CITAC
Cooperation on International Traceability in Analytical Chemistry

CITAC NEWS

APRIL 2020

FOREWORD BY THE CHAIR

CITAC ACTIVITY IN 2019

Michela Sega // INRIM, Italy

The term of my chairpersonship is rapidly coming to its end and it is time to draw some conclusions. The past three years were very successful. Lots of activities have been carried out, fruitful cooperation with other organizations were reinforced, new members joined in, thus enlarging CITAC family, lively meetings were organized. Nevertheless, a lot of work remains for CITAC to face the metrological traceability issues on the global scale of an area in rapid and massive development as metrology in chemistry and biology is.

The cooperation with other International Organizations is a specific feature of CITAC. In 2019, it took place both in the participation in joint projects and in the organization of events in the fields of amount of substance, quality and metrological traceability. On the site of the cooperation with IUPAC, the IUPAC project n. 2019-012-1-500 "Influence of a mass balance constraint on uncertainty of test results of a substance ore material and risks in its conformity assessment" has started in July 2019. It deals with compositional data, as the relevant techniques of data analysis are still not implemented in metrology and analytical chemistry, as well as in conformity assessment, even if there is an extensive literature stressing how traditional statistical techniques may produce inadequate results if applied on raw compositional data without suitable transformation.

A joint IUPAC/CITAC Workshop "Quality of Test results for conformity assessment of a chemical composition - what is good and what is bad?" was held in Tel Aviv, Israel on 21st January. The strong cooperation with the European sister organization Eurachem, gave excellent results also in 2019. The second edition of the Eurachem/CITAC Guide "Measurement uncertainty arising from sampling: A guide to methods and approaches" was published in 2019. It aims to describe various methods to be used to evaluate the uncertainties arising from the processes of sampling and the physical preparation of samples. In 2019 a Eurachem /CITAC leaflet "Metrological Traceability of Analytical Results" was also published. The Eurachem Workshop "Uncertainty from sampling and analysis for accredited laboratories" was held in conjunction with Eurolab and CITAC on 19th-20th in Berlin, Germany.

It is also worthwhile to mention that in 2019 CITAC joined the Stakeholder Advisory Board of the European Joint Research Project "EMUE - Examples of Measurement Uncertainty Evaluation", carried out within the framework of the European Metrology Programme for Innovation and Research (EMPIR). This project provides a comprehensive set of worked examples illustrating how the principles of measurement uncertainty evaluation can support and give added value to normative and related practices. In the same year 2019 CITAC joined also the Stakeholder Advisory Board of the IUPAC Project "Influence of a mass balance constraint on uncertainty of test results of a substance or material and risks in its conformity assessment". This project relates to the

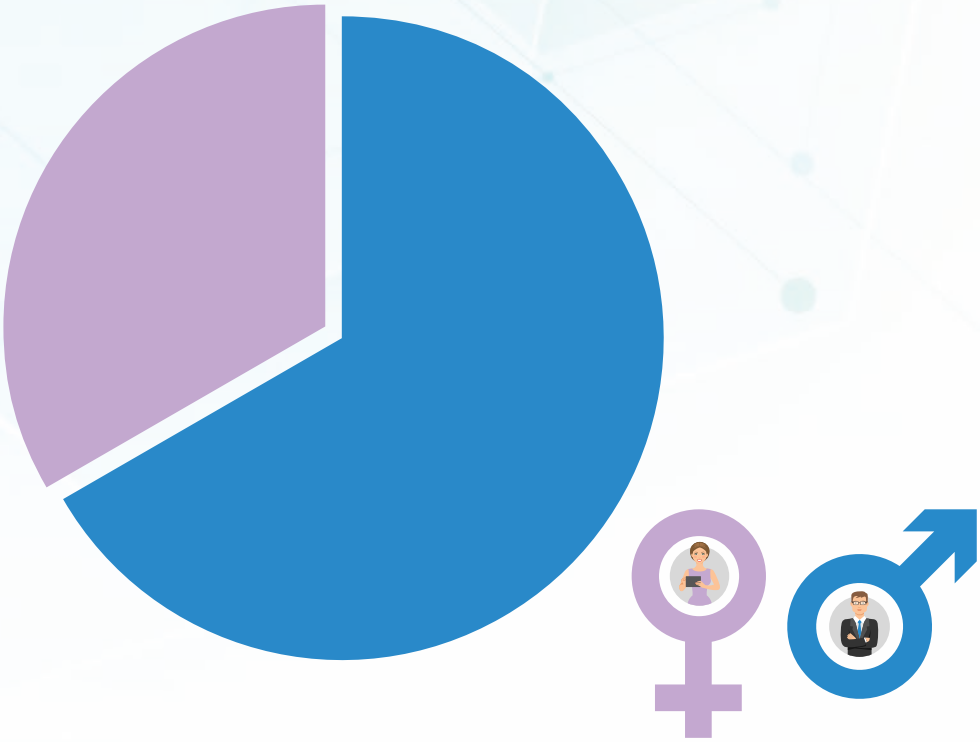

Fig. 1: Gender distribution of CITAC members

cases in which the component contents of a substance or material are linked by a mass balance constraint, i.e. when the sum of their mass fractions, molar fractions or any other positive quantity ratios is 100 % or 1. In such cases the test results of the substance or material are "compositional data" with a "spurious" correlation.

I would like to congratulate the Winners of CITAC Best Paper Award 2018, authors of important and innovative papers in the field of metrology in chemistry, who presented their work in the 34th CITAC meeting held in Sèvres on 13th April 2019: Dr. Robert Wielgosz, BIPM, and his coauthors in Metrologia 55 (2018) S174-S181; Dr. Jeremy Melanson, NRC, Canada, and his coauthors in Anal. Bioanal. Chem. 410 (2018) 6719-6731; Dr. Michael Nelson, NIST, USA, and his coauthors in Anal. Chem. 90 (2018) 10510–10517. According to the best CITAC tradition, the three papers are related to different innovative issues and the presentation of the works raised interesting discussions during the meeting.

These last three years, were particularly successful in renewing the CITAC membership: new colleagues joined CITAC, bringing new skills and competencies and a lot of enthusiasm. I would like to give a special warm welcome to Dr. Dr Narine Oganyan (Russia) who joined CITAC family in 2019.

Due to this new memberships, at present CITAC counts 39 members, coming from all the continents and a 13 of them, a third, are women, as shown in figure 1.

In conclusion, I would like spend some words to express my gratitude to CITAC Executive Committee members, who shared with me all the problems and helped me in finding constructive and active solutions: the Vice-Chair Dr. Bernd Güttler, the Secretary Prof. Ricardo Silva, the Past-Chair Dr. Laly Samuel, the Treasurer and Internet Administrator Prof. Wolfhard Wegscheider and, last but not least, the CITAC News Editor Dr. Ilya Kuselman. Many thanks also to Ms. Karin Schober, the Treasurer Assistant and Webmaster, and to every CITAC member who supported our work in any form. I would like to wish all the success to the next CITAC Board, which will be elected during the upcoming 35th CITAC Members Meeting.

ADDRESS OF THE VICE-CHAIR

Bernd Güttler // PTB, Germany

In some contrast to other fields of metrology, its application in chemistry always needs to be more targeted to the most important requirements of its stakeholders. This is because of the sheer number of possible measurands and applications in chemistry. A strategic approach is necessary that may lead to different priorities depending on the most pressing needs in different economies. Nevertheless, some targets are quite similar in their overwhelming importance and their technical requirements everywhere in the world and are demanding our foremost attention. One of them is biomedicine.

This is not only because of its relevance for human health and well-being (approximately 70% of clinical decisions are based on in vitro diagnostic tests[1]) but also because biochemistry and biomedicine have evolved so rapidly over the last two decades and fostered new measurements for medical diagnosis and new treatment strategies[2,3]. The findings and procedures in this area are especially important for diseases that are leading causes of morbidity and mortality such as cancer, cardiovascular or neurodegenerative diseases. Accurate and precise measurements of quantities of clinical importance are essential to achieve comparable results for patient care in all these cases. Within this context, measurement procedures at the level of DNA, proteins and cells are essential prerequisites for both fundamental biomedical research as well as for their reliable clinical application.

The demand for quality of biochemical measurements is indeed recognized now in biochemical research and in biotechnology. This is because high-class published results often cannot be reproduced by other groups. Venture capitalists in biotechnology estimate that more than one-half of published research results cannot be exploited[4] as a consequence of these and other shortcomings. The situation was described as "reproducibility crisis"[5] and has even driven the German research organisation (DFG) to dedicated statements contemplating about the situation and its consequences for the research community and the general public[6]. Furthermore, measurands such as amounts of specific protein biomarkers in bodily fluids, are measured with not acceptable discrepancies, as shown in interlaboratory comparison studies[7]. Therefore, the measurement results often do not fulfil medical requirements with respect to their accuracy and comparability, which may lead to incorrect diagnoses – with a risk to patients and considerable additional costs for the society healthcare system as a whole.

The accuracy, precision and comparability of related measurement results are mandatory for the concept of personalized medicine. With the rapidly increasing number of different measurement procedures, the demand for correct measurement results is growing especially in areas where measurements results affect treatment decisions for a life-threatening illness. In addition, the assurance of comparability is of high importance for pooling data in clinical multi-centre trials and large-scale biologic databases.

Measurement results for a given measurand should

be comparable within medically meaningful limits, irrespective of the measurement procedure used or the laboratory performing the measurement. This request cannot be satisfied if the results are not traceable to the International System of Units (SI) through higher-order, if possible, primary measurement standards. Linking up working level results obtained in clinical laboratories to internationally recognized and accepted standards is thus an essential component in assuring the accuracy and comparability of clinical laboratory measurements. The issue was recognized and addressed by regulatory bodies on an international scale. In-Vitro Diagnostic Medical Devises (IVDs) became subject to regulation at the European level with the implementation of the EU IVD Directive (IVDD) 98/79/EC. The IVDD requires that traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.

Recently, the IVDD has been revised and strengthened to become the new EU In-Vitro Diagnostic Device Regulation (IVDR) 2017/746. The new IVDR significantly broadens the scope of the former directive and now legally demands metrologically based quality assessment of clinical laboratory testing for IVDs. Until May 2022 full implementation of the IVDR is required.

NMIs and DIs in Europe and elsewhere are very active in this field and provide SI-traceability for a range of relevant quantities. But much more work is necessary on the primary level as well as on the level of reference laboratories and PT providers. At present, neither the total number of measurands considered to be of highest priority is linked to the SI nor has a single national NMI/DI the capacity to provide the full scope of primary standards needed.

The IVDR also emphasizes post-market surveillance requirements that manufacturers must provide for their products on a long-term life-cycle basis. IVDs are subject to continuous performance and risk assessment and require reference measurement procedures and materials which remain stable and reliable for many years. Such CRMs and RMPs of higher metrological order must be traceable to NMIs and DIs whenever possible.

All this requires concerted actions on an international level. No single NMI has the expertise or resource to tackle all or even a significant fraction of the most critical priorities without collaboration. Close collaboration is also needed with the stakeholders in the field. The existing Joint Committee for Traceability in Laboratory Medicine, a collaboration between IFCC, ILAC and BIPM is a very important initiative for this goal on an international level. Further to this it is the task of the recently established European Metrology Network (EMN) for Traceability in Laboratory Medicine to establish a next step. Building up links to the stakeholder community to ensure dissemination to the end users on the basis of concerted actions, to develop and implement a strategic agenda for the NMIs at least in Europe and beyond, if possible, and establish a knowledge base, technology transfer and promotion plan, to ensure that an effective response is put in place.

This task and its joint solution is very close to the mission of CITAC that aims to join forces for reliable measurements in chemistry everywhere in the world.

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7 see e.g. https://www.rfb.bio/cgi/displayAnaStats?rv_type=all&rvTypeForDetails=CM&year=2017&rv_num=1&analyte=Troponin%20I&searchType=analyte&anaV=4

MESSAGE FROM THE CITAC SECRETARY

MORE THAN STATISTICALLY DIFFERENT… METROLOGICALLY DIFFERENT!

Ricardo Bettencourt da Silva // University of Lisbon, Portugal

The incursion of metrology in some scientific areas or activities that depend on chemical analysis results is limited, even when the impact of decisions supported on these results advises the production of reliable and objective analytical information. Some examples of these areas are the quality control of medicines and the academy. The society expects that the quality of medicines is adequate and research data are properly obtained and interpreted.

One of the reasons for this worrying scenario can be the misunderstood difference between statistical and metrological interpretation of analytical data. People tend to believe that classical statistical assessments of chemical analysis results by comparing mean values or replicate results standard deviations through t-tests, F-tests or ANOVA are metrological assessments. In fact, these assessments are "only" statistical since can miss important details about results origin. The statistical assessments compare available numbers and are only sound if some assumption about that numbers are fulfilled, such as the fact that no other relevant random or systematic effects affect data interpretation.

For instance, if two first order degradation rates of the same compound from different catalytic processes are compared by assessing the means of replicate determinations of these degradation rates through a t-test, it is assumed determinations are not affected by systematic effects introduced by used chemical references (e.g. standards), deviations from first order kinetics or other effects driven from the measurement procedures. Some would argue that the "other " effects are irrelevant based on how these assessments are usually performed. However, for sure, some of those would recall cases where the initially observed difference is not confirmed in subsequent assessments declining the initial information. These cases are frequently attributed to the occurrence of outliers that can hide the use of inadequate data interpretation techniques.

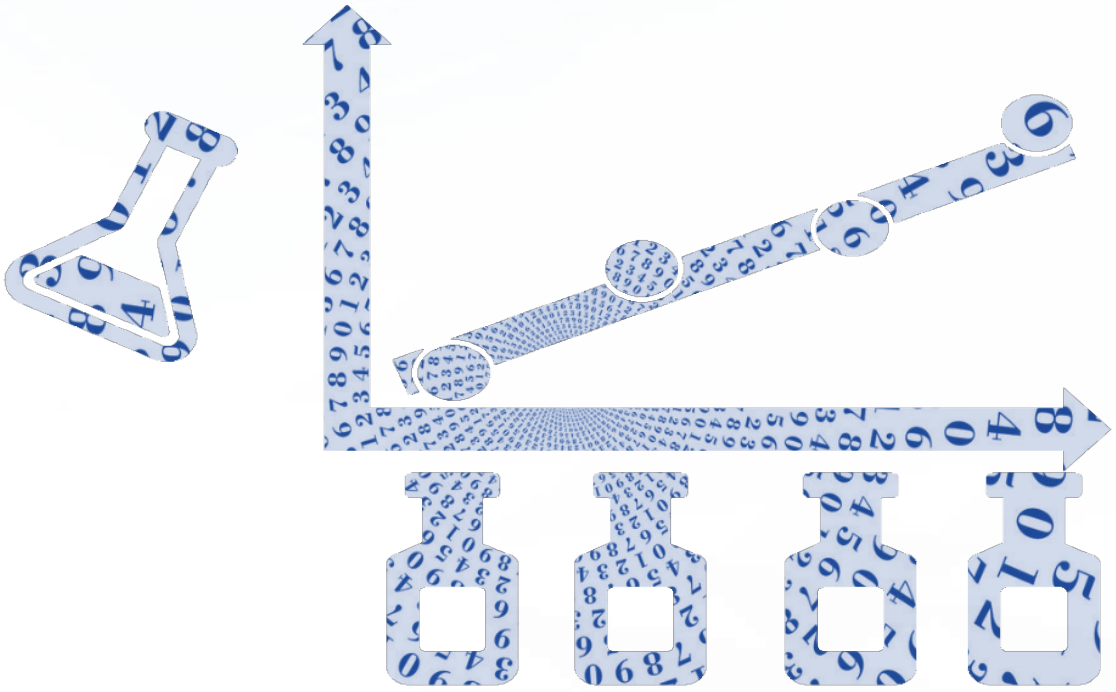
When two mean values are statistically equivalent given results standard deviation that underevaluate measurements uncertainty, the results are also metrologically equivalent. In these cases, the statistical equivalence of results (i.e. the mathematical equivalence of numbers) indicate the metrologically equivalence of tested items (i.e. the material equivalence of items). However, when measurements are not statistically equivalent, these can be metrologically equivalent due to the omission of relevant random or systematic effects

in the statistical assessment.

Metrologists perform the extra work and need the extra expertise to transform numbers in an expression of the reality!

What can be done to change this scenario? For sure the way to change this is long and difficult. In fact, we know how difficult it is to promote sound metrological evaluations in routine conformity assessments just by looking how the International Laboratory Accreditation Cooperation (ILAC) has been tackling this problem. Many work still needs to be done to make all accredited conformity assessments metrologically sound. Some of this work depends on sectorial development of references for the performed measurements that depends on the awareness of that community and respective stakeholders for the need for such improved references.

This is, at least, a task of a lifetime... an important one that must be continued and expanded.



The numbers from chemical quantifications should be processed metrologically... not just statistically!

EDITORIAL: METROLOGY, QUALITY ASSURANCE & CHEMOMETRICS - WHAT IS WHAT?

Ilya Kuselman // Independent Consultant on Metrology, Israel

When I emigrated from Ukraine, formerly part of the USSR, in 1990 and looked for a job in Israel, a widely known professor of analytical chemistry of the Hebrew University of Jerusalem at that time kindly agreed to look through my resume.

- What do you mean, claiming your field of interest as *metrology in chemistry*? - he asked me.

- Such a field does not exist, it is probably a mistaken translation from Ukrainian or Russian.

I tried to explain what *metrology in chemistry* is, using a mixture of poor Hebrew and broken English, and he concluded with a sense of relief:

- This is *chemometrics*.

"Love what you do and do what you love" ... Ten years later, as a member of the board of the Israel Analytical Chemistry Society organizing the Isranalytica 2000 conference, I understood that a number of leading analytical chemists still could not distinguish among *metrology in chemistry*, *quality assurance* and *chemometrics*. Taking that as a challenge, I prepared a lecture on this topic at the conference and published it in Reviews in Analytical Chemistry [1].

The paper did not make any noticeable impact, but today, twenty years later, the new generation of chemists working in analytical laboratories are much more educated and experienced in *metrology in chemistry* and *quality assurance* than chemists of earlier generations. There are now guidelines from JCGM, documents of ISO and ILAC, and guides from CITAC, IUPAC, Eurachem and other sister organizations. Specifically, JCGM 200 [2] defines *metrology* as the science of measurement and its application, including all theoretical and practical aspects of measurement, whatever the measurement uncertainty and field of application, e.g., *in chemistry*. *Quality assurance* is a way of preventing human errors in measurement and keeping measurement uncertainty within the set limits. It is defined in ISO 9000 [3] as a part of quality management focused on providing confidence that the quality requirements will be fulfilled.

Nevertheless, it is known that "God (and the devil) is in the detail": implementation is important and sometimes not simple. Therefore, international journals, as discussed in CITAC News 2018 and 2019, publish papers on new approaches and applications in *metrology in chemistry* and *quality assurance*.

Chemometrics is the science of relating measurements made on a chemical system or process to the state of the system via the application of mathematical or statistical methods, as formulated in the IUPAC Recommendations [4]. There are a number of books and papers on *chemometrics* methods, but these methods are less documented/standardized than *metrology* and *quality assurance* methods. *Chemometrics* methods are used in analytical chemistry mostly in the development of spectroscopic, chromatographic and other multivariate

complex measurement procedures. Since the *quality assurance* strategy requires taking into account the metrological characteristics of the procedure at the very beginning of its development, *chemometrics* methods are useful as at the stage of an experiment design, as at the procedure validation. These methods are also helpful for the treatment of data accumulated in a laboratory, as well as in interlaboratory studies. Thus, *chemometrics* provides tools for performing some *metrology* and *quality assurance* tasks.

It is important to note that analytical chemistry, as a science and service, is continuously enriched by interaction with *metrology*, *quality assurance* and *chemometrics*. However, *metrology* is widely applied outside analytical chemistry: in physics, biology, engineering, etc. *Quality assurance* in analytical laboratories is also only a small part of its applications. The same is concerning *chemometrics*.

What *chemometrics* is currently, one can learn more from publications in the journals "Chemometrics and Intelligent Laboratory Systems", "Journal of Chemometrics", and "Journal of Mathematical Chemistry". Moreover, there are **394** journals that have recently published approximately **52,900** articles on chemometrics, in particular Analytical Chemistry (ACS Publications), the Journal of Analytical Chemistry (Springer), the International Journal of Pharmaceutical Analysis, Biology & Medicine, Physical Chemistry & Biophysics, and others [5].

Quite often, an analytical chemist lacks the knowledge necessary to understand applied mathematical and statistical methods and tries to learn them by "putting one foot in front of the other". However, "if you want to go quickly, go alone; if you want to go far, go together". In other words, joint work with a good mathematician is promising. As to the question of who is "good", there is no answer: "we choose and we are chosen". The problem is also that everyone would like to live and work according to his/her schedule, whereas the world time scale is independent of individuals' desires. This is a common problem of any team: the participants should be able to synchronize their watches ...

Of course, to work successfully each of us needs health. I hope the world will cope with the COVID-19 pandemic and we will meet next year again to discuss our CITAC tasks. Take care!

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LIAISON REPORTS 2019 OF THE SISTER INTERNATIONAL ORGANIZATIONS

AFRIMETS REPORT

Angelique Botha // NMI, South Africa

SUMMARY OF GENERAL ISSUES

The 13th Intra Africa Metrology System (AFRIMETS) General Assembly (GA) took place in Giza, Egypt, from 7 to 12 July 2019. The GA was preceded by seven Technical Committee (TC) meetings. The TCs discussed the results of comparisons conducted during the past year, new comparisons planned for the next 3 years and strategies on how to improve the capabilities of African NMIs. Approximately, 15 inter-laboratory (NMI) comparisons are currently active in AFRIMETS. Two comparison studies are being planned for Chemistry, one in the field of the analysis of pesticides in fruits/vegetables and another for the analysis of toxic and nutritional elements in wheat flour.

Two workshops were held during the GA: one on the implementation of the Revised SI in Africa and a second on the type approval of measuring instruments in Africa OIML member states. The workshops were attended by more than 100 delegates. The BIPM provided a presenter (Dr Sten Bergstrand) for the Revised SI workshop and the director and deputy director of BIML, Mr Anthony Donnellan and Mr Ian Dunmill, presented in the legal metrology workshop.

