CCQM STRATEGY DOCUMENT 2021-2030

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EXECUTIVE SUMMARY

The document sets out the strategy to be followed by the Consultative Committee for Amount of Substance; Metrology in Chemistry and Biology (CCQM) in the period 2021-2030 to deliver its mission of advancing the global comparability of chemical and biological measurement standards and capabilities, and thereby enabling Member States and Associates to make measurements with confidence. In so doing, measurement science will also be progressed, and stakeholder engagement strengthened. In developing its strategy, the CCQM expert groups have identified nine key sectors that are expected to influence and drive the development on National Metrology Institutes' (NMI) and Designated Institutes' (DI) services within the 2021-2030 period and impact CCQM activities for achieving global comparability of chemical and biological measurements. Scientific, economic and social challenges which can be tackled through metrology at the CCQM level are described for the following sectors: Environment and Climate; Healthcare and Life Sciences; Food safety, trade and authenticity; Energy; Legal Metrology; Fundamental metrology and support of the SI; Forensic Sciences and Anti-doping; Advanced Manufacturing; Biotechnology and Drug Discovery.

The CCQM has set seven strategic aims to be progressed in the 2021-2030 period, notably: to contribute to the resolution of global challenges; to promote the uptake of metrologically traceable chemical and biological measurements; to progress the state of the art of chemical and biological measurement science; to improve efficiency and efficacy of the global system of comparisons for chemical and biological measurement standards it conducts; to continue the evolution of Calibration and Measurement Capabilities (CMCs) to meet stakeholders needs; to support the development of capabilities at NMIs and DIs with emerging activities; to maintain organizational vitality, regularly review and, if required, update the CCQM structure for it to be able to undertake its mission.

The strategy foresees contributions to progressing the state of the art in measurement science across all nine technical science areas covered by the Committee including Organic, Inorganic, Gas, Isotope Ratio, Surface, Electrochemical, Protein, Nucleic Acid and Cell analysis areas. Thirty-three activities have been identified where progress is expected, ranging from support for the development of new greenhouse gas, isotope ratio and microplastic standards, to the development of reference measurement systems for biomarkers, surface chemical composition, RNA quantification, food authentication, and cell counting as examples.

A more structured approach to stakeholder engagement is foreseen in the new strategy and considered as a key tool in promoting the activities and impact of the CCQM and of the Chemical and Biological Metrology community in general. A mid- and long-term plan for stakeholder engagement will be developed, including possible extension of the CCQM Liaison Membership, to better represent the expanded technical coverage of the committee, extended collaborations with other Consultative Committees and sector specific fora established by the CIPM, and further use of task and focus groups to deliver the CCQM mission.

A core capability/comparison strategy will be continued with the aim of not increasing overall resources required for comparisons for the 71 institutes worldwide maintaining over 6300 CMCs in the chemistry/biology field. Models for broad claim CMCs will continue to be developed, facilitating broader uptake of these, whilst meeting stakeholder needs, and potentially reducing the resources required to review and maintain CMC database entries.

Strong interaction will be maintained between the CCQM and RMOs, with continued coordination of linked, satellite and supplementary comparisons, and increased focus on capacity building and knowledge transfer including the initiation of mentoring programmes for NMIs coordinating comparisons for the first time.

The implementation of the strategy is supported by the BIPM Chemistry Department providing the CCQM Executive Secretary Role, coordination of comparisons in technical areas prioritized by the CCQM, laboratory-based knowledge transfer programmes for National Metrology Institutes with emerging metrology systems, the JCTLM database and support for engagement with stakeholder communities.

Consultative Committee for Amount of Substance; Metrology in Chemistry and Biology: Strategy Document (2021-2030)

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1. INTRODUCTION

The CCQM was established by the International Committee of Weights and Measures (CIPM) to bring together the world's experts in metrology in chemistry and biology. Created in 1993, it is one of the ten Consultative Committees of the CIPM, and the only one working solely in the domain of chemistry and biology. To cover the different technical disciplines within its sphere of activity, the CCQM currently maintains nine technical subject working groups, a Strategy Planning WG, a Working Group on Key Comparisons and CMCs, and an ad-hoc WG on the mole, and is supported by a scientific and technical programme at the BIPM. The membership of the CCQM is constituted of 45 institutes worldwide (either as members, observers or liaisons), with 56 institutes and over 500 scientists participating on a regular basis in the activities of its working groups. The CCQM work programme has

resulted in the execution of just under 400 inter-laboratory comparison exercises since its creation, with on-average 18 new comparisons initiated each year. The CCQM activities together with those of the RMOs, support over 6300 calibration and measurement capabilities in chemistry and biology from 71 institutes worldwide. The activities of the CCQM have also contributed to the establishment of the Joint Committee for Traceability in Laboratory Medicine (JCTLM), and to which NMI and DIs active in CCQM continue to participate.

The current strategy document has been drafted by the Strategic Planning WG of the CCQM, chaired by the CCQM President, following approval of the vision and mission statements and strategic aims for the 2021-2030 period by the CCQM in 2020. Plans for detailed activities have been developed within each of the technical subject working groups covered by the CCQM, following consultation in 2020 with National Metrology Institutes and Designated Institutes active in these groups. The plans are summarized in this document and detailed technical subject strategies available for consultation. The 2021-2030 CCQM Strategic Plan builds upon and replaces the previously published 2017-2026 CCQM Strategy document. The document has been submitted to the 26th meeting of the CCQM for approval.

2. SCIENTIFIC, ECONOMIC AND SOCIAL CHALLENGES

Reliable chemical and biological measurements are essential for meeting the scientific, economic and sustainability challenges faced by our societies today. Nine key sectors have been identified within the technical subject areas covered by the CCQM, that are expected to influence and drive the development of NMI and DI services within the period 2021-2030 and impact the CCQM strategy for achieving global comparability of chemical and biological measurements. Examples of each sector's reliance of chemical and biological measurements and standards is given below, with more complete descriptions provided in each of the technical subject strategy documents referenced in Annex 3.

a) Environment and Climate

Policies and programmes to protect and restore the environment and biodiversity and provide coordinated action in response to climate change will require: enhanced measurements systems for monitoring, source apportionment and emission control of greenhouse gases, aerosols and air quality pollutants; reliable measurements systems for ocean acidification measurement; reliable measurements of persistent organic pollutants, endocrine disruptor compounds, antibiotics, perfluorinated compounds and other pollutants, regulated and emerging ones, or their indicators, in air, water, soils and sediments. Microplastics and the circular economy in general represent a growing challenge requiring a multidisciplinary approach.

b) Healthcare and Life Sciences

Policies and programmes to advance healthcare will require: reference methods, materials and services for in vitro diagnostic kits to meet regulatory requirements for metrological traceability and consistency of measurement results from different manufacturers; reliable and rapidly deployable reference measurement systems for infectious diseases; reliable measurements for in vitro diagnostics of non-communicable diseases; reliable measurements for regenerative medicine and gene therapy; a measurement infrastructure for the next generation of clinical biomarkers (e.g. breath analysis) for screening and diagnosis.

c) Food safety, trade and authenticity

Programmes and policies to ensure food safety and enable trade will require: reliable measurements for regulated contaminants and residues, nutritional content parameters such as vitamins, food processing and migration contaminants in food; reliable measurements for emerging food contaminants such as fungal or drug metabolites, elemental speciation, microplastics and nano particles; reliable measurements, standards and databases for food authenticity/provenance

determinations; verification of mandatory fortification levels with staple foodstuffs; reliable and comparable measurement systems for food allergens, toxins and pathogens; reliable electrochemical methods for food quality; reliable measurement methods and materials for the identification and quantification of GMO content in food stuffs.

d) Energy

Policies and programmes to develop, provide and trade current and future energy sources will require: globally maintained measurement infrastructure for natural gas composition; appropriate measurements systems for composition of biomethane, LNG and LPG, to facilitate diversification in the supply of energy gases; a global measurement infrastructure for hydrogen purity to move towards a hydrogen economy; enhanced measurements of conductivity of feed water in steam turbines and in biofuels; enhanced measurement systems for the performance of Li-ion batteries and fuel cells; reliable surface chemical analysis of battery and fuel cell electrodes, supercapacitor and graphene materials, and photo-voltaic devices; reliable measurements of heavy metals and sulfur contaminants in fuel.

e) Forensic Sciences and Anti-doping

The areas of forensic sciences and anti-doping will require: reference materials for the identification of novel designer drugs; reference materials and methods for identification and quantification of prohibited substances and their metabolites; reference materials, methods and databases to authenticate provenance of commodities such as timber, food, animal and plant products; reliable measurements for nuclear forensics and the points of origin of nuclear materials and events. New sampling approaches will require reliable measurements for techniques such as dried blood spot testing.

