NMIs responsibility to confirm their own requirements since they differ from country to country, but the risk is low since it will not be live material.

11.9 CCQM WG on Protein Analysis (PAWG)

Dr Park presented a report on the PAWG activities over the last year, noting the 2017 fall meeting held at the NRC. He began by highlighting the progress of CMC claims based on CCQM-K115 on the purity of human C-peptide for which the final report has been published, and he described a new process and flowchart for reviewing Bio CMCs. Dr Park confirmed that CCQM-P137 on the activity of alpha-amylase was also completed and the Draft B report was being finalized, and he noted that a subsequent key comparison is planned. He then presented preliminary results for CCQM-P164 on human growth hormone (hGH) in serum, and reasonable agreement between labs was achieved for this very challenging comparison. NRC and PTB both agreed to perform follow-up experiments to explain discrepancies before a decision is made on proceeding with a key comparison. Dr Park then provided an overview of CCQM-K151 and P191 on Mass fraction of a purity-assessed recombinant protein in an aqueous calibration solution using amino acid-based ID-LC-MS and/or sulfur-based ID-ICP-MS. All samples had been shipped and measurements are ongoing. Dr Park then reviewed the PAWG's 5-year study plan and highlighted a proposal for a new pilot study on quantification of total haemoglobin by PTB.

Dr Park continued by highlighting a workshop on recent technical advances in protein metrology, held earlier in the week in conjunction with the PAWG working group meeting. He also described a workshop held jointly with the IAWG on 18 April 2018, on inorganic approaches for protein quantification. Dr Park also mentioned a workshop on biologics that was held at the autumn meeting in Ottawa, with speakers from NRC and the Korean Food and Drug Administration. Dr Park concluded his presentation by raising the topic of using journal publications to support CMC claims.

Dr May stated that the CCQM has never said journal articles could be the sole basis for CMC claims, but can be part of the ensemble of evidence. Ms Parkes commented that journals typically do not want the type of information that would be required to support CMCs. She added that the *Journal of Biomolecular Detection and Quantification* will be changing its scope to better reflect our needs. Dr May reaffirmed that journal articles may provide supporting evidence, but further evidence is generally required.

12. REPORTS FROM RMOS

All RMOs had been invited to submit written reports on their activities, which had been posted as CCQM documents well in advance of the meeting. The CCQM President invited the RMO representatives to briefly summarize their activities. He asked the representative from GULFMET to give a fuller report, as this was the first time that GULFMET had been represented at a meeting of the CCQM.

12.1 GULFMET

Mr AbdelRahman Alaskar was invited to present an introduction to GULFMET and began by reviewing its members, currently Bahrain, United Arab Emirates, Kuwait, Oman, Qatar, Saudi Arabia, and Yemen. Currently, only Saudi Arabia is engaged in chemical metrology, specializing in organic, electrochemical and gas activities. The Saudi Arabian labs are well-equipped and staff

training has proceeded with UME through a capacity building project. Mr Alasker noted particular experience in the analysis of PAHs by HPLC-FLD and LC-MSMS, measurement of buffer solutions by Harned cell, and the preparation and certification of CO and CO_2 gases. Capacity building is to continue over the next two years, with participation in CCQM and RMO comparisons planned for 2020.

Dr Güttler commented that it is very exciting to see GULFMET getting involved in chemical standards, and since chemistry is a huge area now are priorities being set. Mr Alaskar responded that they are looking at the needs of private laboratories, based on environmental and organic testing requirements. Dr Mester noted that only Saudi Arabia was mentioned, and asked if any other Gulf States were launching new programmes. Mr Alaskar confirmed that United Arab Emirates is considering developing a chemical metrology programme. Dr May asked whether the current set of gas analytes were chosen to gain experience or are these to be provided as standards in the future. Mr Alaskar responded that they are mostly to gain experience as they could be purchased from other NMIs, but they will focus on other needs specific to Saudi Arabia in the future.

13. BIPM PROGRAMME ON METROLOGY IN CHEMISTRY

Dr Wielgosz presented a progress report on the BIPM Chemistry Department and began by reviewing its four major programmes in the theme of international equivalence of chemical and biological measurement standards: (1) air quality and greenhouse gases, (2) organic purity analysis for health, diagnostics, pharmaceutical, food, environmental and forensics, (3) outreach activities with organizations such as JCTLM, IFCC, WADA, CODEX, etc., (4) capacity building and knowledge transfer on areas such as mycotoxins and air quality measurement standards. Dr Wielgosz then reviewed the organizational structure of the department, which currently consists of 10.5 FTEs, noting that Dr G. Martos had joined the Department in October 2017. He then described the highly successful visiting scientists programme at the BIPM, with 20 visiting scientists hosted in 2017 in the department, equating to 7.2 person-years.