Figure 1: Attendees of the 13th AFRIMETS General Assembly held from 7 to 12 July 2019 in Giza, Egypt.

The General Assembly discussed issues such as the technical activities conducted the past year, training and most importantly, how AFRIMETS can introduce a membership fee. The resolutions taken included:

1. To change the Memorandum of Understanding (MOU) of AFRIMETS to include the role of Directors of NMIs.
2. Noting that the operational phase of the Africa Continental Free Trade Agreement (AfCFTA) has commenced on 07 July 2019, the AFRIMETS Secretariat was tasked to develop modalities to introduce a membership fee from 2021. It will be introduced in 3 phases.
3. A technical committee (TC) for the implementation of the Revised SI was established. The convener is Dr Aletta Karsten from the NMISA.
4. Dr Mohamed Berrada from PLEE/LNM, Morocco, replaced Mr Lotfi Khedir on the JCRB delegation.

The TCs discussed results of comparisons conducted during the past year, new comparisons planned for the next 3 years and strategies on how to improve the capabilities in African NMIs.

The TC-QS meeting took place on 8 and 9 July with 22 attendees from 10 countries with approved quality systems (QS) and observers from 4 institutes (three of which will submit their QS for approval in the next few months). The quality systems of 9 national metrology institutes (NMIs) and two designated institutes (DIs) were presented to the committee. All members with approved QS and those applying for approval reported on their migration to ISO/IEC 17025:2017 and ISO 17034:2016. A timeline has also been agreed for all NMIs and DIs with CMCs in the key comparison database (KCDB) to migrate to the new standard by December 2019.

CURRENT TC AND WORKING GROUP CHAIRS AND CONTACT DETAILS

The AFRIMETS structure includes working groups to mirror the international consultative committee working groups (CC-WGs) and are identified as TC-(parameter).

THE CONTACT DETAILS OF THE TC-CHAIRS IMPORTANT TO CHEMISTRY ARE LISTED BELOW:

Function	Name	Details
TC-QM Vice-Chair (Bio analysis)	Dr Angelique Botha Mrs Desirée Prevoo	National Metrology Institute of South Africa (NMISA), Private Bag X34, Lynnwood Ridge, 0040, RSA Tel: +27-12 8413800 e-mail: abotha@nmisa.org Tel: +27-12 8414576 e-mail: dprevoo@nmisa.org
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RMO MEMBERSHIP UPDATE

AFRIMETS has 6 sub-regional metrology organisations (SRMOs), which are primarily based on regional economic blocks, whose individual members are principal members of AFRIMETS. In total the SRMOs have forty-two members, thus AFRIMETS has 42 principal members. Countries not belonging to AFRIMETS through an SRMO are categorised as ordinary members. There are four (4) ordinary members, bringing the total number of members of AFRIMETS to forty-six.

The Associate members are the PTB (Germany), LNE (France), the NIRPR (National Institute of Radiation Protection and Research – Nigerian Nuclear Regulation Authority), GRPI (Ghana Radiation Protection Institute), TAEC (the Tanzania Atomic Energy Commission), INSTN (Madagascar) and the International Atomic Energy Agency (IAEA). Observers include the European metrology organisation (EURAMET), the Arab Federation of Metrology (AFM), the African Committee of Metrology (CAFMET), the African Electrotechnical Standardisation Commission (AFSEC) and the Emirates Metrology Institute (EMI). Three institutes are designated by NMIs to participate in the Metre Convention on behalf of their governments:

South Africa: iThemba Laboratories for Medium and High-Energy Neutron Dosimetry

Tunisia: DEFNAT – Electricity
INRAP – Chemistry

In June 2019 AFRIMETS received the welcome news that the Kingdom of Morocco acceded to the Metre Convention. This brings the number of AFRIMETS signatories to the Metre Convention to 5. The LPEE-LNM subsequently signed the CIPM MRA on 15 July 2019.

The Members of the BIPM and Associates of the CGPM are shown below, as well as the participants in the CIPM MRA.

Figure 2: A map of Africa representing the AFRIMETS members and associate members of the CIPM MRA.

AFRIMETS CMCS

As at 15 November 2019 there were a total of 643 CMCs accepted in Appendix C of the KCDB (General Physics = 482, Chemistry = 122 and IR = 39).

The CMCs originate from:

South Africa = 533 (118 CMCs in Chemistry)
Egypt = 39 (2 CMCs in Chemistry)
Zimbabwe = 19
Kenya = 17 (2 CMCs in Chemistry)
Tunisia = 14
Zambia = 11
Namibia = 7
Botswana = 3

Zimbabwe (SIRDC) published CMCs in temperature recently and Botswana in Mass.

DEVELOPMENT WORK IN CHEMISTRY

Most of the activities in Africa to improve the comparability of measurement results in the field of chemical and microbiological testing still focusses on standardisation. In Tanzania the Tanzania Bureau of Standards (TBS) performs testing over a diverse range of applications from microbiology, which is very important to ensure food safety, pharmaceuticals, cosmetics, and forensic analysis. Tanzania also has more than ten testing laboratories that participate in the SADCMET Water proficiency testing (PT) scheme on an annual basis. In Ghana, the Ghana Bureau of Standards (GBS) also participates in the SADCMET Water PT and supports the mining industry. The Botswana Bureau of Standards (BOBS) and Kenya Bureau of Standards (KEBS) also performs testing to support food safety, water conservation, the mining industry and forensic analysis.

KEBS have also established a capability in metrology in chemistry with an activity in gas analysis for the calibration of breath alcohol analysers and stack gas emission monitoring with a fourier-transform infrared (FTIR) spectroscopy measurement capability. In the field of food analysis KEBS has also started to publish CMCs and the institute also has an interest in a capability for the preparation of calibration standards for elemental analysis and a certified reference material (CRM) for maize, because it is very difficult to import the reference materials (RMs). INRAP, the designated institute for metrology in chemistry in Tunisia has an interest in food safety specifically fish toxins and also experiences difficulties with the import of elemental calibration solutions and CRMs. INRAP is preparing to publish its first CMCs in the field of pesticides in fruits/vegetables and fish and is also developing a CRM. AFRIMETS is planning a comparison study for pesticides in fruits/vegetables in support of this activity.

The National Institute for Standards (NIS) in Egypt has also established a capability for metrology in chemistry and started publishing CMCs in the field of cosmetics and organic solutions. Other countries that have an interest in establishing a new capability for metrology in chemistry in Africa include the Seychelles for medical gases and Ethiopia, who are in the process of establishing its NMI.

The NMISA in South Africa has the most extensive capability for metrology in chemistry with laboratories for organic analysis that focusses on organic contaminants, such as persistent organic pollutants (POPs) and pesticides in food and environmental samples. The laboratory also has an advanced capability for purity assessment of high purity organic materials and most recently established a reference material production facility. From 15 to 17 January 2020, an AFRIMETS peer-reviews visit of the purity assessment capabilities of the NMISA is planned in preparation of the submission of new CMCs in the field of calibration solutions for mycotoxins and matrix reference materials for multi-component mycotoxins in matrices such as white maize, cassava, nuts, etc.

The reference material production facility will focus on the preparation of CRMs relevant to food matrices found in African and is currently preparing for the certification of mycotoxins in a range of matrices such as white maize, as well as ground and tree nuts in collaboration with the national metrology institute (NIM) in China and the International Bureau of Weights and Measures (BIPM) in France. The other laboratories include the Gas Analysis Laboratory that provides binary and multi-component primary reference gas mixtures (PRGMs) for a wide range of air pollutants including volatile organic compounds. The Inorganic Analysis Laboratory is also

preparing to produce CRMs for toxic and nutritional elements in food matrices.

The AOAC International Sub-Saharan Africa Section (AOACI-SSA) held its second annual meeting from 5 to 8 November in Cape Town, South Africa. The theme of the meeting was "Harmonizing of Testing Standards: Critical for the free trade of safe food in Africa". The programme focused its attention on building on the fundamentals of testing, analytical methods alignment and harmonisation as well as delved into some present and emerging food safety issues in order to identify some of the most critical analytical method development needs for the African region. Additionally, two key initiatives were launched, the Young Scientists Development Programme and the Laboratory Mentorship programme, both focused on building capacity and improving performance in testing.

Figure 3: Attendees of the second annual meeting of the AOAC International Sub-Saharan Africa Section held from 5 to 8 November 2019 in Somerset West, South Africa

FUTURE ACTIVITIES

The AFRIMETS General Assembly 2020 will be hosted by the CEMAC region, most probably by Cameroon in July 2020.

The second Africa Food Safety Workshop will be held in Johannesburg, South Africa from 6 to 10 July 2020. An AFRIMETS TC-QM meeting will be held in conjunction with the workshop.

The third annual meeting of the AOACI-SSA will be held in Johannesburg, South Africa from 27 to 30 October 2020.

CONCLUSION

All AFRIMETS structures including the technical and quality system working groups are functioning well. Key and Supplementary comparisons are being conducted and it is expected that several new CMCs will be submitted by Associates during the next 1 to 2 years.

For any further information on the activities in AFRIMETS or the activities of the TC-QM for Chemistry, please contact:

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Head of the Secretariat: Dr Wynand Louw at: wlouw@nmisa.org

TC-QM Chair; Dr Angelique Botha at: abotha@nmisa.org

TC-QM Vice-Chair; Ms Desirée Prevoo-Franszen at: dprevoo@nmisa.org

Figure 4: Invitation to the second Africa Food Safety Workshop to be held in Johannesburg, South Africa from 6 to 10 July 2020.

APMP LIAISON REPORT

Hongmei Li // NIM, China

HIGHLIGHTS

APMP MEETINGS

The 35th APMP General Assembly & Related Meetings

National Measurement Institute, Australia (NMIA) hosted the 35th Asia Pacific Metrology Programme (APMP) General Assembly and Related Meetings in Sydney, Australia. The activities include:

1. The APMP General Assembly;
2. Meetings of the governance bodies: the APMP Executive Committee and Technical Committee Chairs' (TCC);
3. Meetings (and, in some cases, Workshops) of APMP's 12 Technical Committees (TCs);
4. Meetings of the APMP Developing Economies' Committee (DEC);
5. APMP NMI Directors' Workshop;
6. A national Symposium organized by the host NMI;
7. MEDEA CC meeting; and Laboratory tours.

The APMP Mid-year Meeting:

The National Metrology Laboratory of the Philippines (NMLPhil) of the Industrial Technology Development Institute of the Department of Science and Technology (ITDI-DOST) successfully hosted the 2019 APMP Mid-Year Meetings.

CHAIRPERSON AND SECRETARIAT

New Chair Elect for APMP from GA 2019-2022 is Mr. Fang Xiang from National Institute of Metrology , China (NIM).

CHANGES IN EC

Ms Eleanor Howick (MSL, New Zealand) and Dr Tang Lin Teo (HSA, Singapore) were elected as new EC members.

APMP AWARDS

- Winner of the APMP Award for Developing Economies: Dr Benilda S. Ebarvia (NML-ITDI, Philippines)
- Winners of the APMP Young Metrologist Prize: Dr. Takahiro Tanaka (NMIJ/AIST, Japan); and Dr. Woong Kang (KRISS, South Korea)
- Recipients of the APMP Technical Activity Award: Dr Toshiyuki Takatsuji (NMIJ/AIST, Japan) for his leadership and contribution in developing APMP activities as its Chairperson; Dr Osman Zakaria (NMIM, Malaysia), Dr Yu-Ping Lan (CMS/ITRI, Chinese Taipei) & Ms Wei Gao (NIM, China) for their contribution as APMP Executive Committee members; Dr Kazuaki Yamazawa (NMIJ/AIST, Japan), Dr Jinjie Wu (NIM, China), Dr Victoria Coleman (NMIA, Australia) for their contribution as Chairs of Technical Committees; and Dr Takehiro Morioka (NMIJ/AIST, Japan) for his contribution as APMP Executive Secretary.

FOCUS GROUP ACTIVITIES

- Food Safety Focus Group (25-26 Oct 2019)
  Under the theme of '*Case study for food safety metrology capacity building*', a two-day workshop was successfully organized on 25-26 October 2019 in Beijing China by National Institute of Metrology, China
- Focus Group workshop on Climate Change and Clean Air (5 Aug 2019)
  Main topic: '*Air Quality and Climate Change, Ozone Measurement and Calibration, Sources of Air Pollution, Aerosol Measurements, and others.*'
- The 17th Gas Analysis Workshop of APMP/TCQM (from 6 to 7 Aug 2019)
  Day 1: *Purity Analysis, Reference Gas Preparation/ Measurement, Cylinder Absorption, Dynamic Methods for gas mixture;*

  Day 2 (7 Aug 2019): *Morning (Comparison discussion for NMIs only) and Afternoon (Lab/Industry/Cultural visit (TBC)*

TCI AND FGI

The following TCI and FGI Projects have completed in 2019. TCI2020 is now evaluating by EC member, and Focus Group Initiative Project will be reviewed at the 2019 GA.

- TCEM_04_TCI2014: Pilot study on transport behavior of 100-Ω standard registers for use in APMP key comparisons
- EEFG_01_FGI2018: Metrology for energy
- MMFG_01_FGI2018: Pilot study on automated sphygmomanometer accuracy test using blood pressure simulation technique
- FSFG_01_FGI2018: Measurement and capability building in residues of veterinary drugs on meat and seafood
- CWFG_02_FGI2018: Clean Water Focus Group planning workshop
- FSFG_01_FGI2019: Case study for food safety metrology capacity building

UPCOMING APMP MEETING

The 2020 Mid-Year Meetings will be hosted by the Measurement Units, Standards and Services Department (MUSSD), in Colombo, Sri Lanka. The 2020 GA and Related Meetings will be hosted by the National Institute of Metrology, Thailand in Bangkok.

MEMBERSHIP

New full membership affiliation:

- The Metrology Division under the Ministry of Commerce, Industry and Cooperatives, Kiribati (MCIC);
- New associate member affiliation:
- National Measurement and Calibration Center of the Saudi Standards, Metrology and Quality Organization (NMCC/SASO);
- Uzbek National Institute of Metrology, Uzbekistan (UzNIM);

APMP-APAC COOPERATION

The Asia Pacific Laboratory Accreditation Cooperation (APLAC) and the Pacific Accreditation Congress (PAC) have been amalgamated into the Asia Pacific Accreditation Cooperation (APAC) since 1 January 2019.

The first general Assembly of APAC was held in Singapore in the same week of the APMP Mid-year meeting in Cebu, Philippines. Dr Takatsuji, APMP Chairperson attended the meeting and signed on the renewed MoU between two organizations. A number of proficiency testing (PT) programs is expected to be carried out under this MoU.

The APMP-APAC PT Working Group Meeting was held on 1 December 2019 in Sydney, Australia.

Progress reports on on-going programmes:

- APLAC T106 Organochlorine pesticides in ginseng root (running in parallel with APMP.QM-S11)
- APLAC T108 Benzo(a)pyrene in olive oil
- APLAC T109 Measurement of Cadmium in Milk Powder
- APLAC T110 Toxic Metal/Metalloid Species in Powdered Rice
- APAC T111 Genetically modified (GM) maize T25

New proposals for PT programmes:

- Benzoic Acid in fish sauce
- Zearalenone in maize
- Quantification of Staphylococcus aureus in milk powder or flour
- Trace elements in natural mineral water

STRATEGIC INITIATIVES

DEC ACTIVITIES AHEAD OF APMP 2019

The Developing Economies' Committee (DEC) held a very productive meeting as well as two significant workshops during the mid-year meetings in Cebu, the Philippines – one to begin the DEC's work on its next multi-year Strategic Plan, and the other to raise awareness among DEC members of the activities of APMP's Focus Groups. Key recommendations from these meetings include classification of member economies and associated funding criteria, and setting up of Task Groups to drive agreed strategic issues.

MEDEA PROJECT

MEDEA 2.0 project updated. It has finished the first half of the MEDEA 2.0 project term (05/2018 – 04/2021) – the joint project of APMP, APLMF and PTB, funded by the Federal Ministry for Economic Cooperation and Development, Germany.

NIM CB&KT PROGRAMME

Project name: Demonstration Research and Mutual Recognition of Measurement Standards and Technological System for Agro-product Safety (Implementation period from 2017 to 2020.) The project is jointly by NIM, BIPM, NMISA and VMI, HSA, DSS, NPSL, STD-ITDI, , NMC, INMETRO, INTI, etc. So far NIM China has received 9 trainers from above institutes.

STAKEHOLDER ENGAGEMENTS

THE 41ST JCRB MEETING

The GULFMET hosted the 41st JCRB meeting from 9 to 11 September 2019 in Dubai, United Arab Emirates.

PACIFIC QUALITY INFRASTRUCTURE INITIATIVE-REGIONAL WORKSHOP

From 2-6 September 2019, representatives from Pacific Island Forum (PIF) Countries participated in the Workshop on Quality Infrastructure (QI) held in Nadi, Fiji. The Workshop was organized by the PIF Secretariat together with the CARICOM Regional Organization for Standards and Quality (CROSQ), PTB Germany, the Australian Department of Foreign Affairs and Trade (DFAT), the European Union's Trade Committee (EU TradeCom II) facility and the Enhanced Integrated Framework (EIF).

IMEKO TCS JOINT SYMPOSIUM IN ST. PETERSBURG (2-5 JULY, 2019)

The Joint IMEKO (International Measurements Confederation) TCs Symposium organized by the D.I. Mendeleyev Institute for Metrology (VNIIM) and the Russian Academy of Metrology were held in St. Petersburg on July 2-5, 2019. Current trends in fundamental and practical measurements and issues related to interdisciplinary research and education were discussed during the meeting.

SEMICONDUCTOR ADVANCED INSPECTION AND METROLOGY FORUM

During SEMICON Taiwan 2019, CMS/ITRI and SEMI organized a Semiconductor Advanced Inspection and Metrology Forum to discuss the state-of-the-art technologies of semiconductor inspection and metrology.

KEY AND SUPPLEMENTARY COMPARISONS

Data on key and supplementary comparisons in APMP is available on the KCDB website.

FROM 1999 TCQM ORGANIZED:

- 14 key comparisons (12 completed)
- Categories: gases (10) and pH (4)
- 22 supplementary comparisons (12 completed)
- Categories: gases (14) and food (8)
- 34 pilot studies (27 completed, 7 on-going)
- Categories: food and biological materials (23), pH (5), water (2), cosmetics (2), inorganic solutions (1) and surface (1)

NEW PROPOSALS

New proposal APMP.QM-Pxx Quantification of Staphylococcus aureus in milk powder or flour was put forward by Dr. Sui Zhiwei from NIM China.

REPORT OF CCQM

Paola Fisicaro // LNE, France, Vice-chair of the Inorganic Analyses Working Group of the CCQM

The Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) held on 11-12 April 2019 its twenty fifth meeting at the International Bureau of Weights of Measures (BIPM). In conjunction, a workshop has been organized with a Metrologia Focus Issue on 'Advances in Metrology in Chemistry and Biology'.

The meeting and the workshop have been the occasion to conduct a reflection on the history of the CCQM, an update on present status and a look to the future. Dr W.E. May, outgoing president, in his introduction to the meeting, underlined the fact that the CCQM had become the global forum for progressing state-of-the-art in chemical and biological measurement. Its goal is to promote scientific exchange amongst National Metrology Institutes, and highlight novel research and advances being made in Metrology in Chemistry and Biology.

A reflection on the impact of CCQM activities has been conducted by Dr H.G. Semerjian (former NIST Director) and Dr M. Milton (BIPM Director).

Dr Semerjian reviewed examples of the international impact of chemical measurement. In particular, he drew attention to the measurement needs of the Organisation for Prohibition of Chemical Weapons (OPCW), and the climate research, which had led to the Montreal Protocol for restricting refrigerants. Dr Semerjian also described the expansion of chemical metrology around the globe and the considerable developments in the RMOs, which had led to over 6000 CMCs for chemical measurement, supported by a high number of relevant comparisons.

Dr Milton presented his reflections on the CCQM, based on his attendance at all of its meetings as well as those of many other CCs. He underlined the importance of the work done by the working groups and the fact that the regular reports from working groups to the CCQM plenary had been powerful drivers for progress.

The 25th meeting has also been the last meeting for Dr May. He announced that the CIPM had appointed Dr Sang-Ryoul Park, of KRISS, Republic of Korea, as the new President of the CCQM. The meeting welcomed Dr Park by acclaim.

Dr Park, recognizing the responsibility of his new role, said that he looked forward to working with the many highly qualified and enthusiastic members of the CCQM.

He recognized that the CCQM had already contributed greatly to the improvement of measurement and looked forward to the future fruits of the CCQM's endeavours. The success and growth of the CCQM meant that this was an ideal time to reexamine its role, build consensus on the goals of the unique network that is the CCQM, and reaffirm short-term and long-term outputs.

More details about the 25th CCQM meeting can be found on the BIPM website (https://www.bipm.org/utils/common/pdf/CC/CCQM/CCQM25.pdf).

REPORT OF COOMET TC 1.12 "REFERENCE MATERIALS"

S. Medvedevskikh // UNIIM, Russia, Chair of COOMET TC 1.12 "Reference Materials"
O. Kremleva // UNIIM, Russia, Deputy Chair
O. Anfilatova // UNIIM, Russia, The Coordinator

GENERAL CHARACTERISTIC OF COOPERATION

Activities on RMs in the framework of Euro-Asian Cooperation of National Metrology Institutions (COOMET) are carried out by Technical Committee 1.12 "Reference materials" (TC 1.12), the working body, responsible for organizing, coordinating and performing work in the assigned area of cooperation.

Now TC 1.12 is composed of representatives of 18 National Metrology Institutes from COOMET member-countries: Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Cuba, DPRK, Germany, Georgia, Kazakhstan, Kyrgyzstan, Lithuania, Moldova, Romania, Russia, Slovakia, Ukraine and Uzbekistan.

The Chairman of TC 1.12 is Dr. S. Medvedevskikh, Director of Ural Scientific Research Institute for Metrology (UNIIM), Russia. Maintaining the Secretariat of TC 1.12 is assigned to UNIIM.

In 2019 the work within TC 1.12 was carried out on 22 registered COOMET projects. The Coordinator of the projects is Russia. The experts from Belarus, Bosnia and Herzegovina, Bulgaria, Kazakhstan, Russia, Ukraine, Uzbekistan and Switzerland participate in certification analysis of CRMs, being developed within the projects.