f) Advanced Manufacturing

Requirements in advanced manufacturing will include: enhanced measurements systems for high purity gases for advanced manufacturing including semiconductor and organic electronic components; reliable measurements from electrochemical sensors and chemical surface analysis in miniaturized devices; reliable chemical analysis for nanotechnology development; reliable compositional measurements of alloys and other materials.

g) Biotechnology and Drug Discovery

Future developments in biotechnology and process control will require: reliable measures of cell parameters including viable cell concentration, volume and wet cell weight, supporting monoclonal antibody production; reliable measurements for cell authentication; reliable measurements to robustly characterize future cell therapy treatments such as CAR-T cells or induced pluripotent stem cells to ensure their quality, safety and potency. Processes for drug discovery will require: reliable measurements for adherent total and differential cell number for various characteristics including cell viability and cytotoxicity, cell phenotype including molecular cell authenticity testing, or measurement of defined cellular activities or secreted target products.

h) Legal metrology

Implementation of statutory requirements for measuring instruments and methods will require: availability of metrologically traceable standards including those for automotive emissions and breath alcohol and interfering substance testing.

i) Fundamental Metrology and the SI

Analytical methods for chemical measurements require reliable calibration with metrological traceability to calibrations solutions and pure substance reference materials of known purity and isotopic composition. Comprehensive underpinning of metrological traceability will require: reliable databases of reference data for chemical and biological measurement; availability of high accuracy chemical measurement services that underpin the realization of SI units; developments in measurement methods and comparisons that can be used to meet global requirements for reference materials.

The CIPM study on evolving needs for Metrology has started by identifying requirements within 5 grand challenge areas and the horizontal theme of digitalization. These are a subset of the nine sectors considered in the CCQM strategy, and Figure 1 summarizes the topics that will be covered by each of the CCQM technical subject working groups within these sectors in the 2021-2030 period.

Digitalization is a cross cutting theme, and within the CCQM community consideration will be given to the accessibility and availability of chemical and biological reference data. The JCTLM database, isotope ratio scale defining reference material database and Greenhouse Gas Standard databases are initial areas of focus, as well as support for sensor networks and distributed measurements.

Sector	CCQM OAWG	CCQM PAWG	CCQM NAWG	CCQM CAWG	CCQM SAWG	CCQM EAWG	CCQM IAWG	CCQM IRWG	CCQM GAWG
Climate & Environment	POPs Contaminants Microplastics Water/Soil		Species/ microbial surveillance			Seawater pH and salinity	Heavy Metal Contaminants Speciation Water/Soil	GHGs	GHGs Air Quality Emissions Particles
Health & Life Sciences	Diagnostic biomarkers Forensics Anti-doping	Diagnostic biomarkers Therapeutics	Diagnostic biomarkers Gene Therapy	Diagnostic biomarkers	Imaging diagnostics Biocompatibility In-vitro diagnostic devices	Diagnostic biomarkers	Diagnostic biomarkers Toxic Elements	Diagnostic biomarkers Forensics Anti-doping	Breath diagnostics
Food Safety	Toxins Contaminants Residues Authentication	Allergens Authentication	GMO-Foods Pathogens	Pathogens	Packaging materials		Heavy metal Contaminants Speciation	Food authentication	
Energy					Batteries Fuel/Solar cells Catalysts	Batteries Fuel Cells	Fuel Contaminants		Natural Gas LPG/LNG Hydrogen Biofuels
Advanced Manufacturing		Advanced Therapy Development	Biotechnology	Advanced Therapy Development	Nanotechnology Semiconductors Quantum devices	Nanotechnology	Nanotechnology		Trace Gases
Digitialization				Digital Pathology				Isotope Ratio Scale defining RMs Database	GHG Scales Database & Management

Figure 1: Mapping of sectors, identified by the CIPM study on evolving needs for metrology, and summary of measurement needs being addressed by CCQM technical subject WGs as well as areas covered by the JCTLM.

3. VISION AND MISSION

The CCQM's vision: A world in which all chemical and biological measurements are made at the required level of accuracy to meet the needs of society.

The mission of the CCQM is: To advance global comparability of chemical and biological measurement standards and capabilities, enabling Member states and Associates to make measurements with confidence.

The responsibilities of the CCQM are:

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

b. to advise the CIPM on matters related to chemical and biological measurements including guiding international activities related to the definition and realization of the mole and advising on the BIPM scientific programme;

c. to reach out to new and established stakeholders to promote the international measurement system and prioritize needs;

d. to progress the state of the art of chemical and biological measurement science and act as a forum for the exchange of information about measurement research, technical programmes and service delivery;

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

4. STRATEGIC AIMS FOR 2021-2030

In line with the CCQM's vision and mission, the aims of the 2021 to 2030 strategy are:

To contribute to the resolution of global challenges such as climate change and environmental monitoring, energy supply, food safety, healthcare including infectious disease pandemics, by identifying and prioritizing critical measurement issues and developing studies to compare relevant measurement methods and standards

To promote the uptake of metrologically traceable chemical and biological measurements, through workshops and roundtable discussions with key stakeholder organizations, to facilitate interaction, liaison and cooperative agreements, and receive stakeholder advice on priorities to feed into CCQM work programmes.

To progress the state of the art of chemical and biological measurement science, by investigating new and evolving technologies, measurement methods and standards and coordinating programmes to assess them.

To improve efficiency and efficacy of the global system of comparisons for chemical and biological measurement standards conducted by the CCQM, by continuing the development of strategies for a manageable number of comparisons to cover core capabilities.

To continue the evolution of CMCs to meet stakeholders needs, incorporating the use of broad claim CMCs where applicable to cover a broader range of services and considering options to present these in a way that meets stakeholder needs and encourages greater engagement with the CMC database.

To support the development of capabilities at NMIs and DIs with emerging activities, by promoting a close working relationship with RMOs including mentoring and support for NMIs and DIs preparing to coordinate comparisons for the first time and promoting knowledge transfer activities including workshops, as well as secondments to other NMIs, DIs and the BIPM

To maintain organizational vitality, regularly review and, if required, update the CCQM structure for it to be able to undertake its mission and best respond to the evolution of global measurement needs, by prioritizing where new areas or issues should be addressed within the structure and evolving working group remits as required.

5. ACTIVITIES TO SUPPORT THE STRATEGY

Implementation of the strategic aims of the CCQM will be achieved through the sub-structures and tools available to the Committee, notably:

a) The CCQM plenary, to set strategic objectives, oversee activities, establish working groups and liaisons, and initiate new activities;

b) The CCQM technical subject working groups, to develop and implement work programmes in each of their technical subject areas following the CCQM strategic aims;
c) The CCQM Strategic Planning Working Group, to harmonise and align activities between WGs and prepare documents for review and approval of the CCQM;
d) The CCQM Key Comparison and CMC Quality working group, to work with the RMOs in maintaining a coordinated and harmonized system for inter-regional CMC review, with guidelines developed in collaboration with the CCQM technical subject working groups;
e) Support from the BIPM Secretariat, and principally the BIPM Chemistry Department, to implement CCQM strategic aims and CCQM and WG activities;
f) Task groups and focus groups established at the Committee and WG levels to initiate and complete specific tasks, including those requiring engagement with stakeholders, between WGs and with other Committees;
g) Workshops and webinars providing knowledge transfer opportunities between Metrology Institutes and to and from stakeholder communities.
h) Appointment of vice-Chairs for WGs, with documentation of strategy and procedures, to enable effective succession planning.

5.1. PROGRESSING MEASUREMENT SCIENCE

Measurement science is progressed through the activities of the CCQM technical subject working groups and notably through the execution of pilot studies to investigate new methods or measurements areas, workshops and webinars focusing on new measurements challenges, and focus and task groups to define and execute new areas of work.

Activities that will be undertaken within the period 2021-2030 and lead to advances in measurement science are:

1. Supporting greenhouse gas reference material development for isotope ratios
This will support the development of a robust infrastructure for gas phase reference materials for isotope ratios of carbon dioxide for source apportionment, meeting the demand for new standards with the advent of commercial optical spectroscopy for isotope ratio monitoring starting with the CCQM-P204 study.
2. Developing greenhouse gas scale science with traceability to the SI
This will develop protocols to maintain consistency between independently held sets of primary carbon dioxide in air gas reference materials at the 0.02 µmol mol^{-1} level, providing fit-for-purpose standards for GHG monitoring and emissions authentication.
3. Supporting standards development for diversification of the energy gas supply
This will support progress in analytical methods and reference materials to support the quality infrastructure for hydrogen purity (building on CCQM-K164) and for other energy gases.
4. Extending particle metrology
This will improve measurement methods and uncertainties of particle mass, size and number concentration measurements and the characterisation of regulated components, building on initial comparison studies.
5. Supporting reactive gas standard development for air quality monitoring
This will support reference material and spectroscopic analytical method development for the characterization of reactive gases such as nitrogen dioxide, hydrogen chloride and ammonia, building on information gained from comparative measurements.
6. Advancing spectroscopy for absolute gas mole fraction measurement
An initiative to support NMIs developing optical methods based invariant spectroscopic properties of molecules and atoms to measure amount fraction and isotopic abundance of gas mixtures with quantifiable systematic and statistical uncertainties required for SI traceability.