Dr Wielgosz summarized some of the recent outputs of the department and reviewed a series of Gas Metrology comparisons coordinated by the BIPM over the last three years, highlighting results of CCQM-K120 on ambient CO_2 in air. Relative to the original comparison CCQM-K52 (2006) conducted 10 years earlier, CCQM-K120 yielded a 4-fold reduction in KCRV uncertainty and a 3-fold reduction in DoE spread. Dr Wielgosz reviewed BIPM-coordinated organic and peptide comparisons, with bisphenol A purity and oxytocin purity planned for 2018. After reviewing calibration hierarchies in chemical and biochemical measurements, Dr Wielgosz provided an update on the qNMR universal calibrator project which had been started through a collaboration with the NMIJ, and noted the publication of the first qNMR Internal Standard Reference Data (ISRD) document on maleic acid.

Expanding on the BIPM's efforts in CO_2 measurements, Dr Wielgosz noted that calibration requirements for optical instruments necessitates accurate isotope ratio measurements for both carbon and oxygen (calibration in "delta scale space"), which has led to the development of the BIPM Stable Isotope Reference Mixture Generator (SIRM-GEN) Facility. Preparation is under way for a CO_2 isotope ratio key comparison planned for 2020, with comparison samples being prepared at the BIPM

to be fully characterized by 2019. Dr Wielgosz noted that roughly ten NMIs within the GAWG have requested BIPM validation samples to help them in their development programmes prior to the comparison, and he also commented on significant interest from the Isotope Ratio Task Group (IRTG). He continued by describing a joint project with the NIST on an updated version of the NIST Standard Reference Photometer (SRP) for ozone, where the refurbished electronics are expected to extend the lifetime of the instrument by 20 years.

Dr Wielgosz presented an update on the Mycotoxin Metrology Capacity Building and Knowledge Transfer Programme (MMCBKT) initiated in 2016, noting new participation from CODEX, RCM-LIPI (Indonesia), DOST-ITDI (Philippines), NRC, and INM (Columbia) at the 3rd meeting of the MMCBKT held on 13 April 2018 at the BIPM. He reminded members that the MMCBKT project is designed to allow the BIPM and NMIs to work together to: strengthen mycotoxin metrology infrastructure, provide knowledge transfer to scientists developing capabilities in this area, and enable NMIs to characterize selected pure mycotoxin materials (https://www.bipm.org/en/cbkt/safe-food.html). Dr Wielgosz then described progress with mycotoxin material characterization at the BIPM with zearalenone (ZEN), aflatoxin B1 (AfB1), deoxynivalenol (DON), and patulin (PAT) at various stages of development. With all characterization completed, ZEN calibration solutions will be the subject of a Model 2 comparison CCQM-K154.a to be completed in 2018. Dr Wielgosz also reviewed a series of skills-broadening and training secondments established at the BIPM. Four Visiting Scientists are planned for 2018 from NIM (G. Zhen), NMISA (D. Mkhize), and UME (B. Binici and T. Gokcen). Dr Wielgosz concluded the MMCBKT discussion by highlighting two upcoming related workshops, notably the Africa Food Safety Workshop to be held in Pretoria (South Africa) on 4-8 June 2018, and the SIM Mycotoxin Metrology Workshop planned for 18-20 September 2018 in Buenos Aires (Argentina).

Also within the framework of the CBKT programme, Dr Wielgosz presented the "Metrology for Clear Air – Gas Metrology and FTIR" project, where NMIs developing gas metrology capabilities and standards have the opportunity to gain experience with FTIR as a cost-effective measurement technique that can operate at low uncertainties to verify and value assign their standards for a wide range of gases. He highlighted the BIPM's FTIR B-FOS software, now being operated by a growing list of NMIs. Similar to the mycotoxins project, a series of secondments at the BIPM have been established to facilitate knowledge transfer in this area, with three Visiting Scientists for 2017-2018 from NPLI (R. Soman Radha), NMISA (N. Ntsasa), and KazInMetr (A. Nassibulina) supported by voluntary funds from the NPL (UK).

Dr Wielgosz provided an overview of the programme delivery secondment opportunities at the BIPM for 2018-2019, including: (A) CO_2 PVT facility: mole fraction in air value assignment, (B) Preparing and value assigning CO_2 Stable Isotope Standards, (C) qNMR reference data and method development, and (D) High-Resolution Mass Spectroscopy Impurity analysis of peptides.