ACTIVITIES ON THE TRANSITION TO ISO 17034:2016 "GENERAL REQUIREMENTS FOR THE COMPETENCE OF REFERENCE MATERIAL PRODUCERS"

The focus of TC 1.12 activities in 2019 was set on the release of the new ISO International Standard 17034:2016 "General requirements for the competence of reference material producers" and on the related preparation of methodological and organizational documents for the transition of National Metrology Institutes to ISO 17034:2016. COOMET Quality Forum Technical Committee 3.1 presented the Policy and Plan for the transition to ISO 17034:2016. The members of TC 1.12 were proposed as technical experts for participation in peer reviews in the area of reference material production.

At the 20th meeting of COOMET Quality Forum, which took place from 30 September to 2 October in Gebze (Turkey) National Metrology Institutes of Belarus, Kazakhstan and Russia (D.I. Mendeleev VNIIM, VNIIOFI and UNIIM) confirmed the transition to ISO 17034:2016 and received the recognition of Quality Management System in accordance with ISO 17034:2016.

In parallel the Secretariat of TC 1.12 conducted the Analysis of all effective COOMET documents on RMs for harmonization with newly published international documents: ISO Guide 30:2015, ISO Guide 31:2015, ISO Guide 33:2015, ISO 17034:2016, ISO Guide 35:2017. As a result of the Analysis, the Plan for the revision of COOMET documents on reference materials was prepared. The implementation of the Plan is expected in 2020-2022. The first document, scheduled for release in 2020, is COOMET Recommendation "Form and content of COOMET certificate for reference materials of composition and properties of substances and materials".

INTERACTION WITH INTERNATIONAL AND REGIONAL ORGANIZATIONS

To coordinate the issues on RMs to be discussed in the framework of COOMET, the liaisons with the leading international organizations ISO/REMCO, OIML TC 3/SC 3, CIS Interstate Council (NTCMetr), COMAR and others are regularly maintained.

The members of TC 1.12 and the representatives of these organizations mutually participate in international

meetings, presenting the necessary information on the activities of these organizations. Information about the activities of TC 1.12 "RMs" was first presented in the in the news bulletin CITAC NEWS. Information support of the activities of TC 1.12 "RMs" is provided through presentations at seminars, conferences and other events, as well as publications in the journals of the metrological community.

Details of the activities of TC 1.12 can be found on COOMET web-portal http://www.coomet.net/.

INFORMATION ON THE 24TH MEETING OF TC 1.12 (SEPTEMBER, 2019)

The annual 24th meeting of TC 1.12 was held on 25 September 2019 in Minsk (Belarus) at Belorussian State Institute of Metrology (BelGIM).

The meeting was attended by representatives of 7 COOMET member-countries: Belarus, Bosnia and Herzegovina, Kazakhstan, Russia, Slovakia, Ukraine and Uzbekistan; Deputy Chairman of TC 1.8 "Physical Chemistry", Chairman of SC 1.8.3 "Pure Inorganic Substances", COOMET Project Coordinators from UNIIM, Krasnoyarsk V.N. Gulidov Non-ferrous Metal Plant, West-Siberian Testing Centre. Also, the meeting was attended by interested experts in RM area from the leading metrological institutes of Russia - D.I. Mendeleev VNIIM and VNIIOFI and representatives of Bureau of Standards of Interstate Council for Standardization, Metrology and Certification of the Commonwealth of Independent States (CIS EASC).

The agenda of the 24th meeting of TC 1.12 traditionally included items on RM activities, performed by COOMET member-countries, in the framework of international organizations ISO/REMCO, COMAR, OIML TC 3/SC 3, Interstate Council NTCMetr; the information of the Secretariat of TC 1.12 on the progress of the current projects of cooperation, concerning: the development of COOMET CRMs; the development of normative documents on RM problem and the Programme of joint CRM production within COOMET, etc. The reports and presentations of the participants were listened with great attention; the content and target dates of the work were discussed and confirmed. Particular attention at the meeting was paid to the possibility of developing the activities of TC 1.12 in the field of primary reference (PRMP) and reference measurement procedures (RMP) within the framework of COOMET, which could become the main platform for carrying out such work in the Euro-Asian region.

The question of election of TC 1.12 Chairman was considered due to the expiry of his term of office in April 2020 according to COOMET Working Procedure. The participants of the meeting unanimously proposed to recommend Dr. S. Medvedevskikh (director of UNIIM) for the post of TC 1.12 Chairman for a new term.

The next 25th meeting of TC 1.12 is scheduled at UNIIM in Ekaterinburg in September 2020 in conjunction with the IV International Scientific Conference "Reference Materials in Measurement and Technology".

Participants of the 24th meeting of TC 1.12 in Minsk, Belarus, 25 Sep 2019

EURAMET REPORT

Michela Sega // INRIM, Italy

On 20th May 2019, the World Metrology Day that commemorates the anniversary of the signing of the Metre Convention in 1875, the new International System of Units (SI) entered into force, linking the SI units to constants of nature. The members of EURAMET, the European Association of National Metrology Institutes, both with the work carried out within the Technical Committees and through the European Metrology Research Programmes (EMRP and EMPIR), have contributed greatly to the scientific basis for the redefinition. 43 Joint Research Projects have been focused on the broader scope of the SI so far, 10 of which gave a direct contribution to the SI redefinition, with the involvement of 39 National Metrology Institutes and Designated Institutes and researchers coming from academia, research institutes and industry.

EURAMET is currently chaired by Hans Arne Frøystein (JV, Norway); the two Vice-Chairpersons are Erkki Ikonen (VTT, Finland) for EMPIR related matters and Maria Luisa Rastello (INRIM, Italy) for the General Assembly (GA). EURAMET 13th GA took place in Borås, Sweden from 21th to 24th May 2019, hosted by RISE, the Swedish National Metrology Institute. Moldova reached the status of full member, after having been associated member since 2017, thus leading to 38 the number of EURAMET full members. The EURAMET 14th GA will take place in Vienna, Austria, from 25th to 28th May 2020. It will be hosted by BEV, the Austrian National Metrology Institute.

One of the most important initiatives undertaken by EURAMET for the promotion of cooperation conceived in a broader scope towards better partnership, communication, and harmonisation is the European Metrology Networks (EMNs). These are collaborative structures which go beyond joint research to increase the coordination of measurement science across Europe, addressing scientific and societal challenges, infrastructure and services. Currently, there are six EMNs, which were approved in 2018: Mathematics and Statistics, Traceability for Laboratory Medicine, Quantum Technology, Smart Electricity Grids, Energy Gases, and Climate and Ocean Observation. Each EMN, by providing a single point of contact, will underpin regulation and standardisation by stablishing a comprehensive and longer-term infrastructure, promoting best practice and disseminating knowledge in their respective fields. Further EMNs are in preparation or consideration, but there were no new EMNs approved in 2019. More information on EMNs can be found at https://www.euramet.org/european-metrology-networks/.

In September 2019, the European Commission had launched a public consultation, which closed in November, on developing a new Metrology Research Partnership, as part of its Horizon Europe programme, the EU's ambitious €100 billion future research and innovation programme for 2021 - 2027. This consultation recognises the importance of a good metrology system for scientific and technological advancement, and the crucial need for precise and accurate measurements across research and industry. The proposed partnership, starting from the experience gained in the existing European Metrology Programme for Innovation and Research (EMPIR), has among its objectives, to create sustainable European metrology networks for strategic application areas and for support of emerging technologies. It aims also at making strategic use of national funding and private investments in metrology to support standardisation, knowledge transfer, and address regulatory issues. More information can be found at https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2019-4972468_en.

The cooperation among metrology institutes, academia, stakeholders, will be implemented in 2020 with the last call within the EMPIR programme framework, via the usual two stage process, on the following major topics: fundamental metrology, industry, normative, networks. Stage 1, opening on the 8 January, aims at

offering stakeholders from any country the opportunity to influence the projects undertaken by the European Community by identifying potential research topics. The highest priority topics received at Stage 1 will provide the basis for Stage 2 which will open in June. In addition, a call for support for impact projects designed to increase impact of completed projects and a call on capacity building will be launched in July 2020.

Technical collaboration in EURAMET is organised within ten Technical Committees (TCs), focusing on specific areas which represent the forum for scientific and technical cooperation in the respective fields. In addition, two Committees deal with the overall topics Quality and Interdisciplinary Metrology. The TCs are responsible for the execution of the activities required by EURAMET as RMO for the fulfilment of the Mutual Recognition Arrangement of the International Committee of Weights and Measures (CIPM-MRA). The types of technical cooperation carried out within the TCs are: cooperation in research, comparison in measurement standards, metrological traceability, consultation on facilities.

One of the ten TCs is devoted to Metrology in Chemistry (Technical Committee for Metrology in Chemistry, TC-MC), which is concerned with primary methods and reference materials for chemical measurements and research in metrology to support different sectors in the amount of substance fields.

NEWS FROM EURAMET TECHNICAL COMMITTEE IN METROLOGY IN CHEMISTRY (TC-MC)

TC-MC is chaired by Sophie Vaslin-Reimann (LNE, France), who took over in 2019 from Hanspeter Andres (METAS, CH). 28 EURAMET member countries are represented in TC-MC.

The technical activities is carried out within the four technical Sub-committees dealing with gas analysis (SC-GA), inorganic analysis (SC-IA), electrochemical analysis (SC-EA), bio and organic analysis (SC-BOA). The convenors of the subcommittees are: Janneke van Wjik (VSL, NL) for SC-GA, Rainer Stosch (PTB, DE) for SC-IA, Daniel Stoica (LNE, FR) for SC-EA and Mine Bilsel (TUBITAK, TR) for SC-BOA who took over the convenorship from John Warren (previously LGC, UK). In addition, a Strategy Working Group, chaired by the TC-Chair, is also active on the following tasks: advice to TC-Chair and subcommittee convenors, strategic planning of comparisons, support actions, coordination, organisation of workshops.

The TC-MC members are actively participating in the European Metrology Programmes EMRP and EMPIR, being involved in the various targeted programmes (Health, Environment, Energy, Industry, Normative, Research Potential), thus indicating the cross-disciplinary nature of the TC itself.

TC-MC MEETING IN 2019

The annual meeting of the TC-MC was held from 4th to 7th February 2019 in Brno (Czech Republic) and was hosted by CMI. The first day was reserved for the Strategy WG meeting and for a dedicated workshop for DIs without CMCs five years after designation. The goal of the workshop was to understand the needs of the concerned DIs and define together appropriate actions, by discussing in depth all needs and requirements.

The four technical subcommittees reconvened, as usual, ahead of the annual TC-MC plenary meeting on 4th February 2019. A review of new claims as well as the obligatory re-review of a range of existing claims were carried out under cycle XX of the CMC claim period. Running and new projects and comparisons in the framework of EURAMET and EMPIR and also proposals for the upcoming EMPIR call were discussed in detail in all sub-committees.

The plenary meeting took place the 6th and 7th February 2019. Some highlights on EURAMET, BIPM/CIPM, CCQM strategy and activities within its main working groups were given. The convenors of the subcommittees gave an overview of the activities of each subcommittee and of the main outcomes of the meetings carried out in the previous day. A session of the plenary meeting was dedicated to European Metrology Networks (EMNs). After a general introduction on EMNs, an overview on the following EMNs, already approved by the EURAMET GA, dealing with topics related to the amount of substance field, was given: EMN on Climate and Ocean Observation (coordinated by NPL), EMN on Energy Gases (coordinated by VSL), EMN on Laboratory Medicine

(coordinated by PTB). The following potential future EMNs were also presented: EMN on Environment (LNE), EMN on Precision Medicine and Advanced Therapeutics (LGC), EMN on Food Safety (INRIM).

TC-MC MEETING IN 2020

The annual meeting of the TC-MC was held from 4th to 7th February 2020 in Bern (Switzerland) and was hosted by METAS. The first day was reserved for the Strategy WG meeting.

The four technical subcommittees reconvened, as usual, ahead of the annual TC-MC plenary meeting on 5th February 2020. A review of new claims as well as the obligatory re-review of a range of existing claims were carried out under cycle XXI of the CMC claim period. Running and new projects and comparisons in the framework of EURAMET and EMPIR and also proposals for the upcoming EMPIR call were discussed in detail in all sub-committees. A joint SCGA, SCIA and SCBOA workshop on isotope ratio analysis followed the SCs meetings. The workshop, following the birth of a Isotope Ratio Working Group of CCQM established in 2018 to progress isotope ratio measurement science and support measurement applications by providing a permanent forum for NMIs to exchange information, advance capabilities and demonstrate comparability, was organized to inform TC-MC members of this new WG and to share these approaches to prepare future projects in the EURAMET framework.

The plenary meeting took place the 6th and 7th February 2020. Some highlights on EURAMET, BIPM/CIPM, CCQM strategy and activities within its main working groups were given. The convenors of the subcommittees gave an overview of the activities of each subcommittee and of the main outcomes of the meetings carried out in the previous day. A session of the plenary meeting was dedicated to a workshop on the EMNs and their interaction with TC-MC, as strengthening the relationships between relevant EMNs and TCs through transversal collaborations is considered, by EURAMET, of paramount importance. The three currents EMNs relevant for TC-MC were presented: EMN on Climate and Ocean Observation (coordinated by NPL), EMN on Energy Gases (coordinated by VSL), EMN on Laboratory Medicine (coordinated by PTB). The following potential future EMNs were also presented: EMN on Environmental Monitoring (LNE), EMN on Medical Device Regulation (LGC), EMN on Food Safety (INRIM). A brainstorming followed on the impact of the EMNs on TC-MC structure and vice-versa and on possible actions to enhance the interaction between EMNs and TC-MC.

The next TC-MC meeting will be held from 3th to 5th February 2021.

ILAC LABORATORY COMMITTEE REPORT

Maire Walsh // LC liaison, Ireland

ILAC MEETINGS

The 2018 ILAC and IAF Joint Annual Meetings were held in Singapore during 22–31 October. The adopted resolutions of the 22nd ILAC General Assembly held in Singapore can be downloaded from the ILAC website at Resolutions of the Twenty-Second ILAC General Assembly, Singapore, 29 and 31 October 2018.

The ILAC Marketing and Communications Committee (MCC) held their meetings in Washington DC on 11-13 March 2019.

The 2019 ILAC and IAF mid-term meetings will be held at the Hilton Mexico City Reforma, Mexico City during 4–11 April 2019. The ILAC Accreditation Committee (AIC), Inspection Committee (IC), Laboratory Committee (LC),

Joint Working Group A Series, Arrangement Committee (ARC), Arrangement Management Committee (AMC), Joint meeting of the ILAC and IAF Management Committees (JMC), ILAC Executive Committee and Joint meeting of the ILAC and IAF Executives (JEC) will all be held during this period.

The 2019 ILAC and IAF Joint Annual Meetings will be held at the InterContinental Hotel, Frankfurt, Germany during 21–30 October.

Information on future meetings and events can be found in the ILAC Calendar.

THE ILAC MRA

As at 12 March 2019, there are **100 ILAC MRA signatories**, representing **103 economies**. The ILAC MRA covers recognition for accreditation in the areas of calibration (ISO/IEC 17025), testing (ISO/IEC 17025), medical testing (ISO 15189), and inspection (ISO/IEC 17020). The list of signatories to the ILAC MRA is available from the ILAC MRA Signatory Search.

The *ILAC MRA Annual Report 2017* is available from the ILAC MRA and Signatories page.

The ILAC MRA acts as an internationally recognized 'stamp of approval' to demonstrate compliance against agreed standards and requirements. Many specifiers, such as government agencies, have recognised the importance of credible accreditation programs that are developed against internationally recognised standards. Accreditation and the ILAC MRA help regulators meet their own legislated responsibilities by providing a globally recognised system to accept accredited test reports. Case studies and research on the recognition of the ILAC MRA by governments and regulators are available from the Public Sector Assurance website. The website is a collaborative initiative between ILAC, ISO, IAF, IEC and IIOC and in the last quarter of 2018 there were 294 case studies, 85 research papers and 50 supporting materials available to view.

The Business Benefits website was launched in 2017. This is a reference website designed to demonstrate the monetary value of standards, conformity assessment and accreditation for businesses. The website was developed by the ILAC MCC / IAF CMC in partnership with IIOC and ISO and represents another successful collaboration between the 4 organisations. Examples of suitable case studies for inclusion on the Business Benefits website are added as they become available and there is a standing request to the memberships of ILAC and IAF to send in examples as they arise. In the last quarter of 2018 there were 83 case studies categorised into 6 areas of value. All of the case studies identify a clear financial benefit. The site also includes 58 research papers and contains a powerful filter that allows users to source information by standard, economy and sector.

A resolution was adopted at the 2014 ILAC General Assembly (GA) in Vancouver that allows implementation of the extension of the ILAC MRA to include accreditation of proficiency testing providers (ISO/IEC 17043), when the appropriate peer evaluation documents within ILAC are updated to cover this new scope. These document updates have been completed and the evaluations to cover the scope of accreditation of proficiency testing providers are nearing completion.

A resolution was adopted at the 2016 ILAC GA in New Delhi that allows the implementation of the extension of the ILAC MRA to include accreditation of reference material producers (ISO/IEC 17034), when the appropriate peer evaluation documents within ILAC are updated to cover this new scope. These document updates have been completed and the evaluations to cover the scope of accreditation of reference material producers are well advanced.

The ILAC GA and IAF GA agreed that a transition period of 3 years from the date of publication be adopted for ISO/IEC 17011:2017 *Conformity assessment — General requirements for accreditation bodies accrediting conformity assessment bodies*. The revised standard was published on 30 November 2017 and ILAC and IAF members adopted a further resolution during the 2017 Joint General Assembly on the implementation of the transition to the 2017 version of the standard (*JGA Vancouver Resolution 2 - Implementation of transition to ISO/IEC 17011:2017)*. Details of the resolution and the transition plan are available from the Joint ILAC-IAF Documents (A-Series) page in the Publications section of the ILAC website.

ISO and ILAC have issued a joint communiqué that re-confirms the three-year transition period for accredited laboratories to transition to the 2017 version of the ISO/IEC 17025. While both the 2005 and 2017 versions of ISO/IEC 17025 will remain valid during the three-year transition period, accreditations to ISO/IEC 17025:2005 will be invalid from 30 November 2020, as per the ILAC Resolution GA 20.15 adopted in November 2016. The ISO/IEC 17025:2017 Transition Communiqué is available from the ILAC-ISO Partnerships page.

Following the publication of ISO 17034 *General requirements for the competence of reference material producers,* in November 2016, the ILAC GA had agreed that accreditation of reference material producers be conducted in accordance with ISO 17034:2016. The implementation period of 3 years is currently underway.

ILAC MEMBERSHIP

ILAC membership as at 12 March 2019 is as follows:

- 100 Full Members (signatories to the ILAC MRA) representing 103 economies;
- 13 Associates representing 12 economies;
- 10 Affiliates representing 18 economies;
- 24 Stakeholders;
- 6 Regional Cooperation Bodies (includes 5 Recognised Regional Cooperation Bodies)

The ILAC membership consists of 153 organisations from 126 different economies worldwide. Over 76,500 laboratories and more than 10,000 inspection bodies are accredited by the ILAC Full Members (signatories to the ILAC MRA). The latest statistics and graphs on the number of accreditation bodies, accredited laboratories and inspection bodies are available from the ILAC Facts & Figures page.

ILAC EXECUTIVE

The 2018 ILAC GA was notable as being the last General Assembly meeting for the ILAC Chair, Ms Merih Malmqvist Nilsson. The ILAC members and international colleagues took the opportunity to acknowledge and thank Merih for her outstanding contribution to the work of ILAC over many years (since 1998). The ILAC members also offered their thanks to the out-going Committee Chairs; Mr Steve Sidney (Laboratory Committee Chair) and Ms Liliane Somma (ILAC Co-Chair of the Joint Development Support Committee).

The elected Executive Committee members for 2019–2020 are:

Chair	Ms Etty Feller
Vice-Chair	Ms Maribel López Martínez
Arrangement Committee	Ms Dana Leaman
Accreditation Committee	Mr Erik Oehlenschlaeger
Inspection Committee	Mr Arne Lund
Marketing & Communications Committee	Mr Jon Murthy
Joint Development Support Committee	Ms Sharonmae Shirley
Arrangement Management Committee	Ms Jennifer Evans
Laboratory Committee	Mr Jeff Gust

The ILAC Executive Committee continues to review the implementation of *ILAC-R3 ILAC Strategic Plan 2015-2020* and the actions detailed in *Supplement 1 to ILAC R3.* The ILAC Committees and the Executive task force groups established to address the implementation of the ILAC Strategic Plan, continue to progress their respective action items and the results of these efforts were seen throughout 2018, with the number of completed actions rising from 14 to 24. Of particular note, is the progress made on two projects, namely the review of the ILAC Committee structure and the consideration of ILAC's resource needs (now and into the future) and the optimal mechanism for delivering those resources. The ILAC Strategic Plan is a standing item for the agenda of each of the ILAC committees. ILAC-R3 can be downloaded from the ILAC Publications and Resources section.

A major focus for the ILAC Executive Committee since 2016 has been the revision of the ILAC Articles and Bylaws. During the ILAC GA in Vancouver 2017, there was a request from EA to provide an alternative proposal for voting in the General Assembly for consideration. The EA alternative proposal was received in late January 2018 and was subsequently distributed to the ILAC members for information while the ILAC Executive, in consultation with the Dutch Notary, prepared the information package to be distributed to ILAC members to seek their

feedback on the two voting proposals being presented.

The member feedback period concluded on 31 August 2018 and feedback was received from 102 members (65.8%), of which 58% supported the Executive developed proposal based on one vote per AB and 37% supported the EA alternative proposal based on one vote per economy. 42 members also provided written comments as part of their feedback.

Based on the responses from members and the comments received, it was agreed during the 2018 ILAC GA that work would now proceed on the revision of the Articles of Association and would be based on the voting model initially developed by the Executive Committee, and the Executive Committee will include provisions in the Articles of Association aimed at reducing or removing the risk of national domination.