7. Advancing analytical methods for high purity metal characterization

This will support improvement in methods for the determinations of nonmetallic impurities in high-purity metals, based on studies of several nonmetallic elements, building on CCQM-P149 results, and the fundamentals of SI traceability for inorganic measurands.

8. Supporting development of analytical methods for nanoparticle metrology

This will support development of single particle (sp)ICP-MS methods as well as novel techniques such as A4F for measurement of the mean size, size distribution, and number concentration of a population of metal-containing nanoparticles suspended in a liquid, building upon results from CCQM-P194 (Number concentration of colloidal nanoparticles in liquid suspension).

9. Supporting development of element-based quantitation of biomolecules

This will support the development of reliable measurement methods of biomolecules, such as proteins, peptides, nucleotides, DNA, and RNA with element-based measurement methods, building on results of CCQM-P156 (Element-based quantification and purity analysis of a dNMP standard solution) and CCQM-P191 (Determination of the amount content of a purity-assessed recombinant protein in an aqueous calibration solution).

10. Supporting development of small sample and spatially resolved metrology

This initiative will support institutes in developing their capabilities for laser ablation ICP-MS, to provide high quality chemical composition data that is spatially resolved.

11. Supporting methods and standards development for elemental speciation

This initiative will support the wider application of species-specific IDMS as well as fit-for-purpose methods, building on studies of tributyl tin in seawater, inorganic arsenic in rice flour and selenoproteins in human serum.

12. Supporting method development for SI traceability of isotope ratios measurements

This will extend the application of the full gravimetric isotope mixture model (FGIM) for absolute SI traceable isotope ratio determinations, starting with a focus on Cu isotope amount ratios.

13. Supporting metrological traceability development for solid state isotope ratio measurements

This will support the establishment of methods for SI traceability for solid state measurement techniques, such as laser ablation for isotope ratio measurements.

14. Supporting the development of pH scales to complex matrices

This will support the development of pH scales to different non-aqueous solvents, solvent-water mixtures, and high ionic strength matrices such as seawater.

15. Extending conductivity and impedance spectroscopy to more challenging conditions

This will support the extension of conductivity measurements and impedance spectroscopy to challenging matrices including pure water, seawater at high pressures, biofuels and Li-ion batteries.

16. Supporting the extension of coulometry as a reference method

This will support the extension of coulometric methods to bases, reductants and complexing agents (EDTA), and its use in determining antioxidant capacity in complex matrices.

17. Supporting the extension of SI traceable measurements for surface chemical composition

This will support the development of SI traceable measurements of chemical composition of layers of up to 1 µm thickness, chemical mapping of surfaces with lateral scale length of less than 1 mm, and chemical measurements of nanostructured and highly porous materials.

18. Supporting advanced organic purity method development

This will support the development of validated methods for purity assessment of organic molecules, including those with larger molar masses, lacking UV-chromophores and salt materials.

19. Supporting protocol development for reference material commutability studies

This will support the development of best practices in commutability studies required for CRMs used in a calibration hierarchy for clinical diagnostics.

20. Supporting the development of Reference Data as an emergent measurement service

This will initiate the use of well-documented, open source and machine-readable formats for data submitted for comparison results, supporting digitalization activities.

21. Supporting the application of Quantitative Nuclear Magnetic Resonance Spectroscopy (qNMR)

This will support metrological applications of qNMR to more complex molecules and evolving areas of application such as HPLC-qNMR, quantitative NMR for ^{19}F, ^{31}P and ^{13}C as alternative nuclei, and 2D-qNMR.

22. Supporting the application High resolution mass spectrometry (HRMS) in CRM characterization

This will support the assessment of general quantitative performance of HRMS hyphenated techniques for organic analytes and CRM value assignment.

23. Supporting the development of Compound Independent Calibration (CIC)

This will support activities to develop CIC, based on hyphenated Inductively Coupled Plasma Mass Spectrometry (ICP-MS), measuring elemental species, for pure organic or standard solution value assignment with either inorganic element or other organic reference material calibrators.

24. Supporting development of methods for microplastic contaminant quantification

This will support development of methods and reference materials for microplastic characterization and quantification across a range of matrices.

25. Supporting reference measurement system development for protein biomarkers

This will support the development of reference materials and methods for high priority clinical biomarkers as well antigens and antibodies for infectious disease diagnostics.

26. Supporting reference measurement system development for SI traceable measurement of nucleic acids

This will support the development of methods to improve DNA/RNA quantification and purity evaluation and their use in calibration hierarchies for the future of nucleic acid measurement, including infectious disease detection.

27. Supporting reference material development for food origin authentication

This will support the development of reference measurement methods and materials for food authentication, including organic components, mitochondrial DNA sequence analysis, and next generation and Sanger sequencing, and digital PCR techniques.

28. Supporting reference method development for genes, gene expression and epigenetics studies

This will support the characterization of candidate reference methods for measuring actionable genetic, epigenetic and transcriptomic changes.

29. Supporting reference method development for microbial quantification

This will develop reference methods for DNA/RNA copy number quantification studies for microbial identification and concentration determinations in industrial and environmental applications and infectious disease diagnosis and management.

30. Supporting reference method development for counting of cells in suspension

This will support the development of reference methods for cell counting, including flow cytometry, for cells in suspension, building on CCQM-P217 (Enumeration of fixed peripheral blood mononuclear cells in suspension) and CCQM-P205 (Enumeration of membrane intact E. coli).

31. Supporting reference method development for counting of cells adhered to surfaces

This will support reference material development for the counting and characterization of adhered cells building on CCQM-P123 (Number and geometric property of cells adhered to a solid substrate).

32. Supporting method development for cell viability and functional measurement

This will support the development of reference methods and materials to measure cell viability by cell membrane disruption and metabolic methods alongside defined biological activities by quantification of specific cell bound targets (i.e. intracellular cytokines).

33. Supporting method development to practically implement the newly defined 'mole'

This will support various initiatives seeking to develop approaches to directly quantify chemical or biological entities through enumeration, providing SI traceability for measurements that can be readily related to the mole.

5.2. IMPROVING STAKEHOLDER INVOLVEMENT

Assuring appropriate stakeholder interaction has been identified as a key route for CCQM to promote the uptake of metrologically traceable chemical and biological measurements. This is envisaged to be achieved through workshops and roundtable discussions with key stakeholder organizations, which will facilitate interaction, liaison and cooperative agreements, and permit stakeholder advice on priorities to be received and to feed into CCQM work programmes. The mechanisms available to the CCQM for stakeholder interaction include:

a) Granting of CCQM liaison status to organizations that participate within the plenary meeting
b) Workshops and webinars either at the CCQM or WG level;
c) Expert laboratory participation within CCQM pilot studies;
d) Signature of the CIPM MRA and participation within CCQM key comparisons;
e) Participation in CCQM WG Task groups when task completion requires stakeholder involvement.
f) Liaisons established with stakeholder organizations maintained by the BIPM Secretariat.

In many instances, stakeholder engagement is assured directly at the national level through the NMI or DI. However, where strategic interaction and communication with an entire measurement community, including promotion of interaction at national levels, is required, further action from the CCQM can be justified.

Actions to be undertaken by the CCQM in the 2021-2030 period to further stakeholder engagement and achieve its strategic aims are:

a) To undertake a review and document the obligations and privileges for Liaison Members of CCQM and identify additional international candidate organizations whose involvement would be beneficial to the mission of the CCQM;
b) To maintain workshops and webinars, both at CCQM and CCQM WG levels, to facilitate stakeholder engagement and enable knowledge transfer to and from stakeholder communities, based on a mid- and longer-term plan for stakeholder engagement identified by the committee. Recent examples have included both the CCQM webinar series on ‘Reliable measurements in response to the Covid-19 pandemic’, and the CCQM GAWG virtual workshop on Accurate Surface Ozone Measurement.
c) To continue expert laboratory participation in CCQM pilot studies as a method of gaining expert knowledge for the CCQM and engaging additional stakeholder communities;
d) To keep under consideration opportunities for other international organizations providing chemical and biological measurement standards to participate in the CIPM MRA;
e) To utilize Task Groups at the CCQM and WG level to engage with stakeholders in delivering the mission of the CCQM. Recent examples include the establishment of the CCQM GAWG Task Group on Ozone Cross Section Change Implementation;
f) To encourage WGs to include agenda points in meetings on feedback on individual NMI interaction with stakeholder groups of interest to the wider community, for example related to ISO technical committee activities;
g) To establish appropriate structures (liaisons, focus groups or task groups) to maintain communication and input into any CIPM Sector specific structures or other Consultative Committees that have an overlap or would benefit with CCQM engagement;
h) To identify organizations and committees where it would be beneficial for the BIPM Secretariat to establish liaisons to facilitate the implementation of the CCQM mission.