Dr Wielgosz concluded his presentation by describing the activities planned for the 2020-2023 programme, including expansion of the scope of the MMCBKT project to include ochratoxin A (OTA) and a potential new capacity building project on peptide diagnostics standards. Dr May commented that the BIPM programme in chemistry is a very active one, and is a model for how the BIPM will increase its leverage also in its areas of activity related to physical metrology.

14. REPORT FROM THE JCTLM

Dr Maniguet gave an update on the recent activities of the Joint Committee for Traceability in Laboratory Medicine (JCTLM), and began by reviewing the status of JCTLM membership. New National and Regional Member organizations include the Canadian Society of Clinical Chemists (CSCC), All-Russian Scientific Research Institute for Metrological Service (VNIIMS), All-Russian Scientific Research Institute for Optical and Physical Measurements, Rosstandart (VNIIOFI), and D.I. Mendeleyev Institute for Metrology (VNIIM). In addition, 14 new Stakeholder Member organizations were approved for 2018. Dr Maniguet commented on the global reach of JCTLM membership, with 54 members from 19 countries. She also discussed progress in potential expansion of Executive Committee Members Organization beyond BIPM, IFCC, and ILAC, as a discussion has started with the International Council for Standardization in Hematology (ICSH) and a meeting in planned for May 2018 at BIPM.

Dr Maniguet highlighted recent additions to the JCTLM database, including CRMs for tacrolimus in human blood from LGC, and 25-hydroxyvitamin D2 and D3 in lyophilized horse serum by UME. She also noted eight new reference method procedures (RMP) and 15 new reference measurement services (RMS). Dr Maniguet reviewed outcomes of the 2018 JCTLM WG review, noting that a large number of nominations for RMs and RMPs had been rejected, highlighting the need to provide adequate guidance and training to the JCTLM stakeholders with regards to ISO 15194 and 15193 for clarifying key requirements and how to implement certain concepts such as commutability studies, method validation, and extent of equivalence demonstration. She also noted that the large number of submissions had prompted the review team leaders to request additional experts to help with reviews. Dr Maniguet concluded her presentation by reviewing the annual JCTLM Members and Stakeholders Meeting that was held on 4-5 December 2017 at BIPM that had attracted 117 participants from 27 countries. The next stakeholder meeting is planned for 2-3 December 2019.

15. CCQM WORKSHOP AND 25TH ANNIVERSARY CELEBRATIONS AND FUTURE WORKSHOPS

Dr Wielgosz provided an update on planning for the CCQM's 25th Anniversary Workshop entitled "Progressing the state of the art for Chemical and Biological Measurement Science" on 10 April 2019. An associated poster session is planned for the evening of 9 April. The call for abstracts for presentations and posters opens on 1 May 2018 and closes on 1 December 2018, and abstracts can be submitted to the following email address: CCQM2019@bipm.org. The workshops will consist of approximately 12 presentations and 34 posters, where presentations will preferentially be selected from papers accepted for publication in the *Metrologia* Focus Issue on 'Advances in Metrology in Chemistry and Biology'. Papers should progress the state of the art of measurement science in chemistry or biology, including advances in reference measurement methods, certified reference

materials and reference data, as well as papers that contribute to the solution of difficult measurement problems of national/international importance and/or improve the accuracy of measurements of important chemical or biological measurands. Papers published will include novel research contributions as well as invited review articles; each of the technical CCQM WGs has been invited to consider submitting a review article on a topic in their field of expertise. Papers considered for publication will need to meet *Metrologia* guidelines and authors should state in the cover letter that the paper is intended for the 'Focus on' issue. Dr Wielgosz added that papers selected for the Focus issue will be published as they come in, then grouped together electronically for the special issue.

16. ANY OTHER BUSINESS

Dr May initiated a discussion on the format of future CCQM meetings, noting that the agenda was continually growing and it was becoming difficult to fit everything into a two-day meeting. He noted that several years ago there was an idea proposed to have WG Chairs give presentations only every second year to reduce part of the agenda, but this was not considered to be in the spirit of the Metre Convention. Dr Mester commented that there are two sections to the WG reports, the information section and issues arising within the WG portion to be discussed with the CC, so we could consider moving the information section to written reports to allow more time for more discussion of the issues. Dr May clarified that the suggestion is that similar to RMOs, where we would ask all WGs to provide a written report in advance, then allow a subset to provide a more comprehensive presentation. Ms Parkes commented that if this process was adopted the plenary meeting would receive information with a lag time, and would exclude everything covered in the WG meetings earlier in the week. Dr May added that one of the exciting things about the CCQM is that we are reporting on rich data from recent results. Dr Brewer suggested making the presentations shorter and more succinct. Dr Milton inquired whether it really needed fixing at all, and suggested that we should make every effort to remove unnecessary items from the agenda, and potentially be more disciplined in how many meetings a particular key comparison can be mentioned in. Dr Delebeeck commented that as a smaller NMI, she was strongly in favour of having up-to-date presentations, as then there would be no point coming to the meetings if these were not there. Dr Guttler expressed his support for up-to-date reports from WGs. Dr May summarized that there was strong support in the CCQM to maintain the presentations from WGs as they were. The new template for WG presentations allowed for succinct reporting of activities, if carefully followed as demonstrated by the OAWG, and he would work with WG Chairs to ensure that time limits for presentations were met in the future.