Also following the 2018 ILAC GA in Singapore, the Articles and Bylaws were updated to take into account the results of member feedback and the Executive recommendations arising from that feedback. A second formal 60 day member comment period on the ILAC Articles and Bylaws is currently underway and will conclude on 18 March 2019. The next steps then include reviewing and addressing the comments received, commencing the official translations into Dutch and preparing the final versions of these documents in preparation for formal voting to take place during the ILAC General Assembly in Frankfurt in October 2019.

The call for nominations of Team Leaders (Lead Assessors/ Management Systems Experts) and Legal Metrology Experts to participate in assessments of Test Laboratories seeking recognition under the OIML Certification System (OIML-CS) was undertaken in early 2019.

The revised MoU between ILAC, IAF and OIML was signed by the ILAC and IAF Chairs and the CIML President during the 53rd CIML meeting in Hamburg, Germany on 10 October 2018.

The MoU between ILAC, IAF and IEC was revised during 2018 and provided to IEC for a final review. When IEC concludes their review process arrangements will be made for representatives of the three organisations to resign the MoU.

ILAC and IAF also signed MoUs with the World Bank and with IHAF (International Halal Accreditation Forum) on 30 October 2018 during the IAF-ILAC Joint General Assembly held in Singapore. These MoUs provide a framework for cooperation in areas of mutual interest.

The MoU between ILAC and IFCC was re-signed in January 2019.

Information on ILAC's partnerships, including copies of communiqués, joint procedures, press releases and MoUs, is available from the ILAC Partnerships page.

ILAC LIAISONS AND OTHER INTERNATIONAL ACTIVITIES

ILAC carries out a number of regular liaison activities with our international partners, participating in both the routine meetings that underpin these relationships as well as any relevant ad hoc events that may be scheduled throughout the year. During 2018 ILAC has been represented at numerous international conferences, workshops and meetings and this will continue in 2019.

In March each year, the International Bureau of Weights and Measures (BIPM) hosts the annual BIPM and ILAC bipartite working group meeting and the BIPM, ILAC, OIML and ISO quadripartite meeting. The ILAC delegation to these meetings is led by the ILAC Accreditation Committee Chair, Erik Oehlenschlaeger and includes Neville Taylor and Dana Leaman. The 2019 meetings will take place on 18 and 19 March.

ILAC liaison officers, including Erik Oehlenschlaeger, Steve Sidney, Martina Bednarova and Graham Jones attended the following meetings as the ILAC liaisons during 2018:

- Joint Committee for Guides in Metrology (JCGM): WG 1 (GUM) meetings in June and December 2018, Plenary meeting in December 2018.
- Joint Committee for Traceability in Laboratory Medicine (JCTLM): Executive meeting and Members meeting in December 2018.

OIML and BIPM representatives regularly participate in meetings of the ILAC Accreditation Committee (AIC), with the most recent meeting being held in October 2018 in Singapore. The next meeting of the AIC will be in Mexico City on 4 and 5 April 2019.

The (2017–2018) ILAC Chair, Merih Malmqvist Nilsson, represented ILAC at the 53rd Meeting of the International Committee of Legal Metrology (CIML), held in Hamburg, Germany in October 2018.

The first meeting of the OIML-CS Management Committee was held in Sydney, Australia on 21 and 22 March 2018 and was attended by John Styzinski, representing ILAC and IAF and Annette Dever. The next meeting will be held in Delft on 20–21 March and will be attended by Andre Barel.

Merih Malmqvist Nilsson, represented ILAC at the 26th meeting of the General Conference on Weights and Measures (CGPM) in Versailles, 13–16 November 2018. The revised *Joint BIPM, OIML, ILAC and ISO Declaration on Metrological Traceability* was also re-signed by representatives from all four organisations during the CGPM meetings. This document builds on the 2006 tripartite statement and presents the principles that should be used when demonstrating metrological traceability for international acceptance.

ILAC continues to be represented at the ISO/CASCO policy meetings and at a number of ISO technical committee and working group meetings.

In April 2018, the ILAC Secretary Annette Dever, represented ILAC at meetings of the CASCO Chairman's Policy Committee (CPC), the Strategic Alliance and Regulatory Group (STAR), the Technical Interface Group (TIG) and the CASCO Plenary, in Mexico City. Meetings of the CASCO CPC, STAR and TIG and the JSG were also held in Geneva during 26–29 November 2018, where ILAC was represented by Merih Malmqvist Nilsson and Annette Dever.

ILAC representatives, including Jennifer Evans, Arne Lund, Lorraine Turner, He Ping, Zhai Peijun and Pamela Sale have attended a number of CASCO Working Group meetings and ISO TC meetings during 2018 as follows:

- ISO CASCO WG49, ISO/IEC 17000 revision *Conformity Assessment - Vocabulary and general principles*: February 2018 and 19-21 November 2018.
- ISO CASCO WG 23, PROC 33 revision *CASCO Common Elements:* February 2018 and 22- 23 November 2018.
- ISO TC 212 *Clinical laboratory testing and in vitro diagnostic test systems:* May 2018 and October 2018.
- ISO TC 272 *Forensic sciences:* May 2018 and 19–23 November 2018.
- ISO/REMCO meetings: July 2018.

In April 2019, the ILAC Vice Chair Maribel Lopez and the ILAC Secretary Annette Dever, will represent ILAC at meetings of the CASCO Chairman's Policy Committee (CPC), the Strategic Alliance and Regulatory Group (STAR), the Technical Interface Group (TIG) and the CASCO Plenary, in Nairobi, Kenya.

During 2019, ILAC representatives, including Jennifer Evans, Arne Lund, Lorraine Turner, He Ping, Zhai Peijun, Andrew Griffin, Brian Brookman and Pamela Sale are planning to participate in the following meetings as ILAC liaison representatives:

- ISO CASCO WG49, ISO/IEC 17000 revision *Conformity Assessment - Vocabulary and general principles*: 23–25 September 2019.
- ISO CASCO WG 23, PROC 33 revision *CASCO Common Elements:* 26–27 September 2019.
- ISO TC 212 (WG 1, Plenary & revision of ISO 15189 meetings) *Clinical laboratory testing and in vitro diagnostic test systems:* 28–30 May 2019 and October 2019.
- ISO TC 272 *Forensic science:* 20–24 May 2019.
- ISO TC 69 *Applications of statistical methods:* 17–21 June 2019.
- ISO/REMCO *Reference Materials Committee*: 10–13 June 2019.

The IEC-ILAC-IAF Steering Committee meeting was held on 19 October 2018 in Busan, Republic of Korea, with ILAC representatives, Etty Feller and Erik Oehlenschlaeger participating via WebEx. The next meeting is proposed for October 2019.

Etty Feller, (2017–2018) ILAC Vice-Chair, once again represented ILAC at the Organisation for Economic Cooperation and Development (OECD) meeting on "International Regulatory Cooperation: Fostering the contribution of international organisations to better rules of globalisation" in Geneva on 12 and 13 April 2018 and also attended the follow up meeting in Paris on 27 November 2018. The next meeting is scheduled for 10 April 2019 in New York City, USA.

Maire Walsh represented ILAC at the Annual Members meeting of the Cooperation on International Traceability in Analytical Chemistry (CITAC) in Paris during April 2018.

Merih Malmqvist Nilsson also represented ILAC at the UNECE event in Geneva on 26 September 2018 titled *Standards and SDGs.*

Merih Malmqvist Nilsson, began a two year term as Chair of the DCMAS Network in 2018. This organisation has changed its name and scope of activity to become a group for all economies providing a platform for the global organisations in the quality infrastructure to meet and exchange information on relevant topics including opportunities for cooperation. The transition to the new organization is now complete with the new name, International Network on Quality Infrastructure (INetQI) and logo confirmed and the first meeting was held in Geneva on 30 November 2018.

During the first INetQI meeting it was confirmed that ILAC would provide the Chair for 2019 and 2020, and the ILAC Executive subsequently confirmed that the retired ILAC Chair, Merih Malmqvist Nilsson would continue in her role as Chair of INetQI on behalf of ILAC.

Jon Murthy once again participated in the United Nations Economic Commission for Europe (UNECE) Working Party on Regulatory Cooperation and Standardisation Policies (WP. 6) Annual Session, in Geneva on 14–16 November 2018. He then also represented ILAC at the 36th IFIA General Assembly and associated Seminars on 12–13 December 2019 in Paris.

ILAC thanks all of the ILAC liaison officers, and their organisations, who volunteer their time to assist ILAC in carrying out these activities for the benefit of all ILAC members.

The Liaison information page, located in the member's area of the ILAC website, continues to serve as the main repository for the reports and documents produced as part of ILAC's liaison activities. ILAC members can also find copies of all ILAC comments submitted during ISO/CASCO ballots on international standards pertinent to the work of ILAC. The *ILAC Liaison Procedure*, which provides information relating to ILAC's liaison activities, can also be downloaded from this page.

ILAC SECRETARIAT

The ILAC Secretariat is currently staffed as follows: Annette Dever (F/T), Sharon Kelly (F/T), Stephanie Sun (F/T), Nicole Kam (0.6 FTE), Rose De Rota (0.7 FTE) and Joëlle Nicolas (0.8 FTE). Stephanie joined the Secretariat in July 2018 filing the vacant Project Officer role and Nicole joined the Secretariat in January 2019 as the ILAC Finance Officer, working 3 days per week.

In 2019, World Accreditation Day will be celebrated on 9 June and the theme is:

"Accreditation: Adding Value to Supply Chains"

Documents and brochures published since April 2018 are as follows:

ILAC-G28:07/2018 *Guideline for the Formulation of Scopes of Accreditation for Inspection Bodies*

ILAC-G26:11/2018 *Guidance for the Implementation of a Medical Accreditation Scheme*

IAF/ILAC B1:09/2018 *The route to signing the IAF or ILAC Arrangement*

IAF/ILAC B2:09/2018 *How do I gain confidence in an Inspection Body? Do they need ISO 9001 Certification or ISO/IEC 17020 Accreditation*

IAF/ILAC B6:09/2018 *Accreditation: Delivering confidence in the provision of energy*

Many of the ILAC documents and brochures have been translated into a range of different languages.

Follow @ILAC_Official on Twitter to receive the latest ILAC news, including information on meetings, events, liaison activities and new publications.

The latest edition of the newsletter can be accessed via the following link ILAC News 54, October 2018. The next edition of ILAC News will be published in late April 2019. Past editions of the ILAC Newsletters are also available to download from the ILAC website.

You can also subscribe to the ILAC Newsletter.

Subscribe to the latest news to receive updates from ILAC members and liaisons.

IMEKO REPORT

Michela Sega // INRIM, Italy, IMEKO TC8 Chair

IMEKO, the International Measurement Confederation, founded in 1958, is a non-governmental federation of 42 Member Organizations individually concerned with the advancement of measurement technology. It has a consultative status with UNESCO and UNIDO. Its fundamental objectives are the promotion of international interchange of scientific and technical information in the field of measurement and instrumentation and the enhancement of international co-operation among scientists and engineers from research and industry.

IMEKO Secretariat is located in Budapest (Hungary) and the Secretary is Mrs. Judit Farago. More information about IMEKO and its structure can be found on the IMEKO website (www.imeko.org).

The 62nd General Council Session and the Advisory Board, the Technical Board and the Measurement Editorial Board Meetings of IMEKO took place in Berlin, Germany, on 5th-6th September 2019, hosted by the Physikalisch-Technische Bundesanstalt (PTB), the German member organization. A new member organization, the Research Institutes of Sweden (RISE), joined the IMEKO Community. The 63rd IMEKO General Council Session and the related meetings will be held in Denver (USA) on 23rd– 24th August 2020, hosted by the National Institute of Standards and Technology (NIST), the IMEKO US member organization.

The year 2019 was extremely reach of IMEKO events, organized by the various Technical Committees:

- the 16th IMEKO TC10 Conference "Testing, Diagnostics & Inspection as a comprehensive value chain for Quality & Safety" was held in Berlin (Germany) on 3rd-4th September (http://www.imekotc10-2019.sztaki.hu/);
- the 4th IMEKOFOODS Conference "Metrology Supporting Emerging Food Topics" was held in Brussels – Tervuren (Belgium) on 16th-18th September (https://www.imekofoods4.be/);
- the 23rd IMEKO TC4 Symposium took place in Xi'an (China) on 17th-20th September (http://www.imeko2019.org/);
- the Joint IMEKO TC1 and TC2 International Symposium for "Photonics and Education in Measurement Science" was organized in Jena (Germany) on 17th-19th September;
- IMEKO TC17 organised the 22nd "International Symposium on Measurement and Control in Robotics"- ISMCR 2019 in Houston (Texas, USA) on 19th-21th September (http://ismcr.org/);
- the IMEKO TC19 International Workshop on "Metrology for the Sea" was held in Genoa (Italy) on 3rd-5th October; the 2020 edition is scheduled in October 2020(http://www.metrosea.org/);
- the 8th IMEKO TC19 Symposium on "Environmental Instrumentation and Measurements" took place in Sfax (Tunisia) on 29th-30th October;
- the IMEKO TC4 International Conference on "Metrology for Archaeology and Cultural Heritage" - MetroArchaeo 2019, was organized in Florence (Italy) on 4th-6th December (http://www.metroarcheo.com/).

A series of new events is foreseen in 2020. More information is available on https://www.imeko.org/index.php/imeko-news-events/coming-events.

The Technical Committees can select best contributions to IMEKO events to be published, as enhanced versions of the corresponding papers, in Measurement, the official journal of IMEKO, after the event. Additional contributions to IMEKO events can be also published in the IMEKO Online Journal ACTA IMEKO, which published its 4 issues in 2019 (https://acta.imeko.org/index.php/acta-imeko).

The next XXIII IMEKO World Congress will be held in Yokohama (Japan) on 30th August -3rd September 2021, in the Pacifico Yokohama (Exhibition Hall and Conference Center) venue. It will be hosted by the Japanese Member Organization of IMEKO, the Society of Instrument and Control Engineers (SICE), with active

involvement from many Japanese professional bodies, universities and industry. The world congress will be preceded by the IMEKO Annual Advisory Board Meeting, the General Council Session and the Technical Board and the Measurement Editorial Board Meetings which will take place on August 28th and 29th. More information can be found in the website www.imeko2021.org.

The venue and dates for the XXIV IMEKO World Congress were defined. It will take place at the new Congress Center of Hamburg (Germany) on 26th-29th August 2024, hosted by PTB, the German Member Organization of IMEKO. The meetings of the IMEKO Annual Advisory Board Meeting, the General Council Session and the Technical Board and the Measurement Editorial Board will be held on August 24th and 25th.

REPORT FROM ISO/REMCO

Angelique Botha // NMISA, South Africa, ISO/REMCO Chair

The 42nd meeting of the Reference Material Committee of ISO, ISO/REMCO, was held in Daejeon, South Korea from 10 to 13 June 2019, and was hosted by the Korea Research Institute of Standards and Science (KRISS). ISO/REMCO now has a membership of 72 members of the International Organization for Standardization (ISO) and liaison with 16 international organizations and multiple ISO-internal committees (9 'to' and 24 'from' ISO/REMCO). Thirty-two delegates and liaison representatives attended the meeting coming from 11 ISO voting members out of 33 (33 %) and 3 international organizations in liaison out of 16 (19 %).

The scope of ISO/REMCO, as agreed by the ISO Technical Management Board (TMB), is:

- To establish concepts, terms and definitions related to reference materials.
- To specify the basic characteristics of reference materials as required by their intended use.
- To propose actions on reference materials required to support other ISO activities.
- To prepare guidelines for ISO technical committees when dealing with reference material issues.
- To communicate with other international organizations on reference material matters.
- To advise the ISO TMB on reference material issues.

GUIDANCE ON THE PRODUCTION OF QUALITATIVE REFERENCE MATERIALS AND THE ASSIGNMENT OF NOMINAL PROPERTIES

Working group 13 under the convenorship of Dr Stefanie Trapmann started with the work to draft the new ISO Guide 85 to develop guidance for the production of qualitative reference materials. During the past year several examples of qualitative reference materials were collected. using a template focusing on the important aspects of reference material production. A first attempt at the drafting of ISO Guide 85 was to look for common threads in the examples provided in terms of the important aspects and questions asked in the template, including the assessment of homogeneity and stability, as well as the characterization and evaluation of the uncertainty of the certified value.

The examples were summarized in a tabulated format to make it easier to see the similarity in approaches used and during the discussions in the working group the examples were divided into three groups considering structural identity, pharmacopoeia and provenance/ authenticity for the drafting of ISO Guide 85. Good progress was made to also collect missing information from some of the examples and some other aspects that needed clarification. Several technical experts also volunteered to assist the convener with the technical content of the Guide. The plan is to discuss the completed

working draft of ISO Guide 85 at the 43rd meeting of ISO/REMCO early in July 2020 in preparation for the ballot on the committee draft of the Guide towards the end of 2020.

GUIDANCE ON THE PRODUCTION OF HIGH PURITY REFERENCE MATERIALS

ISO Guide 87 has been registered as a new work item with the proposed title: Guidance on the production of high purity reference materials for metals and metalloids. A new working group (WG19) has been established under the convenorship of Dr Zoltan Mester. The membership of the new working group will consist of the existing members of the ad-hoc group 6 that looked at the possibility of developing guidance for high purity reference materials for inorganic elements. The first meeting of the new working group was held during the 42nd ISO/REMCO meeting. The plan is to discuss the first working draft of ISO Guide 87 at the 43rd meeting of ISO/REMCO early in July 2020.

In working group 18 under the convenorship of Dr Takeshi Saito, the drafting process for ISO Guide 86 on the production of high purity reference materials for small organic molecules also started with a collection of examples. Some technical aspects that were already discussed in the working group included the extent to which the impurities need to be certified in a high purity material. There is a clear need to specify the intended use of the material during the production planning.

There were also some discussions about the best practice for the assessment of the homogeneity of the material. The question was asked whether it is allowed to do homogeneity testing on the bulk material or whether the testing must be done on the final packaged material. It was again highlighted that the ISO 17034 requirement is to assess and not necessarily test the homogeneity of the material in the final packaged form. Another issue is also how best to evaluate possible impurity levels that lies below the limit of detection of the measurement methods. A proposal was made for the two working groups working on the guidance documents on the production of high purity materials to have a joined workshop to discuss common problems. This workshop will form part of the meeting schedule for the 43rd annual ISO/REMCO meeting. The plan is also to discuss the completed working draft of ISO Guide 86 at the next ISO/REMCO meeting in order to progress to the committee draft stage towards the end of 2020.

LIAISING WITH INTERNATIONAL ORGANIZATIONS ON ISSUES RELATING TO REFERENCE MATERIALS

At the 41st annual ISO/REMCO meeting, the working group responsible for the terms and definitions related to reference materials were re-activated to draft updated definitions for reference material (RM) and certified reference material (CRM). This update was prompted by discussions with the group responsible for the drafting of the 4th edition of the International Vocabulary on Metrology (VIM4). The REMCO members approved the revised definitions of RM and CRM during a committee internal ballot that was completed by the end of 2018.

During the 42nd annual ISO/REMCO meeting, the comments received from the REMCO members during the committee internal ballot on the definitions were reviewed. The definitions were finalised, and the meeting took a resolution to submit them for a draft amendment ballot of the definitions in ISO Guide 30. The REMCO Chair was asked to draft a letter to the VIM group with the proposed definitions to ask them to consider them for inclusion in the drafting of VIM4 and to use qualitative property value as a synonym for nominal property value going forward.

ISO/REMCO also had fruitful interactions with the ILAC Accreditation Committee (AIC) about the issue of accredited proficiency testing (PT) providers selling their PT materials to customers after completion of the study round. The resale of these PT materials has implications in terms of the requirements that the PT materials must meet in terms of the assessment of long-term stability and stability monitoring. ISO/REMCO also had some discussions with ILAC about the status of the standard ISO 20387 for the third-party accreditation of biobanks and the strong overlap with ISO 17034.

STRATEGIC REFLECTION FOR THE FUTURE AND PROMOTION OF THE WORK OF ISO/REMCO

The work of two ad-hoc groups that investigated the

possibility to start new work items were concluded during the 42nd annual ISO/REMCO meeting. The group that investigated recent advancements in the assessment of homogeneity and stability found six (6) interesting papers in the literature that will be converted into examples and published on the new ISO/REMCO website. Other issues that were identified by the group, such as homogeneity testing on the bulk material and the case of a metal disk being used for spark optical emission spectrometry where the homogeneity is stratified, will be filed for consideration during the next edition of ISO Guide 35.

The group that considered the requirements for reference materials in process analytical technologies submitted a final report, although these types of materials will be very important in the future, the market is still very focused on the pharmaceutical and glass industries at the moment. The state of our knowledge is therefore not sufficient to be able to prepare guidance on internationally harmonised methods and approaches for the production of reference materials for process analytical technologies.

The new ISO/REMCO website will be updated during the course of the coming year with a revision of the REMCO Position Paper on the commutability of reference materials, some news articles will be included to report on the progress with the new work items and other meetings and conferences related to reference materials will also be promoted in the website. The committee is very excited about the prospect of sharing and exchanging new information related to reference materials, such as recent advancements in the assessment of homogeneity and stability of reference materials through the use of the website (https://committee.iso.org/home/remco).

Three of the published guidance documents of ISO/REMCO will be up for systematic review during 2019, i.e. ISO Guide 30 "Selected terms and definitions", ISO Guide 33 "Good practice in using reference materials" and ISO Guide 80 "Guidance for the in-house preparation of quality control materials (QCMs)". The committee members will need to consider whether the contents of these documents are still relevant and up-to-date. The outcomes of the systematic reviews will be considered during the next ISO/REMCO meeting.

The 43rd meeting of ISO/REMCO will be held in Milan, Italy from 30 June to 3 July 2020.

Participants of the 42nd meeting of ISO/REMCO in Daejeon, South Korea, 10-13 June 2019

REPORT FROM ISO/TC 69/SC 6

Tomoyuki Endo // JISC, Japan, ISO/TC 69/SC 6 Secretary

GENERAL

ISO/TC 69/SC 6 'Measurement methods and results' has Secretariat situated in Japan (JISC), 16 participating and 16 observing members. There are in liaison 13 ISO committees and 8 international organizations (European Commission, IDF, IOC, ILAC, IMEKO, OIML, CITAC and EURACHEM). The standards published by ISO/TC 69/SC 6 are listed in the following table.