5.3. PROMOTING GLOBAL COMPARABILITY

The CCQM activities over its first 25 years of existence have done much to promote the uptake of metrological traceability within chemical and biological analytical measurements and laboratories. Within the same time period, there has been growth both in the number of NMIs/DIs providing chemical and biological reference materials and measurement services as well as a broadening of the technical fields in which these services are offered. Seventy-one institutes now have a total of over 6300 CMCs registered in the BIPM key comparison database. The challenge for the CCQM is to maintain a system able to demonstrate the equivalence of chemical and biological measurements standards and capabilities at the required level of quality assurance with a manageable level of comparisons. A second challenge is to ensure that submitted CMCs meet stakeholder needs, and that the resources required for CMC maintenance and review also remain at manageable levels.

The CCQM strategy for maintaining comparisons at manageable levels is to develop and maintain models for core capabilities and comparisons, where one or a combination of comparison exercises can demonstrate capabilities across a broader area of capabilities than the single analyte and matrix studied in the comparison. These are supplemented by specialized comparisons, where particular focus is on a globally important or challenging analyte/measurand. The strategy has been implemented within the WGs with the most mature programmes, with newer WGs developing their measurement programmes with this concept already in mind. As a result, the total number of comparison exercises run each year, is foreseen to remain at or below 18 comparisons per year for the 2021-2030 period. This is consistent with the number targeted in the previous 2017-2026 CCQM strategy, which was 16 to 17, and allows for some additional studies foreseen with the operation of a new WG with CCQM on isotope ratios, which was not accounted for in the previous strategy document.

Maintaining resources for processing CMCs at manageable levels is to be achieved through use of the web based tools of CMC submission and review now available in KCDB2.0, and the development of models for the formatting and required evidence for Broad Scope CMCs. The CCQM strategy is to continue the development of broad claim CMC models within all technical areas covered by the Committee, and available for NMIs to implement if they wish. The 2017 to 2021 period has seen the total number of Chem-Bio CMCs increasing from 6227 to 6346, a rise of 119 over 4 years, which would at first glance indicate a considerable slowdown in the growth of CMCs from the preceding period. However, closer examination of the data reveals that of the 54 countries/Economies holding Chem-Bio CMCs, 38 countries/economies showed increases in the number of their CMCs, and this was offset by 7 countries/economies showing decreases, in some cases substantial, with 9 countries/economies not changing the number of CMCs. As the adoption of broad scope CMC claims is voluntary, and driven by individual national stakeholder requirements, the future evolution of CMCs will be determined by national decisions on implementation of the broad claim option.

The CCQM was instrumental in the development of the JCTLM Database of Reference Materials, Methods and Services for Laboratory Medicine. The database is maintained by the BIPM and the vast majority of entries for CRMs are from NMIs/DIs. In the field of Laboratory Medicine, matrix CRMs are required to exhibit the property of commutability (showing the same behaviour as human test samples within the kits to which they are applied), as well as meeting requirements of specific documentary standards. The JCTLM database remains the only sector specific database of NMI measurement capabilities maintained by the BIPM. A strategic consideration for the CCQM is to ensure that the process of the CIPM MRA and the JCTLM are well aligned.

The CCQM will keep under review the need for further initiatives for sector specific databases, or sector specific applications derived from a machine readable KCDB2.0 to meet stakeholder needs on globally comparable reference measurements. A potential case study would be an initiative to address

the traceability exception that exists within the CIPM MRA for isotope ratio measurement standards for delta scale measurements. A database of reference materials with supporting data meeting FAIR principles, providing a global database of reference points for global scales, would be one approach to meet requirements.

5.4. INTERACTION WITH RMO ACTIVITIES

Effective and efficient interaction between CCQM and RMOs is achieved through:
a) RMO representation at the CCQM Plenary meeting;
b) RMO Metrology in Chemistry TC Chair membership of the CCQM Strategic Planning WG;
c) CCQM technical subject WGs maintaining standing agenda points within their meetings for RMO comparisons and other activities;
d) the CCQM KCWG with representatives from RMOs, CCQM technical subject WGs and the BIPM Secretariat.

As comparisons within CCQM are not normally limited by the availability of a transfer standard (as is often the case in Metrology in Physics) regional key comparisons linked to CCQM ones are less frequent in the Chemistry/Biology measurement space. However, notable exceptions are in the field of gas metrology as well as ethanol in water in organic analysis, where exactly the same measurand needs to be measured on a global level, and in the former case where the cost of preparation of multiple transfer standards limits participant numbers. In these cases, RMO linked key comparisons are foreseen to continue.

RMOs have an active programme in supplementary comparisons to meet comparison needs of their members wishing to demonstrate new or maintained measurement capabilities. To best use resources and avoid unnecessary duplication of efforts, NMIs from other regions can be invited to participate in an RMO's comparisons, and this is facilitated by discussion within CCQM technical subject WGs. This is particularly relevant where RMOs are co-ordinating comparisons of relevance to developing institutes that may not be occurring at the CCQM level.

Capacity building and knowledge transfer (CBKT) programmes originated and are maintained within the RMOs to enable countries and laboratories with emerging metrology systems in chemistry and biology to participate fully in the CIPM MRA processes and comparisons. Since 2016, the regional CBKT programmes have been augmented with activities of the BIPM Secretariat, including the BIPM Chemistry Department running CBKT laboratory projects for laboratories developing organic calibrators and gas standards for food safety and air quality monitoring, with these projects being extend to on-line knowledge transfer and peptide calibrators for laboratory medicine. The expected continued growth in numbers of laboratories and countries with emerging metrology systems wishing to develop and demonstrate compatibility of their chemical and biological measurement standards and capabilities will require these projects to continue. The CCQM would also encourage additional NMIs to become coordinators of comparison exercises, and CCQM Gas Analysis WG is taking the lead in establishing a Task Group on Comparison coordination, with laboratories experienced in comparison coordination partnering and mentoring laboratories wishing to coordinate a CCQM comparison for the first time.

RMOs are also establishing research programmes, which include or result in pilot studies on new technical areas, with EURAMET and the EMPIR/EMP programmes being a notable example. RMO research activities are also reported within CCQM technical subject WGs, and this provides a process for regional pilot studies to be elevated to CCQM level, where there is sufficient interest from other regions of the world.

5.5. WORK PROGRAMME OF THE BIPM LABORATORIES

The implementation of the CCQM strategy is supported by the BIPM Chemistry Department providing the CCQM Executive Secretary Role, coordination of comparisons in technical areas prioritized by the CCQM, laboratory-based knowledge transfer programmes for National Metrology Institutes with emerging metrology systems, the JCTLM database and support for engagement with stakeholder communities.

BIPM laboratory activities enable a long-term commitment to comparison coordination, which is best adapted to periodic comparisons and allowing close monitoring of performance. The CCQM WG strategy plans, for the Gas, Isotope Ratio, Organic and Protein Analysis WGs, foresee BIPM coordinated CCQM comparisons of:

a) NMI/DI primary calibrators/capabilities for prioritized green-house gases and air quality gases
b) NMI/DI calibrators/reference capabilities for $\delta^{13}C$ and $\delta^{18}O$ in CO_2, CO_2 in air and carbonates
c) NMI/DI core capabilities for primary reference materials and calibrators for small organic molecules
d) NMI/DI core capabilities for primary reference materials and calibrators for peptides and proteins

The laboratory-based capacity building and knowledge transfer laboratory activities initiated at the BIPM in 2016 in the fields of Metrology for Safe Food and Feed and Clean Air, supporting KT activities in the RMOs, have had good uptake. The future strategy sees the expansion of these to cover Pesticides and Veterinary Drugs relevant to residues in Food, Dynamic standards for Air Quality Gases, and Pure peptides for Laboratory Medicine. The visiting scientist placement programme will be reinforced with on-line training modules, increasing the possibility of participation in the next period, and support the increased interest in CCQM activities from NMIs with emerging metrology systems.

Implementation of machine-readable databases with data following FAIR principles, will be addressed by the BIPM, in the first instance, with a database for CO_2 scale comparisons in support of the CCQM GAWG Task group on GHG Scale comparisons. This builds on previous database projects, such as the JCTLM, and the development and publication of reference data for qNMR internal standards, which are maintained.