17. DATES FOR CCQM WG MEETINGS TO BE HELD DURING THE 2ND HALF OF 2018

It was noted that the autumn WG meetings for the CAWG, NAWG, OAWG, PAWG, will be held in Chengdu (China) on 8-9 October 2018, hosted by NIM. The IAWG with meet in Ottawa (Canada), from 2-4 October 2018 hosted by NRC, while the GAWG will meet on 8-9 October 2018 at Queretaro (Mexico) hosted by CENAM.

18. DATES FOR THE NEXT MEETING OF THE CCQM

The next meetings of the CCQM Working Groups will take place from 8-9 April 2019 (KCWG on 6-7 April 2019), with the 25th meeting of the CCQM taking place on the 10-12 April 2019.

19. CLOSURE

In the absence of any other business, the President of the CCQM, Dr May, closed the meeting at 15:27 hrs and thanked participants for their contributions, reports and participation in the discussions. He specifically thanked first-time attendees and provided them an opportunity to make any closing comments. Dr May also thanked the staff of the BIPM for their support in hosting the meeting and wished all attendees a safe journey home.

Dr J. E. Melanson

Rapporteur, 29 June 2018

DECISIONS AND ACTIONS FROM THE 24TH MEETING OF THE CCQM

1. As rapporteur, Dr Melanson to draft “Decisions and Actions” document and “Report of 24th Meeting of the CCQM”.
2. The CCQM approved the report of the 23rd Meeting of the CCQM.
3. Outstanding actions from the 23rd Meeting of the CCQM to be progressed as discussed in the report of the 24th Meeting of the CCQM.
4. The CCQM requested that the 'mise en pratique' for the mole be edited to include: the value of the uncertainty of the Avogadro constant prior to re-definition and the values, after redefinition, of the uncertainty in the molar mass constant and the difference between the molar mass constant and its former value (1 g/mol).
5. The CCQM agreed that it would not be requesting an exception to the rule of no overlapping CMCs between institutes in the same country.
6. The CCQM agreed on harmonized terminology for CCQM comparisons: Core Key Comparisons (Track A); Specialized Key Comparisons (Track C); and Pilot Studies (Track D). In addition, comparisons can be carried out with samples sent from coordinating laboratory to participants (Model 1) or samples sent from participants to coordinating laboratory (Model 2). The CCQM noted that the use of shorthand nomenclature (Track A, C and D) whilst in common use, should be deprecated, with preference given to the full names for types of comparison.
7. The CCQM decided to support the recommendation of the Task Group on isotope ratio measurements to create a CCQM isotope ratio working group. The CCQM President confirmed Dr Mester’s (NRC) willingness to serve as the Working Group Chair. The CCQM decision to form the working group will be presented for approval to the CIPM in its June 2018 meeting.
8. The CCQM supported the preliminary criteria established by the Task Group on method-defined measurands chaired by Dr Andres (METAS) and the Task Group has agreed to deliver a final report for the April 2019 meeting.
9. To bring levels of CCQM information on the BIPM website in line with other CCs, CCQM will provide open access to the following types of documents: meeting agendas, workshop and symposium presentations, policy and guidance documents, decisions and actions of the CCQM plenary meetings.
10. The CCQM President confirmed the one result per NMI rule for key comparisons.
11. The CCQM requested that Working Groups and comparison coordinators ensure that Draft A and B reports are drafted and approved according to protocols as set forth in the guidelines for operation of the CIPM MRA.
12. The CCQM confirmed the practice of continuing to use Draft B key comparison reports to underpin CMC claims, noting that only properly completed reports (see # 11) may be used (as per the CIPM MRA guidelines), which contain the final agreed KCRV and calculated degrees of equivalence. The reports will need to be accessible on the BIPM website to enable CMC review, and a written policy for this would be established.

13. The CCQM President requested that going forward working group reports to the CCQM Plenary describe how KCRVs were calculated.

14. The CCQM President requested that terms of reference for the Task Group on Quantitative Measurements with Raman Microscopy that is being established within the SAWG, be developed and presented at the 25th CCQM Plenary Meeting.

15. The CCQM President to write to JRC to request clarification on their future involvement in CCQM and CIPM MRA activities