Reference	Document title
ISO 5725-1:1994	Accuracy (trueness and precision) of measurement methods and results -- Part 1: General principles and definitions
ISO 5725-2:1994	Accuracy (trueness and precision) of measurement methods and results -- Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method
ISO 5725-3:1994	Accuracy (trueness and precision) of measurement methods and results -- Part 3: Intermediate measures of the precision of a standard measurement method
ISO 5725-4:1994	Accuracy (trueness and precision) of measurement methods and results -- Part 4: Basic methods for the determination of the trueness of a standard measurement method
ISO 5725-5:1998	Accuracy (trueness and precision) of measurement methods and results -- Part 5: Alternative methods for the determination of the precision of a standard measurement method
ISO 5725-6:1994	Accuracy (trueness and precision) of measurement methods and results -- Part 6: Use in practice of accuracy values
ISO 10576-1:2003	Statistical methods -- Guidelines for the evaluation of conformity with specified requirements -- Part 1: General principles
ISO 10725:2000	Acceptance sampling plans and procedures for the inspection of bulk materials
ISO 11095:1996	Linear calibration using reference materials
ISO 11648-1:2003	Statistical aspects of sampling from bulk materials -- Part 1: General principles
ISO 11648-2:2001	Statistical aspects of sampling from bulk materials -- Part 2: Sampling of particulate materials
ISO 11843-1:1997	Capability of detection -- Part 1: Terms and definitions
ISO 11843-2:2000	Capability of detection -- Part 2: Methodology in the linear calibration case
ISO 11843-3:2003	Capability of detection -- Part 3: Methodology for determination of the critical value for the response variable when no calibration data are used
ISO 11843-4:2003	Capability of detection -- Part 4: Methodology for comparing the minimum detectable value with a given value

Reference	Document title
ISO 11843-5:2008	Capability of detection -- Part 5: Methodology in the linear and non-linear calibration cases
ISO 11843-5:2008/Amd 1:2017	Capability of detection -- Part 5: Methodology in the linear and non-linear calibration cases -- Amendment 1
ISO 11843-6:2019	Capability of detection -- Part 6: Methodology for the determination of the critical value and the minimum detectable value in Poisson distributed measurements by normal approximations
ISO 11843-7:2018	Capability of detection -- Part 7: Methodology based on stochastic properties of instrumental noise
ISO 13528:2015	Statistical methods for use in proficiency testing by interlaboratory comparison
ISO 21748:2017	Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty evaluation
ISO/TR 13587:2012	Three statistical approaches for the assessment and interpretation of measurement uncertainty
ISO/TR 22971:2005	Accuracy (trueness and precision) of measurement methods and results -- Practical guidance for the use of ISO 5725-2:1994 in designing, implementing and statistically analysing interlaboratory repeatability and reproducibility results
ISO/TS 17503:2015	Statistical methods of uncertainty evaluation -- Guidance on evaluation of uncertainty using two-factor crossed designs
ISO 21748:2017	Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty evaluation
ISO/TS 21749:2005	Measurement uncertainty for metrological applications -- Repeated measurements and nested experiments
ISO/TS 28037:2010	Determination and use of straight-line calibration functions

WORKING GROUPS

WG 1 "ACCURACY OF MEASUREMENT METHODS AND RESULTS": PROF. OJIMA

REVISION OF ISO 5725 SERIES

ISO/PWI 5725-1 *Accuracy (trueness and precision) of measurement methods and results -- Part 1: General principles and definitions*

The project leader, Ms. Soraya Amarouche introduced the latest draft on ISO/PWI 5725-1 which describes the outline of part1. As a result of discussion, ISO/TC 69/SC 6/WG 1 decided to continue the discussion and keep a status of PWI. ISO/TC 69/SC 6/WG 1 asked the project leader to prepare a draft by 2020-03-31 for WG consultation.

ISO/DIS 5725-2 *Accuracy (trueness and precision) of measurement methods and results -- Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method*

The project leader, Dr. Stephen Ellison explained his observation for the comments of ISO/DIS 5725-2. As a result of discussion, WG 1 agreed to skip FDIS stage to go to publication directly, since WG 1 confirmed that changes were not technical changes but editorial changes. WG 1 asked the project leader to prepare an updated draft and necessary materials by 2019-07-31 for publication.

ISO/WD 5725-3 *Accuracy (trueness and precision) of measurement methods and results – Part 3: Alternative*

designs for precision studies

The project leader, Dr. Steffen Uhlig explained the latest working draft and WG 1 agreed to initiate CD ballot. WG 1 asked the project leader to prepare a revised draft by 2020-02-29. WG 1 also agreed to change the title from the current one to " *Accuracy (trueness and precision) of measurement methods and results - Part 3: Intermediate precision and alternative designs for collaborative studies*".

ISO/DIS 5725-4 *Accuracy (trueness and precision) of measurement methods and results -- Part 4: Basic methods for the determination of the trueness of a standard measurement method*

The project leader, Prof. Jiang Zheng explained his observation for the comments of ISO/DIS 5725-4. WG 1 agreed to proceed to FDIS ballot, since WG 1 confirmed that changes include technical issues. WG 1 asked the project leader to revise a draft as agreed changes by 2019-07-31 for FDIS ballot.

ISO/PWI 5725-5 *Accuracy (trueness and precision) of measurement methods and results -- Part 5: Alternative methods for the determination of the precision of a standard measurement method*

WG 1 agreed to start the revision of part 5 as PWI and nominate Dr. Stephen Ellison as a project leader. WG 1 asked Dr. Ellison to prepare an initial draft for WG consultation by 2020-03-31.

ISO/PWI TR 27877 *Precision of binary data*

The project leader, Dr. Jun-ichi Takeshita explained the overview of ISO/TR 27877. WG 1 agreed to register this project as AWI. WG 1 asked the project leader to prepare the working draft by 2020-03-31 for WG consultation.

ISO/WD TS 27878 *Reproducibility of the LOD of binary methods by means of collaborative studies*

The project leader, Dr. Steffen Uhlig explained observations of comments from WG consultation. As a result of discussion, WG 1 agreed to initiate DTS ballot. WG 1 asked the project leader to prepare a revised draft by 2019-12-15 for DTS ballot.

WG 5 „CAPABILITY OF DETECTION“: DR. HAYASHI

ISO/PWI TR 11843-8

Dr. Hayashi, the convenor of WG 5 and Mr. Yoichiro Furukawa explained their observation for comments of WG consultation. The draft will be updated the draft based on discussion, and WG 5 agreed to register this project as AWI.

WG 7 “STATISTICAL METHODS TO SUPPORT MEASUREMENT UNCERTAINTY EVALUATION”: PROF. COX

The revision of ISO 10576-1 *Statistical methods – Guidelines for the evaluation of conformity with specified requirements*

Dr. Michael Morton explained the revision of ISO 10576-1, and WG 7 agreed to start the revision with the current Scope. WG 7 asked the project leader to prepare a working draft by 2020-03-31 for WG

ISO/WD TS 23471 *Experimental designs for evaluation of uncertainty – Use of factorial designs for determining uncertainty functions*

The project leader, Dr. Steffen Uhlig explained the observation for comments of WG consultation. As a result of discussion, WG 7 agreed to initiate DTS ballot. WG 7 asked the project leader to prepare a revised draft by 2019-12-15 for WG consultation.

ISO/WD 24185 *The evaluation of the uncertainty of measurements from an autocorrelated process*

The project leader, Dr. Nien-fan Zhang explained observation of comments from NP ballot. WG 7 agreed to continue the discussion as WD stage, and WG 7 asked the project leader to prepare a working draft by 2020-02-29 for WG consultation.

AHG 1 “Statistical methods to support measurement uncertainty evaluation”: Prof. Suzuki

Prof. Suzuki, the convenor of AHG 1 reported the outcome of meeting in Nagoya, and members discussed whether ISO 13528:2015 should be revised or not. AHG 1 agreed to conduct the minor revision on ISO 13528:2015 with a project leader, Dr. Stephen Ellison, to correct editorial issues which were identified at the meeting on 2019-06-17. AHG1 asked Dr. Ellison to prepare the working draft to start an FDIS ballot by 2019-07-31.

IUPAC ANALYTICAL CHEMISTRY DIVISION REPORT

Zoltan Mester // NRC, Canada, President of the IUPAC ACD

2019-039-3-500 A Review of Current Status of Analytical Chemistry Education. There is plenty of anecdotal evidence for the erosion of analytical chemistry as a discipline. This is impacted by faculty appointments, funding structures and perception of the field as being a service function. Additionally, as instruments become easier to use there is a mistaken belief in some industrial organisations that there is a reduced need for highly trained analytical specialists. There have been warning signs that the current, university chemistry curriculum, often with a does not address the needs of chemistry graduates and future employers and does not enable analytical practitioners to maximise the value of their work. The project will reflect on the interdisciplinary curriculum development efforts which has been the trend in many universities worldwide. This is a significant economic cost, considering that in many economies the most used practical skills of graduates is actually related to chemical analysis. A deep and fundamental understanding of analytical chemistry is required to foster the next generation of analytical scientists who have the insight and capacity to contribute to fundamental new developments in this field as well as the generation of new disruptive technologies.

The project will document the status quo in various regions of the world regarding the health of the discipline, proportion of professorships, funding and quality of analytical chemistry education. It will examine current attempts to address these shortcomings and offer some ways forward. The findings will be published in the form of white paper to support future curriculum development, funding and hiring decision.

2017-031-1-050 IUPAC100 Periodic Table Challenge. As a part of the 100 years of IUPAC and the 150 years of the Periodic Table, a sub project is preparing for The Global Periodic Table Competition. Division input would be appreciated in the form of potential questions. "Questions about the name, chemical or physical properties or discovery are possible. But more importantly, we also need you to provide the correct answer highlighting the role of IUPAC in that particular case or more broadly." This activity is about educating people about the work of IUPAC.

In this context, we also note that: The UN General Assembly has proclaimed 2019 as the "International Year of the Periodic Table of Chemical Elements" (see more in IUPAC news 20th December 2017).

2012-005-1-500 Vocabulary of Concepts and Terms in Analytical Chemistry - the revised Orange Book project. The Orange Book (present title "Compendium of Analytical Nomenclature" 3rd Edition) was published in 1998, and now is in the process of revision.

The new Orange Book will be in a consistent glossary style format with definitions of concepts in different fields of analytical chemistry. The nineteen chapters of the 3rd edition will become eleven in the present revision. We have taken the decision to concentrate on methods and not attempt to venture into the ocean of applications. The first chapter will set the metrological scene with definitions from the Green Book, the International Vocabulary of Concepts and Associated Terms in Metrology (VIM) and selected chemometrics and statistical terms. The project is nearing completing, publication is expected in 2020.

2017-005-3-500 Analytical Chemistry of Nanomaterials. The impact of materials structured at the nanometer scale becomes enormous and continues to increase. Analytical chemistry of nanomaterials belongs to emerging issues in this field. Together with physical and physicochemical characterization of shape, size, and structure nanoparticles, analytical chemistry research considers isolation/purification and detection-

identification/ quantification/ spatial composition characterization of nanomaterials in bulk materials, special nanotechnology products, complex matrices of environmental, biological and food samples, and others. The project intends to produce a guidance document on best analytical chemistry practices for the characterization of such materials.

2016-007-1-500 Risks of conformity assessment of a multicomponent material or object in relation to measurement uncertainty of its test results. To develop an approach for evaluation of the probability of false decisions in conformity assessment of a multicomponent material or object in relation to measurement uncertainty of test (chemical analytical) results of a sample of the material or object. This probability, combining probabilities of false decisions concerning different components of the material or object, will characterize the sample conformity as a whole. The solution to this problem is important for understanding conformity assessment risks in customs control, clinical analysis, pharmaceutical industry, environmental control, and other fields.

2019 DOUBLE CELEBRATION

In 2019 IUPAC and world have celebrated 150 years of the periodic table as outlined by Dmitri Mendeleev in 1869, and the 100 years since the founding of the International Union of Pure and Applied Chemistry (IUPAC). It is stated in the prospectus of the International Year of the Periodic Table: 'In proclaiming an International Year focusing on the periodic table of chemical elements and its applications, the United Nations has recognised the importance of raising global awareness of how chemistry promotes sustainable development and provides solutions to global challenges in energy, education, agriculture and health'. IUPAC along with International Union of Pure and Applied Physics (IUPAP), the European Chemical Society (EuChemS), the International Science Council (ISC), International Astronomical Union (IAU), and the International Union of History and Philosophy of Science and Technology (IUHPS) spearheaded this effort celebrating chemical science and its contribution to development and betterment of life. The official opening of this year of celebration took place at the UNESCO in Paris, France on January 29th; followed events around the globe: conference in Moscow, Russia on Mendeleev's birthday, February 8; the IUPAC100 global breakfasts on 12 February; and, following the International Day for Women and Girls in Science, the International Symposium on Women and the Periodic Table in Murcia, Spain, on February 11–12. Other major meetings through the year included the IUPAC Congress in Paris, in July, and Mendeleev 150 Conference, otherwise known as the 4th International Conference on the Periodic Table, in St Petersburg, Russia on July26–28, https://www.iypt2019.org/.

ORGANIZATION

ANALYTICAL CHEMISTRY DIVISION

As results of the 2019 election of Analytical Chemistry division membership the composition of the division for the 2020-2021 biennium is as follows: **Division President** - Zoltán Mester, **Division Past President** - Jan Labuda, **Division Secretary** - Derek Craston, **Division Vice President** - David Shaw; **Titular Members** - Vasilisa B. Baranovskaia, Hasuck Kim, Petra Krystek, M. Clara F. Magalhães, Takae Takeuchi, Susanne Kristina Wiedmer; **Associate Members** - Resat Apak, Jiri Barek, Franziska Emmerling, Erico Marlon de Moraes Flores, Ilya Kuselman, Hongmei Li; **National Representatives** - Maria Filomena Camoes, Orawon Chailapakul, Attila Felinger, D. Brynn Hibbert, Serigne Amadou Ndiaye, Mariela Pistón, Rufus H. Sha'Ato, Luisa Torsi, Frank Vanhaecke.

COUNCIL

The IUPAC Council meet in Paris in July 2019. The following actions were taken by the IUPAC Council: https://iupac.org/wp-content/uploads/2019/08/50th-Council-Decisions-and-Actions_Paris.pdf. Summary of actions:

- Council voted for the site and dates of the 50th World Chemistry Congress and 53rd General Assembly in 2025 by written and secret ballot. Institute Kimia Malaysia, IKM will host the 50th World Chemistry Congress and 53rd General Assembly 11-18 July 2025 in Kuala Lumpur, Malaysia.
- Council received reports of the Standing Committees and Bureau Committees and Interdivisional Committees;

approved the future appointment of the Centenary Endowment Fund Board of Directors including external Directors by the Executive Committee and also the Executive Committee, to progress in the formation of the fund and its guiding documents.

- Council approved McMillan, Pate and Company, LLP as auditors for IUPAC for the financial year 2019 onwards.
- Council voted against the Executive Committee Recommendation to Dissolve/Disestablish CHEMRAWN.
- Council approved the motion that the Chairs of CPCDS, ICTNS, CCE, COCI, and ICGCSD should be full voting members of Bureau, and the motion that a working group be established to undertake a complete review of the organizational structure of IUPAC.
- Council approved of the Proposed Budget for 2020-2021.
- Council approved the motion for removal of SEANAC and EFCE as IUPAC Associated Organizations of IUPAC (AO), and also removal of Ghana Institute for Pure and Applied Chemistry as ANAO of IUPAC.
- Council reauthorized the Commission on Physicochemical Symbols, Terminology and Units, the Commission on Isotopic Abundances and Atomic Weights, and the IUBMB- IUPAC Joint Commission on Biochemical Nomenclature (JCBN).
- IUPAP Letter of Recognition of IUPAC's Centenary was read during Council to the delegations.

IUPAC PUBLICATIONS OF INTEREST FROM THE LAST BIENNIUM

Holden, Norman E. / Coplen, Tyler B. / Böhlke, John K. / Tarbox, Lauren V. / Benefield, Jacqueline / de Laeter, John R. / Mahaffy, Peter G. / O'Connor, Glenda / Roth, Etienne / Tepper, Dorothy H. / Walczyk, Thomas / Wieser, Michael E. / Yoneda, Shigekazu. IUPAC Periodic Table of the Elements and Isotopes (IPTEI) for the Education Community (IUPAC Technical Report). Pure Appl. Chem., Vol. 90/12, pp. 1833-2092.

Labuda, Ján / Bowater, Richard P. / Fojta, Miroslav / Gauglitz, Günter / Glatz, Zdeněk / Hapala, Ivan / Havliš, Jan / Kilar, Ferenc / Kilar, Aniko / Malinovská, Lenka / Sirén, Heli M. M. / Skládal, Petr / Torta, Federico / Valachovič, Martin / Wimmerová, Michaela / Zdráhal, Zbyněk / Hibbert, David Brynn. Terminology of bioanalytical methods (IUPAC Recommendations 2018). Pure Appl. Chem., Vol. 90/7, pp. 1121-1198.

Camões, Maria F. / Christian, Gary D. / Hibbert, David Brynn. Mass and volume in analytical chemistry (IUPAC Technical Report). Pure and Applied Chemistry, Vol. 90/3, pp. 563-603.

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Possolo, Antonio / van der Veen, Adriaan M. H. / Meija, Juris / Hibbert, D. Brynn. Interpreting and propagating the uncertainty of the standard atomic weights (IUPAC Technical Report). Pure Appl. Chem., Vol. 90/2, pp. 395-424

Marquardt, Roberto / Meija, Juris / Mester, Zoltan / Towns, Marcy / Weir, Ron / Davis, Richard / Stohner, Jürgen. A critical review of the proposed definitions of fundamental chemical quantities and their impact on chemical communities (IUPAC Technical Report). Pure Appl. Chem., Vol. 89/7, pp. 951-981.

Participants of the IUPAC Analytical Chemistry Division in Paris, France, 6-7 July 2019

CITAC
Cooperation on International Traceability in Analytical Chemistry

MOST INTERESTING/IMPORTANT PAPERS ON METROLOGY IN CHEMISTRY IN 2019

SUMMARY OF "A NEW METHOD FOR THE SI-TRACEABLE QUANTIFICATION OF ELEMENT CONTENTS IN SOLID SAMPLES USING LA-ICP-MS"

J. Anal. At. Spectrom., 2020, 35, 126-135

Lena Michaliszyn[1], Tongxiang Ren[2], Anita Röthke[1], Olaf Rienitz[1]
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Tongxiang Ren


Anita Röthke


Olaf Rienitz

INTRODUCTION

Already in the 1980s the combination of a laser ablation (LA) system and an inductively coupled plasma mass spectrometer (ICP-MS) offered the possibility to analyse solid samples directly. Many areas, like geology[1], medicine[2] and among other things chemical analysis established this technique according to their research field long ago. With this technique a lot of applications are conceivable. Next to the investigation of biological[3] and medical[4] processes, for example a depth-profiling[5] can be done. Furthermore, LA-ICP-MS can be used for quantitative measurements. There are already several techniques, each with its own advantages and drawbacks.

With the internal standardisation it is possible to improve the accuracy and precision as well as to compensate the effect of variation in e.g. laser output energy. But with this technique only a normalisation of

the signal intensity is possible, meaning this method is not completely quantitative.[6,7] The application of certified reference materials (CRMs) is one of the most common techniques. Because of the matrix depending ablation and fractionation processes it is essential to use a matrix-matched CRM. The number of commercially available CRMs is limited[8] and there is no chance to influence the composition of the solid material. Even if there is the possibility for homemade CRMs, these can never match the sample matrix perfectly. Also, it is difficult and time consuming to prepare a CRM.[7]

Aside there are also the approaches of standard and online addition. For the latter, the ablated material and a solution are simultaneously introduced into the plasma. An improvement in plasma robustness is a side effect of this setup.[9] For a quantification knowledge about the mass flow is necessary. This is the most critical point because the mass flow can only be calculated via an estimation about the mass of the ablated material.[4]

Even though different quantitative approaches are already established a continuous improvement and further developments are necessary to meet the increasing demands.[7] "Thus, in this work a new quantification method using the sample itself as the matrix-matched reference material is introduced."[10]

MATHEMATICAL BACKGROUND AND EXPERIMENTAL

This method is based on the proportionality of the measured intensity $I(^j\mathrm{A})$ and the flow rate of particles .

$$I(^j\mathrm{A}) = k \times \dot{N}(^j\mathrm{A}) \tag{1}$$

By successively replacing the quantities, equation (2) can be obtained. First of all, the flow rate of particles can be replaced by the number of particles N with respect to time. N can be expressed with the Avogadro constant N_A and the amount of the measured analyte isotope $n(^j\mathrm{A})$. The amount of the isotope can be substituted by the isotopic abundance of the measured isotope $x(^j\mathrm{A})$ and the amount of the element $n(\mathrm{A})$ whereat in turn $n(\mathrm{A})$ can be exchanged with the mass $m(\mathrm{A})$ as well as the molar mass $M(\mathrm{A})$ of the analyte element. Then the mass is replaced by the mass fraction $w(\mathrm{A})$ and the mass of the sample m which is introduced into the plasma.

$$I_x(^j\mathrm{A}) = k' \times \dot{N}_x(^j\mathrm{A}) = k' \times \frac{N_A \times x_x(^j A) \times w_x(\mathrm{A}) \times m_x}{M_x(\mathrm{A}) \times t} = k' \times \frac{N_A \times x_x(^j A) \times w_x(\mathrm{A}) \times \dot{m}_x}{M_x(\mathrm{A})} \tag{2}$$

The new method is based on a simultaneous introduction of the ablated sample material (x) and a standard solution (z) out of a concentration series – similar to the principle of the online addition. For both parts, an equation has to be set up. The measured intensity is the sum of the intensity resulting from the solid sample $I_x(^j\mathrm{A})$ and the solution $I_z(^j\mathrm{A})$. Consequently, the corresponding equations have to be summed. By rearranging the quantities within the resulting equation, the form of a linear equation is obtained. For this technique the same plasma conditions ($k' = k''$) and a constant mass flow for the entire experiment as well as the same isotopic pattern in the solid sample and the standard solution ($x_x(^j\mathrm{A}) = x_z(^j\mathrm{A})$, $M_x(\mathrm{A}) = M_z(\mathrm{A})$) is assumed.

$$\underbrace{I(^j\mathrm{A})}_{=y} = \underbrace{\frac{k' \times x_x(^j\mathrm{A}) \times \dot{m}_x \times N_A}{M_x(\mathrm{A})} \times w_x(\mathrm{A})}_{=a_0} + \underbrace{\frac{k'' \times x_z(^j\mathrm{A}) \times \dot{m}_z \times N_A}{M_z(\mathrm{A})}}_{=a_1} \times \underbrace{w_{z,i}(\mathrm{A})}_{=x} \tag{3}$$

The mass fraction of the analyte element, which is the quantity of interest, is obtained by dividing the y-intercept a_0 by the slope a_1 from the linear regression of the data according to equation (3). Because of the unknown mass flows a reference element (R) with an exactly known mass fraction in the same solid sample $w_x(\mathrm{R})$ must be measured as well. For this element equation (3) can be transformed to an expression for the ratio of the unknown mass flows.

$$w_x(\mathrm{A}) = \frac{a_0(^j\mathrm{A})}{a_1(^j\mathrm{A})} \times \frac{\dot{m}_z}{\dot{m}_x} \quad \text{with} \quad \frac{\dot{m}_z}{\dot{m}_x} = \frac{a_1(^j\mathrm{R})}{a_0(^j\mathrm{R})} \times w_x(\mathrm{R}) \tag{4}$$

Figure 1 shows the principle of the described method. The method requires the solid sample itself with an unknown mass fraction of the analyte and a known of the reference element. In addition, a concentration series made of standard solutions has to be prepared for each element. In this work lead (Pb) as well as rubidium (Rb) were quantified according to this technique in two different standard reference materials (SRM 610 and 612, NIST). Because of the glass-based samples, silicon (Si)

was used as the reference element. To fulfil the demand of constant and equal plasma conditions all solutions were prepared in 0.15 mol/kg HNO_3. One measurement sequence contained 48 ablation spots: 36 spots were ablated and analysed together with the concentration series, 12 spots were used to measure the background (carrier and sample gas, HNO_3, no ablation).