The CIPM evolving needs in metrology study for 2030+ foresees the establishment of interdisciplinary fora for discussion of identified challenges and development of international metrology actions to support them. The sectors that have initially been identified by the CIPM are: Climate change and Environment; Health and Life Sciences; Food Safety; Energy; Advanced Manufacturing; Digital Transformation; and ‘New’ Metrology. The fora will require support from the BIPM Secretariat and notably the Chemistry Department, with a considerable number of themes having strong technical overlap with the CCQM. Initial activities together with the EMN on Climate and Ocean Observation have already been initiated to support for the organization of a ‘Metrology for Climate Action’ Workshop planned for 2022.

A detailed strategy for the BIPM activities, together with short terms and longer-term actions is described in Annex 4.

ANNEXES

ANNEX 1: GENERAL INFORMATION

CC Name: **CCQM**
Date Established: **1993**
Number of Members: **26 members; 13 Observers; 6 Liaisons**
Number of Working Groups: **12**
Number of Participants at last meeting: **101**
Number of Institutes participating in CCQM WGs: **56**
Periodicity between Meetings: **1 year**
Date of last meeting: **26-28 April 2021**
CC President: **Dr Sang-Ryoul Park, KRISS**
Number of KCs organized (from 1999 up to and including 2020): **235 Key comparisons**
Number of Pilot studies organized (from 1999 up to and including 2020): **159 stand-alone pilot studies**
Number of CMCs published in KCDB supported by CC body activities (As of March 2021): **6346**

ANNEX 2: LIST OF PLANNED KEY AND SUPPLEMENTARY COMPARISONS AND PILOT STUDIES

Comparisons that are planned with a formal start date can be found on the BIPM website at the address below and are updated by the CCQM on a 6-monthly basis.
https://www.bipm.org/documents/20126/41532304/Planned+Future+CCQM+Comparisons/e8683f8f-0dd4-8d79-3e9c-e3eae0b806a4 Individual WG strategy documents contains further information of plans for future comparisons, and this data has been summarized in the table below.
A summary of registered comparisons that are active or completed is available at https://www.bipm.org/documents/20126/48101949/CCQM_KCs_PSs.xlsx/eaf57589-7beb-52d0-60c6-ca8e21481c03 , and has been used to summarize WG comparison activities in the 2017-2020 period in the table above.

CCQM Working group	Number* of registered Key comparisons 2017-2020	Number* of registered (standalone) Pilot Studies 2017-2020	Estimated Number of Key comparisons for 2021-2030	Estimated Number of (standalone) Pilot Studies for 2021-2030
Gas Analysis Working Group (GAWG)	14	1.5[a]	24	3
Organic Analysis Working Group (OAWG)	13	1	26	3[b]
Inorganic Analysis Working Group (IAWG)	8.5	1.5	28[c]	6[c]
Electrochemical Analysis WG (EAWG)	6	1	18	3[b]
Surface Analysis Working Group (SAWG)	3	1	12[d]	10[d]
Isotope Ratio Working Group (SAWG)	1	2.5	8[e]	6[b]
Nucleic acid Analysis Working Group (NAWG)	0	3	4[f]	8[b]
Protein Analysis WG (PAWG)	3.5	2.5	9[b]	6[b]
Cell Analysis Working Group (CAWG)	0	1	1	6[g]
Total number of CCQM comparisons (2017-2020)	49	15	-	-
Average number of CCQM comparisons per year (2017-2020)	12	4	-	-
Estimated total number of CCQM comparisons (2021-2030)	-	-	130	51
Estimated average number of CCQM comparisons per year (2021-2030)	-	-	13	5

Table Annex 2: Estimations of the number of key comparisons and stand-alone pilot studies that are foreseen to be run each year during the period 2021-2030 by each of the current CCQM WGs, and data from 2017-2020.

[a] Non integer numbers occur in the table as comparison is run across 2 WGs

[b] Based on pilot study organization rate in 2017-2020

[c] Based on comparison organization rate planned for 2019-2023

[d] Based on comparison organization rate planned for 2021-2025

[e] Includes comparisons planned with GAWG

[f] Based on historic rate of KC organization within WG

[g] Based on mixture of pilot study organization rate in 2017-2020 and 2 year plan within WG strategy

ANNEX 3: REFERENCES TO INDIVIDUAL TECHNICAL SUBJECT AREA STRATEGIES FOR 2021-2030

Description	Link
CCQM CAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/2071059/CCQM-CAWG+Strategy+document+2021-2030.pdf/19b75816-2e60-b1a5-1f83-78b8ef550d19
CCQM IRWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465585/CCQM-IRWG+Strategy+document+2021-2030.pdf/41d93edc-c543-8ed4-883b-26e97ac93867
CCQM GAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465561/CCQM-GAWG+Strategy+document+2021-2030.pdf/868de3d5-f89e-3eaf-a3da-b0bb7b9c985f
CCQM OAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465491/CCQM-OAWG+Strategy+document+2021-2030.pdf/786d14ba-829d-9c77-7481-19529759e19a
CCQM EAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465543/CCQM-EAWG+Strategy+document+2021-2030.pdf/5ca7b44b-9962-8f51-9615-0fcbc3743f05
CCQM PAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465501/CCQM-PAWG+Strategy+document+2021-2030.pdf/a3159c77-5198-7432-474c-33e84d891d08
CCQM IAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465575/CCQM-IAWG+Strategy+document+2021-2030.pdf/56c8a480-f539-0ea2-b486-7c0fee0e0c1c
CCQM SAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465515/CCQM-SAWG+Strategy+document+2021-2030.pdf/a0778065-5ab3-8a4f-f8a2-45a2d11a6e2e
CCQM NAWG Strategy Document 2021-2030	https://www.bipm.org/documents/20126/57465599/CCQM-NAWG+Strategy+document+2021-2030.pdf/77097cb9-1089-643c-fa29-5fc3232badd1

ANNEX 4: WORK PROGRAMME OF THE BIPM LABORATORIES (2021-2030)

The implementation of the CCQM strategy is supported by the BIPM Chemistry Department providing the CCQM Executive Secretary Role, coordination of comparisons in technical areas prioritized by the CCQM, laboratory-based knowledge transfer programmes for National Metrology Institutes with emerging metrology systems, the JCTLM database and support for engagement with stakeholder communities.

Key outputs from the work programme of the BIPM Chemistry laboratories in support of the CCQM and participating NMIs and DIs in the 2016-209 programme included:

- 14 comparison exercises coordinated by the BIPM with 291 NMI participations covering NMI standards/ reference capabilities for Greenhouse Gases; Air Quality Gases; Organics; Proteins/Peptides;
- 19 peer reviewed publications supported by 16 seconded visiting scientists, including papers on reference methods for Greenhouse Gases and isotope ratios; accurate surface ozone measurements; application of quantitative NMR; protein/peptide clinical analytes;
- A knowledge transfer programme on Mycotoxin standards for Food Safety Analysis developed with support from 7 visiting NMI scientists with training secondments by 11 NMI visiting scientists;
- A knowledge transfer programme on Application of FTIR for gas standard analysis as part of Metrology for Clean Air programme with training secondments completed by 13 NMI visiting scientists;
- 7 measurement guidelines on the application of internal standards for qNMR characterization of organic standards published.

Interaction between the BIPM laboratory and NMIs has been particularly strengthened by strong uptake of visiting scientist placements in the BIPM Chemistry Department, with 47 visiting scientists undertaking placements within the department, usually for periods between 3 months and 18 months during the 2016-2019 period.

The future CCQM strategic plan relies on a range of comparisons underpinning a broad range of NMI capabilities through core capability comparisons in addition to specific analyte-matrix comparisons which are required when uncertainties are challenging and critical to the application of the capability. In consequence, CCQM comparisons include both:
a) core comparisons which underpin fundamental and a broad range of capabilities following a model and periodicity determined by the concerned CCQM WG;
b) specialised comparisons which can have regular repeat periodicities to closely monitor long term performance of capabilities;

BIPM laboratory activities enable a long-term commitment to comparison coordination, which is best adapted to periodic comparisons and allowing close monitoring of performance. The CCQM WG strategy documents, for the Gas, Isotope Ratio, Organic and Protein Analysis WGs, foresee BIPM coordinated CCQM comparisons of
a) NMI/DI primary calibrators/capabilities for prioritized green-house gases and air quality gases
b) NMI/DI calibrators/reference capabilities for $\delta^{13}C$ and $\delta^{18}O$ in CO_2, CO_2 in air and carbonates
c) NMI/DI core capabilities for primary reference materials and calibrators for small organic molecules
d) NMI/DI core capabilities for primary reference materials and calibrators for peptides and proteins

The BIPM comparison coordination activities provide substantial support to the specific working groups for whom they have been prioritized. The relative level of support provided is demonstrated

in Figure 1 of Annex 3, where the resources of individual institutes to comparison coordination of CCQM GAWG comparisons is depicted. Similar levels of support are provided for the CCQM Organic WG, Protein WG and newly formed Isotope Ratio WG.