The ablated material was analysed together with one solution after the other, resulting in a regression line for the analyte element (Pb or Rb) and one for the reference element (Si).

The measurement was done with a UV laser (NWR 213, ESI) coupled to an ICP-MS (Element XR, Thermo).

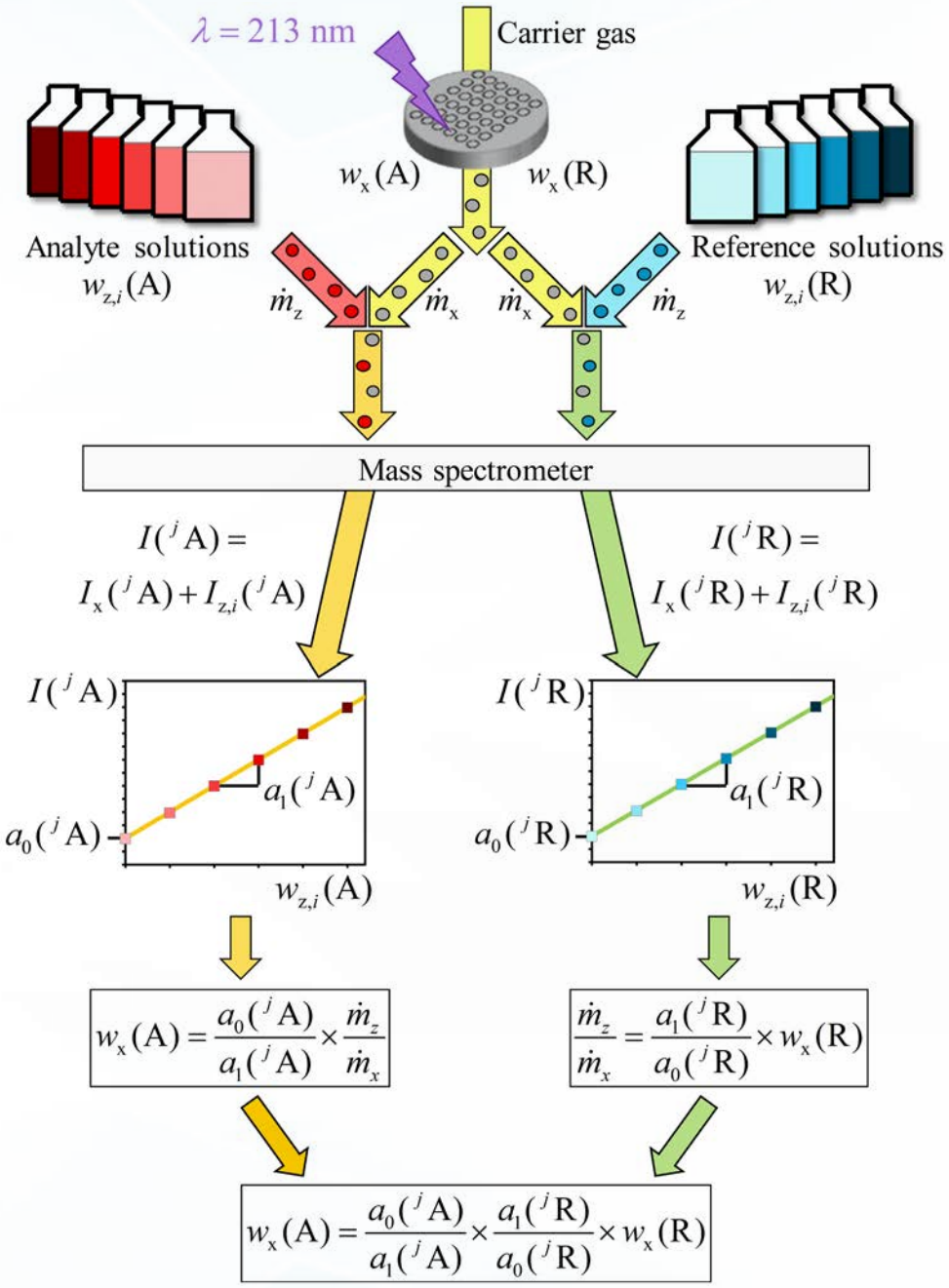

Fig. 1: Scheme of the measurement procedure. The laser ablated material transported by helium is introduced into the plasma. Further specific solutions are injected as well. First, solutions for the reference element (R) are added, afterwards standard solutions prepared of the analyte element (A). Reproduced from Ref. 10 with kind permission from the Royal Society of Chemistry.

RESULTS AND DISCUSSION

After one measurement sequence the parameters from the linear regression of the analyte as well as the reference element were calculated. The parameters a_0 and a_1 were used together with the mass fraction of the reference element to calculate the mass fraction of the analyte element in the solid sample. Because in this work some SRMs were used as samples and a matrix element acted as the reference element it was possible to take w_x(Si) from the certificate.

With the first 8 ablation spots the reference element was measured (with a concentration series) followed by 8 spots for the analyte element. This sub-sequence was repeated two more times for both elements. The quantification was done on three different days (table 1, No. 1-3). With this procedure it was ensured that some effects like fluctuation in laser energy, transport efficiency, plasma stabilisation etc. could be cancelled out or effect all results in the same way.

Table 1: Obtained mass fractions for lead and rubidium in NIST SRM 610 and NIST SRM 612 (U with k = 2) and the relative differences (Δ) between calculated and certified values. Reproduced from Ref. 10 with kind permission from the Royal Society of Chemistry.

Sample		NIST SRM 610				NIST SRM 612			
Analyte	Measurement	w_x / µg/g	U / µg/g	U_{rel} / %	Δ / %	w_x / µg/g	U / µg/g	U_{rel} / %	Δ / %
Pb	No. 1	402	82	20	- 6	38.4	5.5	14	- 0.4
	No. 2	413	76	18	- 3	43.9	7.8	18	+ 14
	No. 3	401	70	17	- 6	41.0	11.0	27	+ 6
	Mean	**405**	**76**	**19**	**- 5**	**41.1**	**8.4**	**21**	**+ 7**
Rb	No. 1	402	45	11	- 6	30.6	3.9	13	- 3
	No. 2	458	78	17	+ 8	31.7	6.5	21	+ 1
	No. 3	420	100	24	- 1	31.2	5.9	19	- 1
	Mean	**427**	**78**	**18**	**+ 0.2**	**31.2**	**5.5**	**18**	**- 1**

The results for all measurements done in this work are shown in table 1. The mass fractions and their corresponding uncertainties were calculated according to the Guide to the Expression of Uncertainty in Measurement (GUM). Due to the small variations in laser output energy, the small local differences in the composition of the sample and a time depended material transport efficiency out of the ablation crater, a relatively large expanded uncertainty of the single measurements was obtained. Nevertheless, it is not possible to distinguish between the measured and certified values – within the scope of measurements uncertainties (figure 2). The quantification of Rb (M = 85 g/mol)[11] and Pb (M = 208 g/mol)[11] shows the applicability of the new method for elements over a wider mass range. Because of the direct influence of w_x(R) on the result w_x(A) this technique is especially suitable for samples with an extremely well-known mass content of the reference (matrix) element near to 1 g/g.

In comparison to other quantifications[12–14] of Pb and Rb in SRM 610 and 612 the range of uncertainty is nearly the same but the new method produces SI-traceable and therefore internationally comparable results.

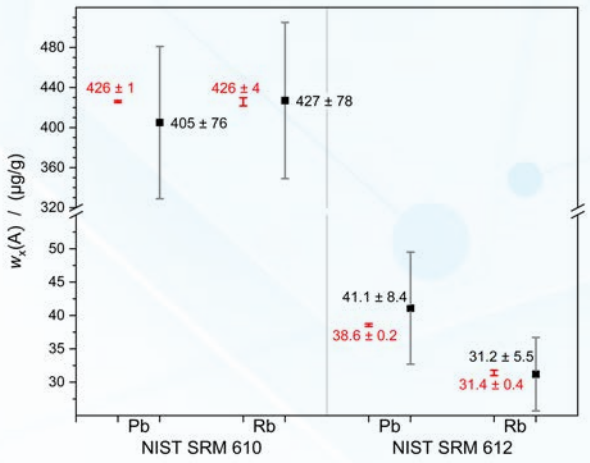

Fig. 2: Measured mass fractions of lead and rubidium in NIST SRM 610 and 612 (black) compared to the certified values (red); error bars denoting the expanded uncertainties *U* with *k* = 2. Reproduced from Ref. 10 with kind permission from the Royal Society of Chemistry.

CONCLUSION

Due to a straightforward uncertainty estimation and the SI-traceability this method is a step forward for quantitative LA-ICP-MS measurements. The sample itself acts as the perfectly matrix-matched reference material. This guarantees exactly the same ablation, transportation and ionisation behaviour. Using the principle of the online and standard addition, the knowledge about the ablated volume or the mass flow is not required anymore. Next to the standard solution only the mass fraction (and its uncertainty) of one element in the sample is necessary. Therefore, this method is predestined "to determine impurities in highly pure samples with a mass fraction of the matrix element close to 1 g/g."[10]

Even if the preparation of the standard solutions and the measurement itself are time-consuming, the main advantages – the SI-traceable results with a reliable measurement uncertainty – prevail clearly.

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SUMMARY OF "A MULTIVARIATE STATISTICAL APPROACH FOR THE ESTIMATION OF THE ETHNIC ORIGIN OF UNKNOWN GENETIC PROFILES IN FORENSIC GENETICS"

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INTRODUCTION

The robust evaluation of data from DNA profiling of biological evidence such as those recovered from crime scenes, mass-disaster areas or missing person investigations is one of the most debated topics in forensic sciences [1]. DNA typing is nowadays more and more employed, exploiting large sets of genetic markers that can be simultaneously analyzed on a single biological sample or trace, even if containing only a few copies of DNA. Currently, different panels of Short Tandem Repeats (STRs) markers (or loci) are widely utilized for personal identification in the interpretation process of single source samples and DNA mixtures collected e.g. during crime scene investigation activities [2]. Up to date, while autosomal STRs markers are the elective tool for personal identification, they have been poorly employed as Ancestry Informative Markers (AIMs) as STR alleles equal in state occur in diverse populations, mostly because of recurrent mutation (homoplasy).

Bayesian statistics have been applied to estimate the ethnic affiliation of unknown genetic profiles obtained with autosomal STRs in well-known software such as STRUCTURE [3], the Snipper App suite [4] and PopAffiliator 2 [5]. These approaches perform Bayesian evaluations by inferring the relationships between the allele frequencies of specific populations and the alleles observed in the individuals, which are recognized as part of such populations. This is done by computing the likelihood values of membership to each of the tested population groups, according to their relative allele frequencies. In the present study, we employed multivariate methodologies such as Sparse and Logistic Principal Component Analysis (SL-PCA) [6], Sparse Partial Least Squares-Discriminant Analysis (sPLS-DA) [7] and Support Vector Machines (SVM) [8] on autosomal STRs data sets. These multivariate techniques were selected as they turned capable of dealing with the nature of the genotypic data, which can be easily binarized. In particular, our goal was to develop robust multivariate approaches (which are largely employed in the field of Chemometrics) for the interpretation of DNA profiles to better estimate the biogeographical ancestry information of personal genetic profiles, rather than using the "traditional" Bayesian approach, by building dynamic and flexible models that could be easily modified according to the number of tested populations and the number of markers in the profile and the reference panel.

DATA AND MULTIVARIATE MODELS

Several population datasets were selected for this study. In order of decreasing heterogeneity, the first evaluated dataset was extracted from the NIST U.S. population database [9], and consisted of genotypic data from 24 STRs markers for U.S. African-American, Asian and Caucasian individuals. Further datasets have been tested, too, involving: (i) Northern and sub-Saharan African populations analyzed for 16 autosomal STRs loci (using the AmpFℓSTR® NGM SElect™ PCR Amplification Kit from Thermo Fisher Scientific – manuscript under submission); (ii) two central Asian populations from Afghanistan [10] and Iraq [11] genotyped for 15 autosomal STRs loci (using the AmpFℓSTR® IdentifilerTM PCR Amplification Kit panel from Applied Biosystems); (iii) two populations involving Italian [12] and Romanian [13] individuals genotyped for 16 autosomal STRs loci (using the AmpFℓSTR® NGM SElect™ PCR Amplification Kit from Thermo Fisher Scientific). All the genotyped subjects were unrelated one another. As mentioned above, powerful multivariate techniques such as SL-PCA, sPLS-DA and SVM were employed on the available datasets and their discriminating power was also compared aiming to obtain reliable models for the estimation of the BGA information of unknown genetic profiles. Each STR profile was converted into a row of zeros and ones by means of an in-house code developed in the R software (version 3.6.0.) [14] statistical environment. In details, for all the tested individuals, a value equal to 1 was reported for the alleles x and y (where x is equal to y in case of homozygosity) recorded for a specific marker Z, while a value equal to 0 was reported for the other n available alleles of the previously cited marker Z. Consequently, the STRs DNA profile of each individual was converted into a series of zeros and ones (i.e. binary dataset). Since the matrices obtained by using such computational approach turned to show many zeros as compared to the number of ones, sparse algorithms were preferred

when calculating the multivariate models. Initially, SL-PCA was utilized as an exploratory analysis tool to verify the capabilities of multivariate statistics in recognizing specific pattern regarding the biogeographical origins of the individuals based on their STR profiles, especially when dealing with binary data (as reported above). PCA, here employed in the sparse and logistic version reported in [6], is one of the most exploited technique in the field of multivariate statistics; it allows to graphically represent the information contained into large data matrices by providing useful visual representations of data distributions, similarity trends, classes and outliers. After the preliminary evaluation of SL-PCA modelling, sPLS-DA and SVM models were applied, to assess their predictive capabilities in blind inference of the ethnic affiliation of DNA profiles. sPLS-DA is the sparse version of the combination of Partial Least Squares (PLS) and Discriminant Analysis (DA) techniques [7]. In practice, sPLS-regression finds the factors that capture the greatest amount of variance in predictor variables by simultaneously modelling those X predictors that optimally correlate the responses of the Y matrix. On the other hand, DA is a supervised classification method whose goal is to discriminate different classes of objects by evaluating the optimal boundaries among them. Originally developed by Fisher [15], DA allows discriminating objects of different classes by examining the probability distributions of the classes to which the objects may belong. Finally, SVM is a Multivariate Data Analysis methodology whose aim is to provide a decision rule in terms of a special type of hyperplanes, defined as "optimal separating hyperplanes" and also known as "delimiter" or "margin" [8], capable of recognizing and discriminating the objects of different sets or classes. The delimiter is optimized as the distance between the separating decision boundaries (hyperplanes) and the closest objects to these hyperplanes, which are defined as support vectors. SVM techniques map the objects matrix X into a high-dimensional space called "feature space"; then linear or nonlinear functions (such as kernels) may be adopted in order to build an optimal separating hyperplane in this space.

DISCUSSION OF THE EXPERIMENTAL RESULTS

For the NIST dataset, three main clusters (Figure 1) corresponding to the African-American, Caucasian and Asian individuals were observed in the space of the first two Principal Components in SL-PCA and in the first two latent variables in sPLS-DA. A good separation was also observed for both SL-PCA and sPLS-DA models regarding

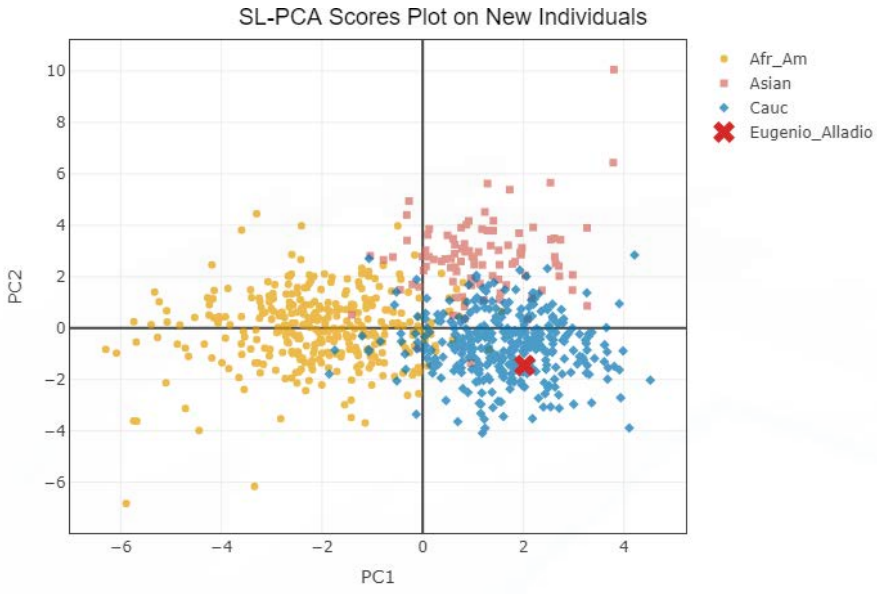

Figure 1. 2D SL-PCA Scores Plot on African-American (yellow circles), Asian (red squares) and Caucasian (blue diamonds) individuals. The red cross shows the BGA prediction for the corresponding author of the manuscript (from Torino, Italy).

the evaluation of Northern African and Sub-Saharan African individuals. This result can be ascribed to the fact that the Sahara Desert acted as a strong geographic barrier to gene flow between the cited populations in the last five thousand years [44].

On the contrary, a robust separation could not be observed in the case of less genetically differentiated populations such as the Afghan and the Iraqi individuals, as well as the Italian and the Romanian subjects, when using SL-PCA. Better results were observed when evaluating Afghan and Iraqi subjects using sPLS-DA (i.e. a classification accuracy of 94% was achieved), while insufficient results were obtained once again when evaluating the Italian and the Romanian populations (i.e. a classification accuracy of 58% was calculated). Finally, SVM was applied to the experimental datasets and a 100% accuracy as observed for the following tested populations: African-American vs. Asian vs. Caucasian individuals (NIST U.S. data), Northern vs. Sub-Saharan individuals and Afghan vs. Iraqi individuals. No misclassifications were observed both with tested cross-validated training sets and the extracted test sets. On the other hand, an accuracy equal to 89.1% was calculated for the SVM model as applied to the Italian vs. Romanian population, corresponding to an overall number of 27 misclassifications out of 209 Italian individuals and 27 misclassifications out of 287 Romanian subjects. Consequently, SVM turned out to be a very powerful model, with high specificity and sensitivity values, for all the ethnic groups, thus proving once again the reliability of multivariate statistics to extract BGA information from autosomal STRs DNA genetic profiles. These approached have been recently tested also on datasets obtained by generating simulated genotypes using the simugeno function that is available in the forensim R package [16]. In particular, the allele frequencies of individuals from the Macedonia region [17] were used to simulate the genotypes of unknown individuals to be compared with those available for the Italian population. The calculated sPLS-DA model is reported, as an example, in Figure 2. The multivariate approaches proved successful once again and, particularly, SVM provided the best result with an accuracy of 93%.

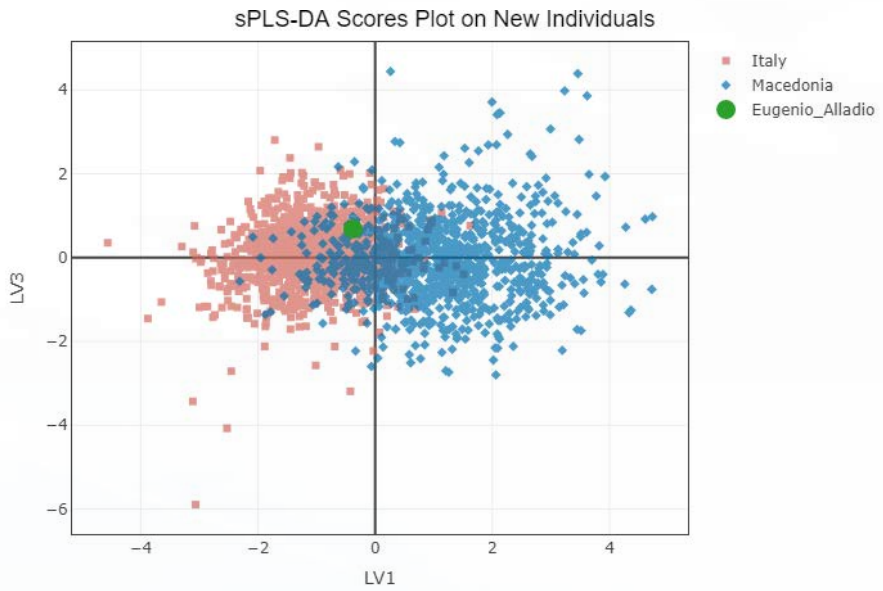

Figure 2. 2D sPLS-DA Scores Plot on Italian (red squares) and Macedonian (blue diamonds) individuals. The green circle shows the BGA prediction for the corresponding author of the manuscript (from Torino, Italy).

CONCLUSIONS

The predictive power of the tested multivariate techniques turned extremely high, indicating that the adoption of multivariate models may represent a powerful and useful tool for the investigative authorities to ease their decision processes when estimating the BGA of individuals. Future perspectives include the application of these multivariate strategies in discriminating even more locally-restricted populations. Further research studies with sPLS-DA and SVM techniques are already planned and will be performed in our laboratories using Next Generation Sequencing (NGS)/Massive Parallel Sequencing (MPS), by combining their data with the autosomal STRs results or developing the cited multivariate approaches on other forensic genetic markers such as Y-chromosome STRs, Single Nucleotide Polymorphisms (SNPs), mitochondrial DNA (mtDNA) and microhaplotypes (MH) variants. An open-source software, already developed in the R environment, will be made available soon, too.

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SUMMARY OF "ESTABLISHMENT OF MEASUREMENT TRACEABILITY FOR PEPTIDE AND PROTEIN QUANTIFICATION THROUGH RIGOROUS PURITY ASSESSMENT – A REVIEW"

IN THE SPECIAL ISSUE "FOCUS ON ADVANCES IN METROLOGY IN CHEMISTRY & BIOLOGY"

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INTRODUCTION

The health of their populations and efficient health care systems are of critical importance to the economic and social well-being of nations. Accurate and comparable peptide/protein measurements are required in support of diagnosis, prognosis, monitoring and treatment of widespread diseases (e.g. diabetes). The required consistency of measurement results can be achieved by making them traceable to stated references and through the development of Reference Measurement Systems. This review highlights the progress made in the *Protein Analysis Working Group* of the *Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM-PAWG)* in establishing Primary Calibration Reference Services in the emerging area of health markers such as peptides/proteins. Primary Calibration Reference Services are technical capabilities for composition assignment, commonly as the mass fraction content, of pure substances or solutions thereof. It is a core technical competency for *National Measurement Institutes (NMIs)*. A limited number of key comparisons, foreseen by the *CCQM-PAWG* strategy, are discussed that enable *NMIs* providing measurement services in peptide/protein analysis to test and demonstrate their capabilities. In addition, the review examines the development and improvement of analytical methods and metrological models that are required to meet the needs of *NMIs* and associated clinical stakeholders.

SUMMARY

Accurate peptide/protein measurements are increasingly demanded in different fields of bioanalysis particularly in support of diagnosis, prognosis, monitoring and treatment of prevalent diseases [1-3]. Pure peptide reference materials are needed to improve the comparability of measurement results obtained by different laboratories on a global scale [4]. International equivalence and acceptability of measurements can only be achieved by quality controlled *certified reference materials (CRMs)* and if corresponding purity values have been accurately measured with a stated uncertainty.

Accurately and rigorously characterized pure peptide primary calibrators are essential for the development of *Reference Measurement Systems (RMS)* for clinical chemistry and laboratory medicine and for the dissemination of metrologically traceable measurements. *RMS* are demanded for key peptides/proteins biomarkers for, e.g. hypertension (angiotensins), diabetes (insulin and C-peptide) or chronic kidney disease (parathyroid hormone). Primary standards within the supporting *RMS* should be pure substance reference materials if routine measurements are calling for a high degree of precision and accuracy [5-8].

Reliable characterization of the purity of peptides/proteins is not only required in the field of diagnostics but also for therapeutics as active pharmaceutical ingredient peptides/proteins are increasingly produced through chemical synthesis [9,10]. Chapter 2 of the paper provides deeper insights into the peptide/protein production processes for chemical synthesis, isolation from their natural sources, recombinant techniques used in biochemical protein expression, or a combination of these routes. Common impurities (Figure 1) obtained during chemical synthesis are generally characterized by similar sequence to the desired peptide (such as truncated forms, additional amino acids, oxidated, deamidated or acetylated).

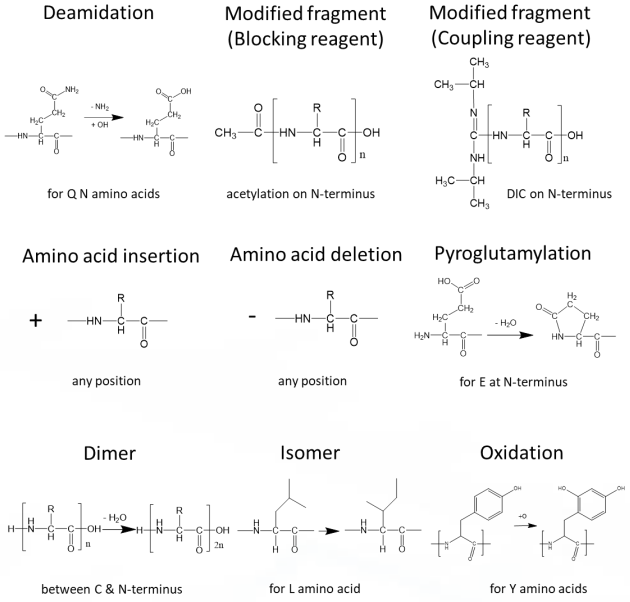

Figure 1: Generic overview of typical peptide impurities

In addition, remaining trifluoroacetate or acetate frequently occur as counter ion impurities of synthetic peptides at high mass fractions levels. Recombinant

production is of interest when longer peptides/proteins containing post-translational modifications (PTMs) and multiple disulfide bonds have to be produced. Proteic contaminants derived from heterologous expression are more abundant and diverse. This requires multiple purification steps to separate a protein of interest from the bulk extract. The identification of those contaminants can be quite difficult without previous knowledge of the host cell system.

Higher order reference measurement procedures, pure substances, and matrix *CRMs* are well established for well-defined small molecules. The provision of such required metrological tools in the field of peptides/proteins is more demanding.

The majority of *National Metrology Institutes (NMIs)* have adopted procedures for the provision of pure substance primary calibrators that rely on the mass balance approach. The mass balance approach provides a measure for the main component of the material through identification and estimation of the mass fraction of the individual impurities and/or distinct classes of impurities present in the material and, by subtraction from 100%. Increasingly, *NMIs* have successfully applied approaches that directly measure the mass fraction or mole amount fraction of the main component in the field of small molecules [11].

It is difficult to apply these concepts directly to peptides/proteins as higher order structures can occur, and the characterization of the primary structure may not be sufficient to correlate the amount of the molecule to its biological activity. However, the quantification of the primary structure purity of a peptide/protein is inevitable for the establishment of a primary calibrator material, where the quantity of interest is the mass fraction of the peptide/protein.

Another hurdle for the provision of traceable peptide/protein measurements is the limited availability of pure peptide/protein material (usually less than several hundred milligrams) making it difficult to implement different techniques required for the application of the classical mass balance approach. Traditionally, this has resulted in the harmonization of many peptide/protein measurements by the establishment of accepted practices, methods and/or standards. The development and increased use of targeted hydrolysis-based digestion and peptide quantification strategies has permitted the determination of protein amounts using prototypic peptides [12-14] by proteotypic peptide based isotope dilution mass spectrometry. These approaches are described in detail in Chapter 6.3 and have been investigated for the routine analysis of human growth hormone (hGH) and its biomarkers [15,16]. Higher order measurement procedures for the analysis of purified protein calibrators and serum-based matrix materials have been developed by various *NMIs* [17,18]. In general, these approaches show great promise for the standardization of key protein measurands. However, proteotypic peptides of known purity are required for the mass fraction value assignment of such proteins.

The degree of purity of both proteotypic and intact (bioactive) peptides can be controlled during the production process. Synthetic or recombinant production is affecting the impurity profile. The most common peptide purity assessment approaches are described in Chapter 5 [19].

The purity can be assessed by using the mass balance approach (Chapter 5.1) requiring different analytical methods for the determination of water, volatiles, non-volatiles, counter ions and inherent structurally-related peptide impurities [20]. The determination of the different types of impurities is performed by orthogonal validated methods calibrated with standards of certified purity so that results are SI traceable. The final calculated peptide mass fraction value carries low associated uncertainty, usually fit for any higher-order application. It is therefore the gold standard approach when sufficient material is available. However, in many cases there is not sufficient peptide material available to perform a mass balance approach.

In Chapter 5.2 peptide impurity corrected amino acid (PICAA) analysis is described in detail. It is an alternative to the mass balance approach requiring only a few milligrams of peptide material. Absolute quantification of pure peptide or protein calibrators by amino acid analysis (AAA) relies on the absolute quantification of amino acids released during peptide/protein complete

hydrolysis in acidic conditions. Chemical hydrolysis of peptides into amino acids for their subsequent quantification is a well-established technique and can be performed according to a variety of protocols and detection methods. The peptide solution can be transferred directly to the acidic solution (liquid-phase hydrolysis), freeze-dried and placed in contact with the acid vapors at high temperatures in a special desiccator (gas-phase hydrolysis) or in a microwave system (microwave-assisted hydrolysis) [14]. Meticulous sample preparation and hydrolysis completeness are essential to obtain accurate measurement results. SI traceability can be achieved through suitable amino acid *CRMs* of known purity, provided that complete hydrolysis is achieved. Liquid chromatography isotope dilution mass spectrometric techniques (LC-IDMS) are, in many cases, the method of choice for its recognition as a potential primary ratio method. Overall expanded uncertainties of well below 5 % can be obtained applying this method and sufficient hydrolysis replicates [14].

Structurally-related peptide impurities must be identified and quantified to achieve most accurate results. They are the most critical class of peptide impurities that are formed during synthesis, storage and transportation processes. These impurities have similar sequence, structure, and thus properties (Figure 1), which can significantly alter the biological activity of the material. It is extremely important to identify the peptide impurities, especially in the fields of clinical diagnostics and therapeutics [21,22]. The importance of peptide impurities separation, identification and classification of peptide impurities is discussed in Chapter 3. Particularly, quantification of the pre-identified and closely related peptide impurities is crucial in obtaining accurate values for peptide purity assignments as several approaches require correction for amino acids originating from inherent structurally-related peptide impurities [19]. Currently, liquid chromatography coupled to high resolution or tandem mass spectrometry (LC-hrMS or LC-MS/MS) are the most frequently applied techniques. Chapter 4 elaborates on the importance of the purity assessment of impurity standards, peptides impurities quantification by LC-MS and the uncertainty evaluation.

Quantitative nuclear magnetic resonance (qNMR) [23] with a correction for structurally-related peptide impurities (PICqNMR) (Chapter 5.3) and nitrogen determination by elemental analysis (CHN/O) [24] with a correction for nitrogen originating from impurities (PICCHN) (Chapter 5.4) are alternative approaches for the assessment of peptide purity that require only minor quantities of peptide material. Cross-linked peptides containing disulfide bridges and/ or metallo-peptide/proteins can be assessed by sulphur determination by elemental analysis (CHN/S) with a correction for sulphur originating from impurities or ICP-MS with a correction for structurally-related peptide impurities, respectively. The approaches traditionally used for the purity assessment of primary peptide calibrators as presented before enable to identify, quantify and correct related peptide impurities. Also other methods are discussed in Chapter 5.4. For example, ion mobility coupled to mass spectrometry (IM-MS) as a promising approach to be used for the characterization of the peptide/protein standards, providing the added value of the structural characterization of the peptide/protein to scrutinize its native state.

Furthermore, metrological considerations and SI traceability are debated in Chapter 7 with a special focus on clinical considerations regarding measurand definition, protein digestion efficacy and protein polymorphism and the fitness for purpose taking into account uncertainty suitability and commutability. Measurement uncertainties are required to be sufficiently small to meet the medical needs. Considering that measurement uncertainties increase all along the traceability chain, it is generally agreed that measurement uncertainties of a *RMP* should be about 2 to 3 times smaller than those of the corresponding routine method. It also needs to be ensured that methods and purity *CRMs* aimed at providing traceability for clinical measurements should be commutable to clinical routine measurement procedures and designed in agreement with other international standardization initiatives.

Chapter 8 on key comparisons for peptide/protein purity provides insights of the work undertaken within the *CCQM-PAWG*. Key comparisons as the provision of Primary Calibration Reference Services has been identified as a core technical competency for *NMIs*.

The CCQM-K115/P55.2 comparison series is presented addressing the assignment of the mass fraction content of purity peptide/protein materials to directly support *NMI* services and *CRMs* currently being provided by *NMIs*. A model to classify peptides in terms of their relative molecular mass, the amount of cross-linking, and modifications has been developed within *CCQM-PAWG* and is discussed.

CONCLUSIONS

This article aims to present a review of the developments in pure reference material production and measurement techniques to underpin mass fraction measurements of peptides/proteins relevant for diagnosis, prognosis, monitoring and treatment of diseases to improve health care. Current practices and developments for the primary realization within the *CCQM-PAWG* are reviewed and how the state-of-the-art in measurement techniques and accurate peptide/protein purity assessment approaches evolved and improved in recent years.

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GARSHOM PRAVASI VANITHA AWARD 2019 – LALY SAMUEL

Garshom International Awards, the most prestigious awards for Non Resident Keralites was initiated in the year 2002 to honour people from Kerala, India, who have contributed their might to uplift the community in their place of residence and have achieved success in life through their ingenuity and hard work. The 14th Garshom International Awards presentation was held at Hotel Scandic Solli, Oslo, Norway on 24th August 2019. Since the introduction of this award, many from the southern state of India, Kerala, who have ventured out and written a success story for themselves by their sheer determination, innovation, hard work and drive in the land which gave them the opportunity and in turn contributed to improve the situation for their fellowmen have been brought to the limelight by Garshom.

Garshom foundation is a non-profit organisation which engages with diverse groups who care about people and the community they serve. The intent is to create socially viable solutions that contribute to the holistic development of the communities they work with, especially the underprivileged and vulnerable children, women and youth. They also seek to change the cycle of poverty that afflicts the poorest of Indian society at the grassroots level by focusing on investing in the future of children through programs that equip them with the skills and tools needed to become productive members of the society.

In 2019, the 14th edition of the prestigious Garshom International Woman award was presented to the Past-Chair of CITAC Dr. Laly Samuel from New Zealand for her contribution to the society as scientist, being inspirational to Keralite women and being a model for the young generation to look up to and emulate. She was selected from nearly a thousand nominations submitted to the foundation from various backgrounds. The jury's decision was unanimous based on her outstanding performance. Among the many nominated esteemed personalities from all over the world originating from Kerala, Dr. Samuel's name emerged at the top of the list. She was selected as her activities have been found to be a role model for others to follow and for her contribution in bringing honour to the non-resident Keralites.

Dr. Laly Samuel was the team leader of chemical standards programme at the Measurement Standards Laboratory of New Zealand. She has contributed her expertise to the field of analytical chemistry by establishing the Virtual Institute of Metrology in Chemistry (VIMC) providing a cost-effective implementation of chemical metrology in New Zealand. Honouring her contributions to chemical and technological research and development found her a place among the 2000 outstanding scientists of the 20th century by the International Biographical Centre in 2000. She was listed as one of the top 100 influential women of New Zealand in 2016.

Dr. Laly had completed her post-doctoral studies at Rikkyo St. Paul's University in Japan under the Bishop William memorial fund scholarship and is now working as a scientist in New Zealand. Apart from her passion in science contributing a lifetime to the achievements in the field of analytical chemistry.

Dr. Samuel is also a humanitarian involved in acts of charity in several countries. Currently she is settled in New Zealand with her husband and two children.

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NEW AND RENEWED GUIDES WITH PARTICIPATION OF CITAC

IUPAC/CITAC GUIDE: EVALUATION OF RISKS OF FALSE DECISIONS IN CONFORMITY ASSESSMENT OF A MULTICOMPONENT MATERIAL OR OBJECT DUE TO MEASUREMENT UNCERTAINTY – A SUMMARY

Ilya Kuselman // Independent Consultant on Metrology, Israel

The Guide was developed by IUPAC projects 2016-007-1-500 and 2018-004-1-500 (https://iupac.org/projects/) by the task group consisted of Francesca R. Pennecchi, INRIM, Italy; Ricardo J.N.B. da Silva, University of Lisbon, Portugal; and D. Brynn Hibbert, UNSW Sydney, Australia; chaired by me. The work was supported by CITAC. Currently the Guide is approved by IUPAC Analytical Chemistry Division and CITAC for publication in Pure and Applied Chemistry – the IUPAC journal.

1. THE RISKS CLASSIFICATION, MODELLING AND EVALUATION

Risks of a false decision on conformity of chemical composition of a multicomponent material or object due to measurement uncertainty were defined in the Guide using the Bayesian approach. This approach allows to combine the prior probability density function (pdf) of concentrations or contents of components of a material or object and the likelihood function into posterior pdf. The posterior pdf, containing all the available information, is used for the risks evaluation.

Even if conformity assessment for each particular component of a material is successful, the total probability of a false decision (total consumer's risk or producer's risk) concerning the material as a whole might still be significant. This relates to the specific batch, lot, sample, environmental compartment or other item of material or object (specific consumer's and producer's risks), as to a population of the items (global consumer's and producer's risks) characterizing the material production or object globally. Hence, there are four kinds of particular risks for each i-th particular component concentration or content, and four kinds of total risks for the material or object as a whole. Therefore, for $n>1$ components under control one can distinguish $4(n+1)$ kinds of risks of false decisions. For example, for two components this means – 12, for three components

– 16, and for four components – 20 kinds of risks.

A model of the total probability of a false decision for cases of independent actual ('true') concentrations or contents of the components and corresponding measurement results was formulated based on the law of total probability. It was shown that a total risk can be evaluated as a combination of the particular risks in conformity assessment of components of the item. For a more complicated task, i.e. for a larger number of components under control, the total risk is greater.

Correlated actual values of the components' concentrations or contents, as well as correlated measured values, were modelled by multivariate distributions. Then, a total global risk of a false decision on the material conformity was evaluated by calculation of integrals of corresponding joint posterior probability density function. A total specific risk was evaluated as the joint posterior cumulative function of actual property values of a specific item lying outside the multivariate specification (tolerance) domain, when the vector of measured values obtained for the item was inside this domain. The effect of correlation on the risk is not easily predictable.

There are following implementation remarks in the Guide.

2. TOLERANCE DOMAIN

The tolerance/specification lower and upper limits of concentrations or contents of the components, T_{Li} and T_{Ui} respectively, form a multivariate tolerance domain of permissible compositions of the material or object $T_1 \times T_2 \times ... \times T_n$. However, there might be also constraints of the mass balance to be satisfied, and/or technological constrains. These constraints lead to a multivariate sub-domain of feasible compositions, which may influence calculation of the risks.

3. PRIOR PDF

A large enough dataset of results of tested items of the same material produced at the same factory, as well as results of monitoring the same environmental compartment, can be used for approximation of the prior pdf. The assumption is that the actual concentration values are approximated by the test/measurement results adequately, since measurement uncertainty is negligible in comparison with item-to-item (batch-to-batch) variations caused by changes of conditions of the material production, environmental conditions, etc. Known statistical criteria of goodness-of-fit of experimental and theoretical distributions (normal, lognormal, etc.) are applied. A choice of the theoretical distribution may be based also on the chemical understanding of the material nature. If there is no detailed prior knowledge about distribution of the component concentrations or contents in the tested item, the prior pdf is vague. In such cases, a uniform pdf may be used, limited by the least and the greatest possible values of the component concentrations or contents.

When actual values of the concentrations or contents c_i are correlated, the prior covariance matrix has variances σ_i^2 of prior distributions as diagonal elements, and covariances $cov_{ij}=r_{ij}\,\sigma_i\,\sigma_j$ as off-diagonal elements, where r_{ij}, $i \neq j$, are the correlation coefficients.

4. LIKELIHOOD FUNCTION

The likelihood is a function describing the plausibility of the actual values of a component concentration or contents for a given measurement result. In practice, a distribution of measured values at a given actual concentration or actual content c_i of component in a sample of a multicomponent material or object, caused by measurement uncertainty u_i, is available from the analytical method validation data. This distribution of the measured values, regarded as a function of c_i, is nothing else than the likelihood function itself.

When measured values c_{im} are correlated, the likelihood is a multivariate pdf having covariance matrix with variances equal to the squared measurement uncertainties u_i^2 as diagonal elements, and covariances $cov_{ij} = r_{ij}\,u_i\,u_j$, $i \neq j$, as off-diagonal elements.

5. POSTERIOR PDF

The posterior distribution can be expressed as the posterior pdf of actual concentration values or actual content values at the same measured values of the component's concentrations or contents in an item. It is

the normalized product of the prior and the likelihood. For example, a multivariate normal prior pdf and a normal likelihood function generate a multivariate posterior pdf, which is also normal.

6. COMPUTATIONAL DETAILS

In this Guide calculation of parameters of posterior multivariate normal distributions and descending risk values were performed in the R programming environment. Simulation of a posterior distribution is also possible by Markov Chain Monte Carlo (MCMC) method, using the Metropolis-Hasting algorithm with MS Excel. Global risks evaluated as with R, as using Monte Carlo (MC) simulation and Cholesky decomposition of the covariance matrix with MS Excel, produced satisfactorily close calculation results.

6. LIMITATIONS

Any model is a simplified reflection of reality and can be useful if one remembers about its limitations. There are some limitations, relevant for this Guide.

The assumption of negligible definitional uncertainty of actual component concentration or content c_i may influence the prior pdf. In particular, inhomogeneity and/or instability of an item of the multicomponent material or object lead to an increase of the standard deviation (and variance) of the prior pdf and its skewness. Adequacy of the use of a dataset of item-to-item (batch-to-batch) test/measurement results for modelling the prior pdf is a not simple question including the necessary volume of this dataset, the time of its accumulation, possible changes of raw materials for production during this time, etc. The goodness-of-fit of experimental and theoretical distributions are to be also taken into account.

Measurement uncertainty evaluation is important for formulation of the likelihood function. Note, the multivariate tolerance domain may be large enough for a doubt, if the same measurement uncertainty can be applied in this domain, e.g. when the uncertainty value u_i is depending on the measurand – the component concentration or content c_i.