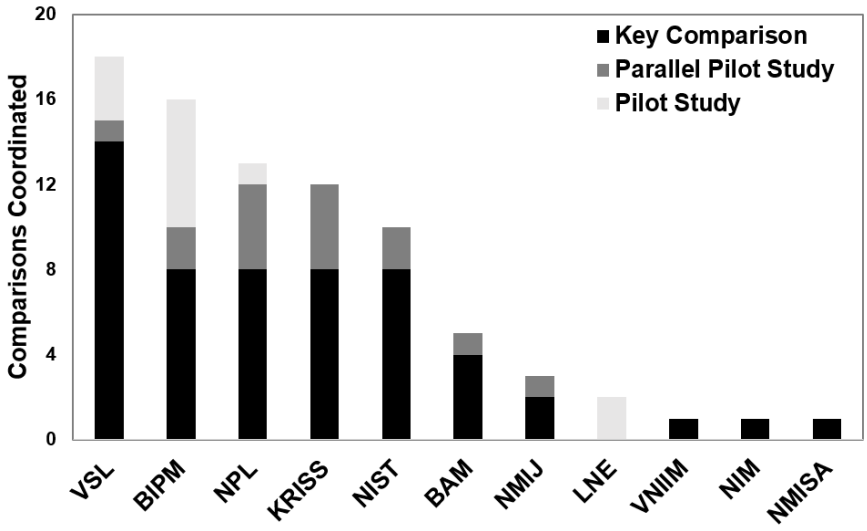

Figure 1 Annex 3 Bar chart from CCQM GAWG strategy document showing previous coordinators of CCQM GAWG key comparisons, pilot studies and parallel pilot studies.

The BIPM also offers comparisons run as a series of bilaterals, with BIPM.QM-K1 being the long-standing example for Ozone standard Photometers, and in the future strategy this will be extended to CO_2 in air standards, and Isotope ratios in CO_2 (pure and in air matrix). The benefits for NMIs/DIs of this series of comparisons is the fast turnaround time and ability to monitor for potential biases over time against an independent stable reference. These facilities also serve as the basis for future Knowledge Transfer programmes.

The laboratory-based capacity building and knowledge transfer laboratory activities initiated at the BIPM in 2016 in the fields of Metrology for Safe Food and Feed and Clean Air, supporting KT activities in the RMOs, have had good uptake. The future strategy sees the expansion of these to cover Pesticides and Veterinary Drugs relevant to residues in Food, Dynamic standards for Air Quality Gases, Pure peptides for Laboratory Medicine. The visiting scientist placement programme will be reinforced with on-line training modules, increasing the possibility of participation in the next period.

Implementation of machine-readable databases with data following FAIR principles, will be addressed in the first instance with a database for CO_2 scale comparisons in support of the CCQM GAWG Task group on GHG Scale comparisons. This builds on previous database projects, such as the JCTLM, and the development and publication of reference data for qNMR internal standards, which are maintained.

The CIPM evolving needs in metrology study for 2030+ foresees the establishment of interdisciplinary fora for discussion of identified challenges and development of international metrology actions to support them. The sectors that have initially been identified by the CIPM are: Climate change and Environment; Health and Life Sciences; Food Safety; Energy; Advanced Manufacturing; Digital Transformation; and 'New' Metrology. The fora will require support from the BIPM Secretariat and notably the Chemistry Department, with a considerable number of themes having strong technical overlap with the CCQM. Initial activities and support for the organization of a 'Metrology for Climate Action' Workshop planned for 2022 have already been initiated.

A more detailed description of BIPM Chemistry Laboratory activities in support of the CCQM mission during the period 2021-2030 is described in the following table.

Detailed strategy	Plans (2022-2023)	Long Term (2024-2029)
To demonstrate and improve equivalence and support the establishment of national measurement standards and services for: – **greenhouse gases**, at performance levels required to support national energy and environmental priorities; – **major air quality gases**, at performance levels required to support national health and environmental priorities.	*To coordinate CCQM and BIPM on-going comparisons of standards for:* • *methane and carbon dioxide in air, with uncertainties congruent with global and urban monitoring requirements;* • *isotope ratios of carbon dioxide with uncertainties congruent scale definitions and emission source apportionment* • *surface ozone for accurate air quality monitoring;* *To provide on-line knowledge transfer courses for NMIs establishing:* • *NO_2 air quality dynamic standards* • *Reactive gas standards and FTIR facilities*	• *To provide the suite of highest-priority comparisons of standard gas mixtures addressing global energy and environmental priorities.* • *To provide knowledge transfer activities within regions and to NMIs establishing clean air metrology programmes for greenhouse gas, isotope ratio and air quality standards, and with emerging metrology systems.* • *To support programmes to mentor NMI scientists coordinating gas standard comparisons for the first time*
To demonstrate and improve equivalence and support the establishment of national reference measurement capabilities and services in organic and biochemical measurement for: – **small organic molecules**, at performance levels required to support reference measurement systems for laboratory medicine, food safety and trade in primary produce, forensics, environmental analysis and pharma. – **peptides and proteins**, at performance levels required to support reference measurement systems for laboratory medicine and health care sectors.	*To coordinate CCQM comparisons on calibration standards for:* • *viral antibodies (monoclonal SARS-CoV-2 antibody).* • *small molecule organics (Pesticides and Veterinary drugs)* • *diagnostic peptide biomarkers (PTH(1-84))* • *mycotoxin food contaminants (PAT and DON)* *To provide reference data on ^{19}F internal standards for qNMR, supporting NMI measurement services.* *To provide on-line knowledge transfer courses and studies for NMIs establishing:* • *Mycotoxin in food reference systems* • *Pesticide and Veterinary Drug Residue in Food Refence Systems*	• *To provide the suite of comparisons for large and small molecule calibrators of the highest global importance.* • *To provide knowledge transfer activities within regions and to NMIs establishing food safety and laboratory medicine reference measurement capabilities, and with emerging metrology systems.* • *To support programmes to mentor NMI scientists coordinating organic and peptide calibrant standard comparisons for the first time*
To promote and develop the use of SI traceable standards and measurements with inter-governmental and other stakeholders for use in chemical and biochemical analysis.	*To support CCQM task groups in:* • *Coordinating a global change in ozone reference measurements;* • *Developing an extended global greenhouse gas measurement system* *To develop the JCTLM Database with machine readability for greater uptake of reference measurement systems in clinical diagnosis* *To develop a Greenhouse Gas measurement and meta data database following FAIR principles enabling greater uptake of NMI standards* *To work with stakeholder communities in running the Metrology for Climate Action Conference and Reliable measurements in response to the Covid-19 Pandemic Webinar Series*	• *To increase participation in the CIPM MRA and uptake of NMI measurement services by International Organizations with laboratory networks active in chemical and biochemical measurement.* • *To support CCQM task groups in interfacing with and providing technical solutions to global stakeholder communities* • *To support the availability of FAIR data for chemical and biochemical reference measurement systems, with the development of appropriate databases* • *To support sectoral and cross committee efforts in promoting and developing the use of the SI, notably in the health, environmental, food safety and advanced manufacturing sectors.*

Table 1 Annex 3 BIPM activities in support of the CCQM Strategic plan 2021-2030.

ANNEX 5: SUMMARY OF WORK ACCOMPLISHED (2017-2020)

Summaries of work accomplished in the 2017-2020 period in each of the technical subject CCQM working groups is described within their individual strategy documents. A number of highlights and CCQM achievements are described here.

a) Global system of comparisons for chemical and biological measurement standards
Organization and coordination of CCQM key comparisons and pilot studies has followed the planning outlined within the 2017-2026 CCQM Strategic plan document. Fourty-nine key comparisons and fifteen stand-alone pilot studies were registered as starting in the CCQM WGs between 2017 and 2020, resulting in on-average 16 new comparison studies initiated each year during this 4-year period, meeting the estimation of 16 to 17 annual comparison studies foreseen in the 2017-2026 strategy document.

b) Evolution of CMCs to meet stakeholder needs
During 2019 and 2020 the CCQM Key Comparison and CMC Quality WG (CCQM-KCWG) have worked with the RMO Metrology in Chemistry Technical Committee Chairs and the BIPM KCDB Office to ensure an orderly transition towards the use of the web-based system with KCDB 2.0 for CMC submission and review. This has been achieved in a system that retains a yearly timetable for CMC submission and review with cycle XXII CMCs being the first to follow this process. The change in procedures have been fully documented by the CCQM KCWG in their guideline document available at https://www.bipm.org/documents/20126/48767434/CCQM-KCWG_Guidance_document_2020.pdf/4befce10-c278-2832-dd6b-70799e2ba106

The technical subject WGs of CCQM are developing guidelines for drafting and review of broad claim CMC claims. As the guidelines are developed for these, they are made publicly available and referenced in the KCWG guidance document.

c) Ensuring reliability of measurements in response to the Covid-19 pandemic

The CCQM NAWG and PAWG initiated comparisons in 2020 to support NMI efforts to develop reference materials and methods to support the reliability of testing in response to the Covid-19 pandemic. CCQM-P199.b, on SARS-CoV-2 copy number quantification, was launched by the CCQM NAWG, with preliminary results reported in 2020. CCQM-P216, on SARS-CoV-2 monoclonal antibody quantification, was launched by the CCQM-PAWG in 2020, with results to be reported in early 2021.

The comparison study (CCQM-P199.b) organized by the CCQM Working Group on Nucleic Acid Analysis (CCQM-NAWG) and coordinated by the National Measurement Laboratory at LGC (UK), NIM (China), NIBSC (UK) and NIST (US), required quantification of the same viral genetic sequences targeted by many of the diagnostic tests. The RT-dPCR results were found to agree very well with each other and different SI-traceable non-molecular orthogonal methods; most values were within +/-40% of mean. The reproducibility of the method is unprecedented for absolute molecular measurements, where orders of magnitude of spread in reported copy numbers can be found using conventional molecular diagnostic methods. This work, made possible by over a decade of CCQM led collaborative efforts within the bio-metrology community, represents the most comprehensive example of highly reproducible and sensitive measurement of RNA and opens the possibility for SI-traceable quantification of viral genes. The methods and results are already being used by National Metrology Institutes to value assign reference materials that underpin the quality of SARS-CoV-2 diagnostic tests. The comparison was conducted under an accelerated timeline, with the worldwide comparison

completed in under six months, and the final report expected in early 2021. In the longer term, these capabilities have far wider implications as they can provide a global foundation for ensuring the accuracy of associated molecular methods whether applied to COVID-19, as preparation for any future global pandemic or for wider diagnostic uses such as in testing for antibiotic resistance or cancer.

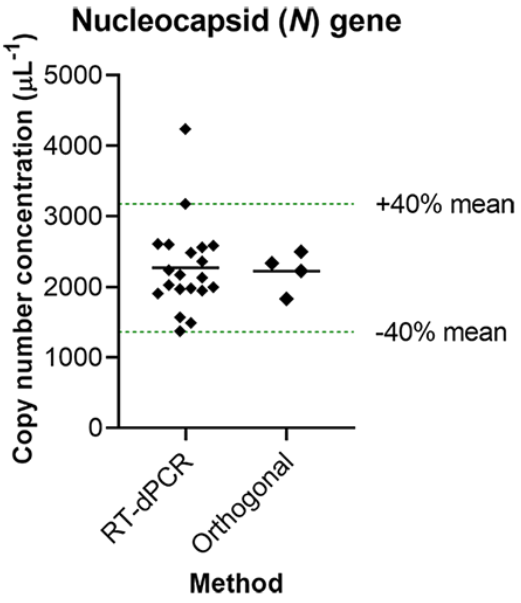

Figure illustrating results from part of the study demonstrating that laboratories performing molecular RT-dPCR methods are able to perform with good agreement with each other and the SI-traceable orthogonal methods (isotope-dilution mass spectrometry and single molecule flow cytometry), the latter providing the basis for the RT-dPCR method's claimed accuracy. The RT-dPCR results were compared with orthogonal methods using different concentrations of the same RNA material. The different concentrations were prepared using gravimetric dilution. Diamonds show individual laboratories' results with solid black line (mean) and dotted green lines +/-40% of mean value.

The CCQM initiated a series of webinars on 'Ensuring the reliability of measurements in response to the Covid-19 pandemic' with the first two held in July and December 2020. Invited expert speakers, who were working on establishing tests and testing schemes within countries or running proficiency tests for these were invited to present their activities and raise on needs for standards and controls in these processes. Recordings of the webinars are available for viewing vias the BIPM YouTube channel at: https://youtu.be/0Jh65cEPIrI https://youtu.be/V_B02SfY_CQ https://youtu.be/AMdRJhEZAy0

d) Advances in Metrology in Chemistry and Biology

The CCQM Workshop on Advances in Metrology in Chemistry and Biology, marking the 25th anniversary of the CCQM, was organized at the BIPM in April 2019, and resulted in nineteen publications in the related Metrologia Special issue (listed below) highlighting advances in various fields of chemical and biological measurement science including a paper on Amount of substance and the mole in the SI.

1) SI traceability and scales for underpinning atmospheric monitoring of greenhouse gases

Paul J Brewer *et al* 2018 *Metrologia* **55** S174 https://doi.org/10.1088/1681-7575/aad830

2) A higher order method for the determination of total phosphorus in human serum

Fransiska Dewi *et al* 2018 *Metrologia* **55** S195 https://doi.org/10.1088/1681-7575/aae27d

3) Cobalt determination in the hair of patients after metal-on-metal hip implants by instrumental neutron activation analysis

G D'Agostino *et al* 2019 *Metrologia* **56** 014001 https://doi.org/10.1088/1681-7575/aaee37

4) Metrologically traceable quantification of trifluoroacetic acid content in peptide reference materials by ^{19}F solid-state NMR

Andreas Brinkmann *et al* 2019 *Metrologia* **56** 024002 https://doi.org/10.1088/1681-7575/ab04e3

5) Comprehensive certification of a testosterone calibration standard facilitating the investigation of charged aerosol detection for the quantification of impurities of related structure

Stephen R Davies *et al* 2019 *Metrologia* **56** 024004 https://doi.org/10.1088/1681-7575/ab0cbb

6) Total evaporation technique for high-accuracy isotopic analysis of isotopically enriched molybdenum by negative thermal ionization mass spectrometry

Panshu Song *et al* 2019 *Metrologia* **56** 024005 https://doi.org/10.1088/1681-7575/ab0a11

7) Recommendation of a consensus value of the ozone absorption cross-section at 253.65 nm based on a literature review

J T Hodges *et al* 2019 *Metrologia* **56** 034001 https://doi.org/10.1088/1681-7575/ab0bdd

8) Conventional and new traceability schemes of organic standards for safe water supply in Japan

9) Masahiko Numata *et al* 2019 *Metrologia* **56** 034002 https://doi.org/10.1088/1681-7575/ab04c6

Metrological advances in reference measurement procedures for electrolytic conductivity

Steffen Seitz *et al* 2019 *Metrologia* **56** 034003 https://doi.org/10.1088/1681-7575/ab1527

10) Characterization of water in methylcyclohexane as a certified reference material for determination of trace water content in liquids

Shinsuke Inagaki *et al* 2019 *Metrologia* **56** 034004 https://doi.org/10.1088/1681-7575/ab1444

11) The role of ICP-MS in inorganic chemical metrology

M Sargent *et al* 2019 *Metrologia* **56** 034005 https://doi.org/10.1088/1681-7575/ab0eac

12) Advances in reference materials and measurement techniques for greenhouse gas atmospheric observations

Paul J Brewer *et al* 2019 *Metrologia* **56** 034006 https://doi.org/10.1088/1681-7575/ab1506

13) Measurement of the number concentration of gold nanoparticle suspension by scanning electron microscopy

Kazuhiro Kumagai and Akira Kurokawa 2019 *Metrologia* **56** 044001 https://doi.org/10.1088/1681-7575/ab1f37

14) Amount of substance and the mole in the SI

Bernd Güttler *et al* 2019 *Metrologia* **56** 044002 https://doi.org/10.1088/1681-7575/ab1fae

15) Nitrogen content of amidosulfuric acid assayed by coulometric titration with electrogenerated hypobromite ions: establishment of SI traceability of nitrogen involving amidosulfuric acid, ammonium chloride and sodium chloride

Toshiaki Asakai 2019 *Metrologia* **56** 044003 https://doi.org/10.1088/1681-7575/ab27ea

16) An FTIR method for accurate CO_2 mole fraction measurements with correction for differences in isotopic composition of gases

Edgar Flores *et al* 2019 *Metrologia* **56** 044005 https://doi.org/10.1088/1681-7575/ab2941

17) Establishment of measurement traceability for peptide and protein quantification through rigorous purity assessment—a review

Ralf D Josephs *et al* 2019 *Metrologia* **56** 044006 https://doi.org/10.1088/1681-7575/ab27e5

18) SoGAT—25 years of improving the measurement of nucleic acids in infectious disease diagnostics (a review)

Clare Morris *et al* 2019 *Metrologia* **56** 044007 https://doi.org/10.1088/1681-7575/ab2aa3

19) Determination of the isotopic composition of hafnium using MC-ICPMS

Shuoyun Tong *et al* 2019 *Metrologia* **56** 044008 https://doi.org/10.1088/1681-7575/ab2995

e) CCQM resolution in support of accurate atmospheric monitoring

The CCQM passed Recommendation 1 (2020): On the recommended value of the ozone absorption cross-section per molecule at 253.65 nm (air) for applications including the measurement of atmospheric ozone amount fractions.

It recommended that:

- the 2019 value of **1.1329×10^{-17} cm^2** and standard uncertainty **0.0035×10^{-17} cm^2** be adopted for the ozone absorption cross-section per molecule at 253.65 nm (air) for use in ozone measurement standards maintained at the BIPM and for the calculation of the reference value for the BIPM.QM-K1 on-going comparison of surface ozone measurement standards,
- the BIPM and the NMIs work with the atmospheric monitoring community and other stakeholders towards a global implementation of the 2019 value for the ozone absorption cross-section per molecule at the mercury-line air wavelength,
- the date of implementation of the 2019 value for the ozone absorption cross-section per molecule at 253.65 nm (air) be decided after consultation with stakeholder communities, including the CCQM-GAWG workshop scheduled for October 2020,
- all NMIs / DIs adopt the new value and uncertainty of the ozone absorption cross-section per molecule at 253.65 nm (air) at the date of implementation to ensure international comparability of surface ozone measurements is maintained.

f) Strengthening stakeholder engagement

Memorandums of Understanding were signed by the CIPM President between BIPM and two liaison organizations of the CCQM, IUPAC and IFCC in 2019 and 2020 respectively. The agreements pave the way to strengthening stakeholder engagement within the CCQM.

g) Capacity building and Knowledge Transfer activities for NMIs with emerging metrology systems

The first comparison organized through the CCQM OAWG and coordinated by the BIPM was launched in 2018 and completed in 2020. This was the first in a series of comparisons on mycotoxin calibrations solutions to support National Metrology Institutes that have participated in the BIPM Metrology for Safe Food and Feed CBKT Programme and which are establishing measurement capabilities and certified reference materials for their food testing sectors.

The first comparison, CCQM-K154.a, focused on Zearalenone calibration solutions. Zearalenone is a mycotoxin produced by certain Fusarium and Gibberella species of fungi and may be found world-wide in a number of cereal crops such as maize, barley, oats, wheat and rice. Mycotoxins can cause a variety of adverse health effects in humans and animals, and regulations have been established world-wide for certain food- and feedstuffs to protect their health. The comparison underpins NMI capabilities for producing and value assigning mycotoxin calibrants, which provide the basis for accurate and traceable measurements in the food analysis sector. The comparison series on mycotoxin calibrants will also cover aflatoxin B1, deoxynivalenol, patulin and ochratoxin A.

h) CCQM structural changes to support its mission

The CCQM established a new working group on Isotope Ratios in 2018.

In April 2017 the CCQM formed a task group to investigate on the current state of isotope ratio metrology and to draw conclusions concerning a potential engagement in this field. In April 2018, this task group presented its report the CCQM. The report and its conclusions convinced the CCQM to establish a new working group on isotope ratios (IRWG). The IRWG took up work immediately and organized regular meetings since then, one in April and one in October of each year. In parallel to the meetings work started on strategic issues such as identifying the measurement spaces, required comparisons to cover those spaces and on harmonizing CMC formats in isotope ratio measurements. Practical work focused on the planning and initiating of the first Key Comparison and Pilot Studies of the IRWG.

<u>CCQM-P204 (Start 02/2020)</u>

The Pilot Study CCQM-204 is aimed at evaluating the level of compatibility of laboratories' measurement capabilities to value assign isotope ratios in samples of pure CO2 gas, (δ^{13}C vs. VPDB and δ^{18}O vs. VPDB-CO_2). It will also provide insight into the traceability chains and reference standards being employed to currently achieve these measurement results. The comparison is organised by the BIPM and the IAEA. It will consist of pure CO_2 samples being prepared by the BIPM. The BIPM will fill and send to each participating laboratory four 50 mL cylinders containing pure CO_2, each one filled with a gas with a different nominal δ^{13}C value vs VPDB: -1 ‰; -9 ‰; -35 ‰; and -42 ‰. Laboratories wishing to participate in the comparison will be required to purchase and send the 4 small cylinders and valves (mandatory models recommended by the BIPM) for filling.

Results of the comparison will be compiled by the BIPM and evaluated jointly by the BIPM and the IAEA. All calculations will be performed based on the comparison results and the values and uncertainties submitted by the participants and the study coordinators. Nominal values for each gas sample distributed to participants will be based on measurements performed at the BIPM and the IAEA with traceability to standards maintained at the IAEA. Proposals for reference values for the samples will be calculated from the results from the participants. The results of the comparison are expected to provide a description of the current level of performance of laboratories and the state of the art to be achieved, as well as information for planning a future Key Comparison.

CCQM-K167/P211/P212 (Start 11/2019)

Verification of the authenticity of food items is essential to ensure the quality and safety of food products. Carbon isotope delta, $\delta^{13}C_{VPDB}$, measurements are routinely used to determine the authenticity of food products by determining the source of the food product and detecting adulteration of the food products via addition of unreported additives.

The first Key Comparison for $\delta^{13}C_{VPDB}$ measurements (CCQM-K140) was conducted in 2015-2016, and honey samples were measured. The October 2018 meeting of the IRWG in Ottawa, Canada, included a need for more Key Comparisons for SHNOC measurements. This proposed Key Comparison will support Calibration and Measurement Capability (CMC) claims for $\delta^{13}C_{VPDB}$ measurements, allowing for institutions to demonstrate and improve core capabilities in this area. The goal of this Key Comparison is to establish current best achievable uncertainties for $\delta^{13}C_{VPDB}$ measurements.

The Key Comparison is coordinated by NRC Canada and is focusing on $\delta^{13}C_{VPDB}$ measurements in pure vanillin. In parallel to K167 the Pilot Study P211 is organized, which gives less experienced institutes the chance to participate. In addition, P212 is conducted, which evaluates the coherence of $\delta^{13}C_{VPDB}$ values assigned to the various international reference materials in a multi-laboratory intercomparison.

CCQM-P213 (Start 02/2020)

Accurate and precise isotope ratio measurements are playing an increasingly important role in modern analytical sciences. Significant and often unique applications include terrestrial and extra-terrestrial investigations involving geochronology, archaeology, provenance studies (chemical “finger-printing”), life/medical sciences, forensic sciences, environmental and atmospheric sciences, as well as traditional analytical chemistry and physics. Most studies are reporting isotope ratios in a delta notation, which allows small isotopic differences to be expressed unambiguously without the need for the exact knowledge of absolute isotope ratios of the standard, and which is fit for purpose for many studies. After numerous discussions at Isotope Ratio Working Group (IRWG) meetings (October 2018, April 2019 and October 2019), it was decided to conduct a Pilot Study on delta Cu isotope ratio measurements relative to NIST SRM976 Cu isotopic standard in high purity materials first, to demonstrate measurement capabilities of NMIs/DIs.

ANNEX 6: EXAMPLES OF IMPACT OF CCQM ACTIVITIES (2017-2020)

Seventeen case studies of the impact of CCQM activities from the 2017-2020 period are provided within the technical subject CCQM Working Group strategy documents.

Case Study N°	Description	Document describing case study
1	Primary Methods and Standards for Organic Measurements: qNMR internal standards and related techniques	OAWG strategy document
2	Pefluorinated alkyl substances (PFAS) – A persistent Global environmental issue	OAWG strategy document
3	Mycotoxins in Foodstuffs	OAWG strategy document
4	Measurement Services Supported by OAWG Key Comparisons on Clinically Relevant Small Molecule Organic Biomarkers	OAWG strategy document
5	GMOs in Food	NAWG strategy document
6	Support for equivalence of pH CRMs	EAWG strategy document
7	pH of seawater	EAWG strategy document
8	Conductivity in the pure water range	EAWG strategy document
9	Roadmap for purity determination (high-purity elements and inorganic compounds)	IAWG strategy document
10	Copper calibration solutions (CCQM-K143/P-181)	IAWG strategy document
11	Counting nanoparticles	IAWG strategy document
12	Toxic and essential elements in bovine liver	IAWG strategy document
13	New generation reference materials for Greenhouse Gas Monitoring	GAWG strategy document
14	A new recommended value for the Ozone Cross Section at 253.65 nm	GAWG strategy document
15	Diversification of gas supply	GAWG strategy document
16	Absolute SI quantification of DNA	NAWG strategy document
17	Towards SI traceable RNA measurement	NAWG strategy document

ANNEX 7: DOCUMENT REVISION SCHEDULE

Document name; type of revisions; date

Document Reference	Type of revision	Date
Version 0.3	Draft by SPWG sent to CCQM for comment	02/04/2021
Version 1.0	Updated by SPWG based on CCQM comments	21/06/2021