A correct choice of the mathematical statistical method with or without the raw data transformation should be fit-for-purpose, and that requires also formulation of clear criteria.

7. EXAMPLES

Examples of evaluation of the risks are provided for conformity assessment of denatured alcohols when two or three denaturants are used; total suspended particulate matter in ambient air near to three independent stone quarries; a cold/flu medication with four active pharmaceutical ingredients; and a PtRh alloy in which contents of Pt and Rh, as well as of sum of three precious impurities and of sum of eight precious and nonprecious impurities, were under control.

More details are available in the following references.

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NEW EDITION OF EURACHEM/CITAC GUIDE ON MEASUREMENT UNCERTAINTY ARISING FROM SAMPLING

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The second edition of the Eurachem/CITAC Guide on measurement uncertainty arising from sampling (UfS) has recently been published [1]. It has been updated to explain how several new research ideas can be used to improve the way that we estimate and express UfS. The Guide considers the whole measurement process, which usually begins at the point where a primary sample is taken. It retains the basic structure of the first edition, describing the estimation of UfS by both empirical and modelling approaches, and includes six worked examples across several application sectors, including food, animal feed, soil and water.

THE UNCERTAINTY FACTOR

One significant new development is the option of using the Uncertainty Factor as an alternative way to express measurement uncertainty. The upper and lower confidence limits of a measurement value are expressed by multiplying and dividing the measurement value by the uncertainty factor, rather than by the traditional approach of adding and subtracting the uncertainty. This approach is more accurate when the relative expanded uncertainty value is large, typically over 20%, and also where the frequency distribution of the uncertainty is approximately log-normal rather than normal. These two conditions often apply to measurement uncertainty that arises from the sampling process, particularly when the spatial distribution of the analyte in the test material is substantially heterogeneous. The Guide explains how the expanded uncertainty factor (${}^{F}U$) can be calculated as ${}^{F}U = \exp(2s_G)$, where s_G is the standard deviation of the log-transformed measurement values. An updated worked example, for Pb-contaminated soil, is provided to show how ${}^{F}U$ can be evaluated in practice using the 'duplicate' method. Duplicated Pb analyses are made on duplicated samples taken at 10 of the 100 sampling targets placed in a grid across a contaminated land site in the usual way. However, the natural logarithms of the Pb measurement values are taken before the analysis of variance (ANOVA) is made. This log-transformation is necessary because the frequency distribution of the Pb measurements on the 100 sampling targets is approximately log-normal (Fig 1a), but much closer to normal after the transformation (Fig 1b). The frequency

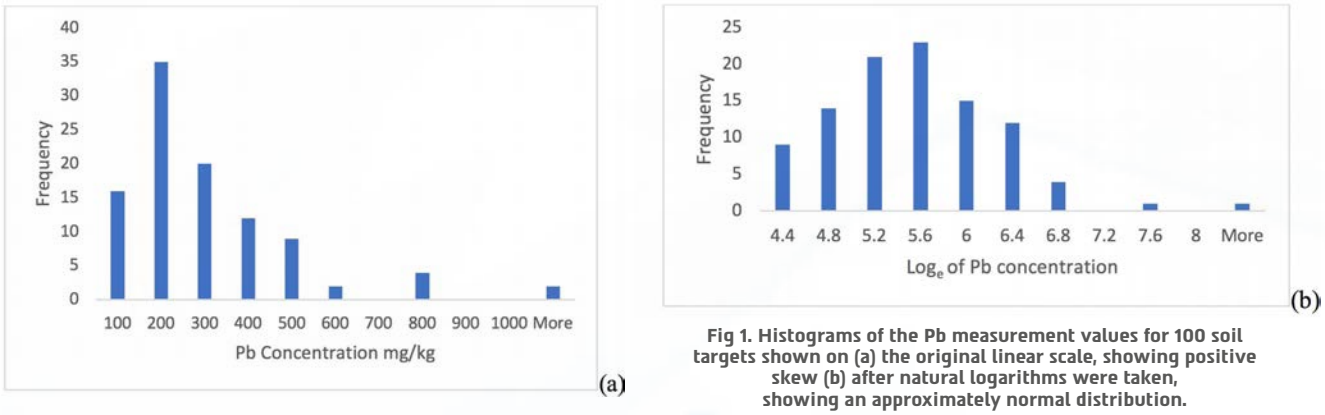


Fig 1. Histograms of the Pb measurement values for 100 soil targets shown on (a) the original linear scale, showing positive skew (b) after natural logarithms were taken, showing an approximately normal distribution.

distribution of the measurement uncertainty, as judged by the duplicated samples, is also made closer to normal by this transformation [2].

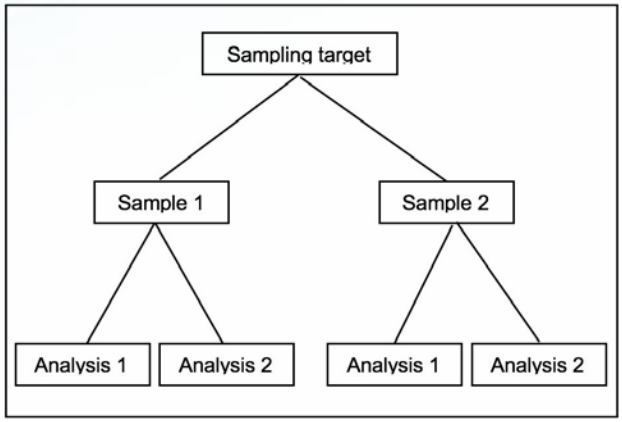
The results of the ANOVA then give not only the expanded uncertainty factor of the measurement (${}^{F}U_{meas}$=2.62), but also that arising from the sampling (${}^{F}U_{sampling}$=2.60) and from the chemical analysis (${}^{F}U_{analysis}$=1.12). The upper confidence limit of a typical Pb measurement value of 300 mg kg^{-1}, can then be calculated as 784 mg kg^{-1} (300 x 2.62), and the lower confidence limit as 115 mg kg^{-1} (300/2.62).

The Guide also explains two options for how measurement uncertainty can be calculated by adding the component arising from sampling, expressed as an uncertainty factor (${}^{F}U_{sampling}$), with that arising from chemical analysis, expressed in the traditional way as a relative uncertainty ($U'_{analysis}$). One option is to have both the sampling and analytical uncertainty components calculated and expressed in the log-domain. A second option is to assume, for the analytical component, that the relative standard uncertainty ($s'_{analytical}$) is approximately equal to the standard deviation of the natural logarithms ($s_{G,analytical}$). This is an acceptable approximation when the $s'_{analytical} < 0.2$, which is usually the case. The two components can then be added as variances in log-space, as in the first option.

AN UNBALANCED EXPERIMENTAL DESIGN TO REDUCE THE COST OF ESTIMATING UfS

A second new development in the methods described in the Guide is the use of an unbalanced experimental design to reduce the cost of estimating UfS by the duplicate method. The first edition of the Guide described the use of a balanced design for the empirical estimation of the measurement uncertainty as a whole, and its two components from the sampling and analytical steps. This balanced design has analytical duplicates on both of the two sample duplicates (Fig 2a). The new edition of the Guide stresses the advantage of using an unbalanced design, with an analytical duplicate on only one of the two sample duplicates (Fig 2b). This design reduces the extra cost of estimating the uncertainty by 33% (i.e. reducing the number of extra measurements required from 3 to 2 per sampling target) [3]. It reduces the number of degrees of freedom on the analytical component, but retains the same number for the sampling component, which is usually the more dominant. Anecdotal evidence suggests that one of the reasons that UfS estimation has not been more widely adopted is the extra cost that is required. This new more economical approach may therefore help to increase the number of application sectors where UfS estimation is fully adopted.

[a]



[b]

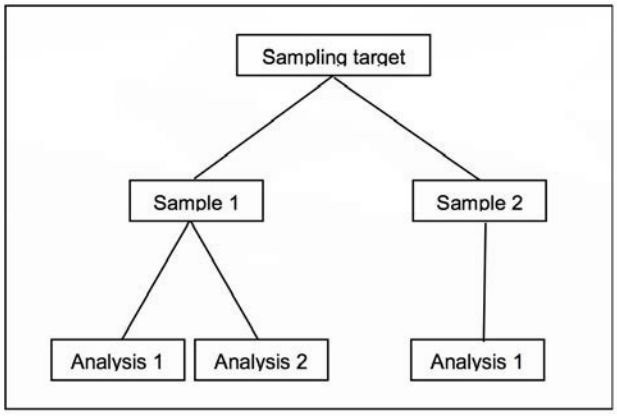


Fig 2: Comparison between (a) the full balanced design, and (b) the unbalanced design proposed in the new edition of the Guide. This reduces the extra cost of estimating the measurement uncertainty due to both the sampling and chemical analysis by 33%.

UfS ESTIMATION USING SAMPLING PROFICIENCY TESTING

A more comprehensive method for the estimation of UfS is by the use of measurements made in Sampling Proficiency Testing (SPT). In the first edition of the UfS Guide this approach was discussed in theory, but the new

edition now refers to the first practical example of the use of SPT data for UfS estimation [4]. In this approach multiple samplers each apply whatever sampling protocol they consider appropriate to achieve the same stated objective for the same sampling target. Using a balanced design across all of the different samplers, it is then possible to included the 'between-sampler' bias in the estimate of UfS, in addition to the components that were previously included. The first practical SPT concerned the measurement of the moisture content of a 20 ton batch of fresh butter. The established duplicate method, using a single sampler, gave an estimate of the expanded relative measurement uncertainty (U') of 0.39%. Interestingly, the use of the SPT results gave an U' estimate of 0.87%, which is a factor of 2.2 larger. This is clear evidence of between-sampler bias, but could conceivably be due to a few poorly performing samplers. When the z-score of the sampler were investigated, there were two samplers that did indeed have potentially non-proficient z-scores ($z > 3$). However, when these two non-proficient samplers were removed from the study, the estimates uncertainty was still 0.69%, which is still 1.8 times larger than the estimate made by the single-sampler approach. The conclusion of this study was that the use of an SPT for the estimation of UfS would give a more reliable, and probably larger estimate of the uncertainty. The multi-sampler approach using an SPT is clearly more expensive to undertake, but in situations where the UfS value has a large economic consequence, such as the estimation of the mass of gold in a potential new mine, it may well be financially justified.

APPLICATION OF UfS ESTIMATION TO NEW SITUATIONS

Another development covered in the new Guide is the increased range of measurement situations where UfS estimation has been applied and reported. One such application is for measurements made *in situ*, where the test material has not been removed from its original location but measured in place. For *in situ* measurements, the taking of a sample is almost indivisible from the rest of the measurement process. This means that situation is more complex than for traditional *ex situ* measurements made in an external laboratory, partially because of the spatial heterogeneity of the analyte concentration in the test material. Even when an *in situ* measurement probe is placed at the same nominal location on the sampling target, the analyte heterogeneity will thereby increase measurement uncertainty. This is due to the higher level of UfS that is present in an *in situ* measurement when compared against an *ex situ* measurement, where the test material has been homogenized. UfS can be estimated for *in situ* measurements using an empirical approach such as the duplicate method [5]. Duplicated positioning of the measurement probe, using the same sampling protocol, can be used to give a 'sample duplicate'. Similarly, duplicated measurements made without moving the probe can be used to give an 'analytical duplicate'. The systematic component of the uncertainty cannot be estimated only with measurements on a matrix-matched certified reference materials (CRMs). This is because a CRM is usually a dried, ground, homogenized and often compacted material that is physically very different from the test material, which may well be moist, unground, heterogeneous and un-consolidated in the measurement situation. Comparison will also be required, therefore, between the measurements made *in situ* and those made *ex situ*, with an independent analytical method for the same measurand, on samples taken from the same sampling target.

'On site' measurements, are made when a sample has been taken from its original location, and usually prepared and homogenised, but it is measured close to its original location. This situation is intermediate in complexity between the traditional *ex situ* measurements, and the *in situ* measurements just discussed. For an example of the determination of total petrol hydrocarbons (TPH) in stockpiled soil, the *ex situ* measurement made by the on-site method can be compared against those made in a remote laboratory under more controlled conditions. Problems can arise from differences between the definitions of the measurand for the two analytical methods for TPH, and in deciding which is correct [6].

UfS IN PASSIVE MEASUREMENTS OF RADIOACTIVE DECAY.

Application of UfS estimation to the measurement of

^{137}Cs in soil, by gamma ray spectrometry at a nuclear decommissioning site, has illustrated some interesting new issues [7]. The passive nature of sampling for *in situ* use of γ-ray spectrometry, means that a very large mass of test material (e.g. 200 - 1000 kg) can form the 'test portion' of this analytical method. This contrasts with the very limited mass of test material (e.g. ~ 0.5 kg) usually physically extracted for the *ex situ* measurement by γ-ray spectrometry. When the duplicate method is applied, the measurement uncertainty from sampling (UfS) for the *in situ* measurements was found to be much lower than that for the *ex situ* measurements. This is undoubtable due to the much greater mass interrogated by the *in situ* γ-ray spectrometry, which is therefore much more representative of the sampling target. This effect is slightly offset by the 50% lower analytical component of the uncertainty, due to the longer counting time typically used for *ex situ* determinations, making the overall expanded measurement uncertainty comparable at around 40%. However, the cost of each *in situ* measurement is about one tenth of an *ex situ* measurement, so it is economically justified to take many more *in situ* than *ex situ* measurements. Overall, when four times more *in situ* are made than *ex situ* measurements, it was found that the standard error on the mean value of ^{137}Cs for the whole site is reduced by a factor of two using the *in situ* measurement approach, at half the cost.

UfS ESTIMATION AT THE MICRO SCALE

The final area of new application of UfS estimation is to a range of different spatial scales. This is particularly the case for instrumental measurements made using 'beam sampling' at scales ranging from the millimetre to the micron scale [8]. At these smaller scales, analyte heterogeneity become increasing important. The heterogeneity is often the main component of the UfS and hence the dominant source of the measurement uncertainty. Studies using PXRF at the millimetre scale, and SIMS at the micron scale, have used the duplicate method to estimate both the UfS, and the analyte heterogeneity. When the UfS is included in the uncertainty estimate, it is possible to show that these *in situ* measurements can be fit-for-purpose (FFP, such as the spatial mapping of element concentration), despite having higher uncertainty than is usual for bulk analysis. With an increasing use of *in situ* measurement devices in many sectors of society, at all spatial scales, reliable methods of estimating the UfS of beam measurement procedures can enable their FFP to be judged.

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VISIT A CITAC MEMBER AT HIS/HER LAB

INRIM LABORATORY "PRIMARY GAS MIXTURES AND ORGANIC ANALYSIS" AT APPLIED METROLOGY & ENGINEERING DIVISION

Michela Sega, Francesca R. Pennecchi, Francesca Rolle , INRIM, Italy

INRIM, the National Institute of Metrological Research, is a public Italian research centre having the institutional role of National Metrology Institute (NMI). In this framework, it realises, maintains, and develops the national reference standards of the measurement units of the International System (SI). It is located in Torino, in the northern part of Italy.

INRIM research activities are also devoted to many other areas such as materials science, nanoscience, quantum optics, studies on the fundamental constants of physics. Basic and applied research and the development of new measurement technologies and instruments enhance the metrology activity.

Apparently, INRIM has a short history as it was founded just in 2006. Actually, it has quite an age since it was created by the merging of two research centres, the Istituto Elettrotecnico Nazionale Galileo Ferraris (IEN) and the Istituto di Metrologia Gustavo Colonnetti (IMGC) of the Italian National Research Council, both established in Torino in the last century.

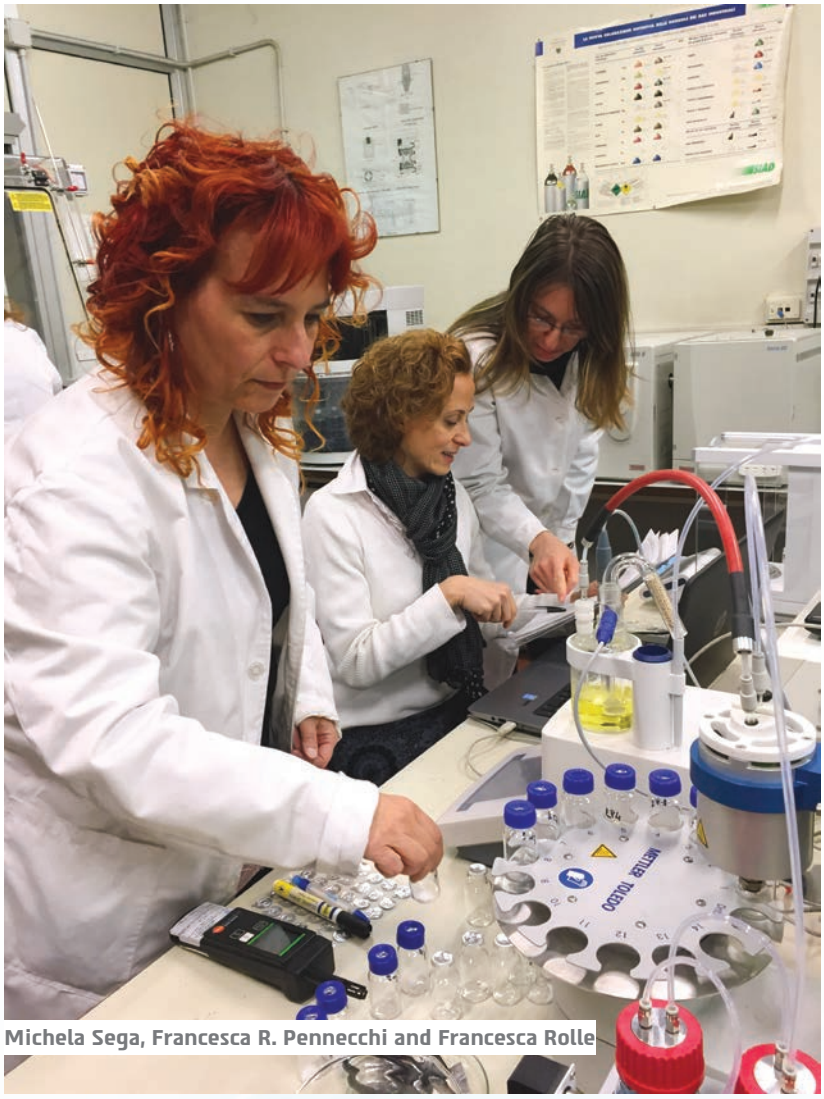
INRIM is organised in three scientific Divisions: Advanced material metrology and life sciences – ML (Head: Paola Tiberto), Applied metrology and engineering - AE (Head: Michela Sega), Quantum metrology and nanotechnologies – QN (Head: Davide Calonico). Each of them carries out activities in the three institutional pillars of INRIM: scientific research, role of NMI, knowledge transfer.

The Division AE develops metrological science and technologies with attention to engineering and industrial needs. It is articulated in five scientific sectors. One of them, Applied Thermodynamics, deals with industrial and environmental applications of thermodynamics in thermal measurements, radiative processes, chemistry of gaseous substances. It has among its topics the environmental monitoring and climate: in this framework, some activities are devoted to chemistry by the research group working in the laboratory Primary reference gas mixtures and organic analysis.

The group has well established experience in gas analysis, mainly of carbon dioxide (CO_2) and nitrogen

oxides (NO_x). The laboratory is equipped with facilities for the preparation of reference gas mixtures by primary methods, like gravimetry and dynamic dilution by mass flow controllers. The group takes part on regular basis in international interlaboratory comparisons in the CCQM and EURAMET TC-MC framework. One of the most important research field deals with climate changes and activities are currently developed within the European Joint Research Project "SIRS – Metrology for Stable Isotope Reference Standards", a project co-funded by the European Commission within the EMPIR programme. In this context, new gaseous reference standards are under development to underpin measurements of stable isotopes of CO_2, the major greenhouse gas, which enable its origin to be identified, with the objective of obtaining more accurate and comparable data to separate anthropic emission sources from natural ones. Another EMPIR Project in which the group is involved is "EMUE - Examples of Measurement Uncertainty Evaluation". In this framework, some examples of uncertainty evaluation and conformity assessment are under development concerning several applications, such as the preparation of standard gas mixtures via dynamic dilution and the quantification of low masses of benzo[a] pyrene in atmosphere. In such case studies, great attention is devoted to appropriately model covariance terms effecting the uncertainty budget and to choose the more suitable procedure, such as the Monte Carlo method, for propagating the uncertainty through the measurement model.

Considering how the atmosphere and the hydrosphere are closely related, in order to deal with climate and environmental issues, the metrological traceability of the results associated with the determination of marine and oceanic parameters (the Essential Oceanic Variables, EOVs, a subgroup of the Essential Climate Variables, ECVs) is of utmost importance. Some activities are therefore devoted to the uncertainty evaluation of chemical and physical parameter measurements (e.g. pressure, temperature, electrical conductivity and salinity) and to the feasibility study of gas reference standards to be used in the determination of partial pressure of CO_2 (pCO_2) in marine water. These activities are carried out in close collaboration with other Italian Research Institutes that have specific competences and expertise in marine and oceanic measurements, as well as within European frameworks, like the joint action on European Marine Sensors Calibration Network of the European Joint Programming Initiative "Healthy and Productive Seas and Oceans" (JPI OCEANS), which puts together the marine research community, NMIs and industry from the participating countries.



Michela Sega, Francesca R. Pennecchi and Francesca Rolle

Another important research field is devoted to the establishment of sound metrological traceability paths to the determination of water content in real matrices, by combining and comparing the outcomes of thermogravimetry, the technique usually employed in moisture determination in materials, to more selective and high specific electrochemical methods, like the coulometric Karl-Fischer titration and the Evolved Water Vapour analysis.

In the framework of a joint collaboration between CITAC and IUPAC, members of the group are also actually involved in two joint Projects, namely n. 2018-004-1-500 "IUPAC/CITAC Guide for evaluation of risks of conformity assessment of a multicomponent material or object due to measurement uncertainty" and n. 2019-012-1-500 "Influence of a mass balance constraint on uncertainty of test results of a substance or material and risks in its conformity assessment". The former, being an extension of a previous project on "Risks of conformity assessment of a multicomponent material or object in relation to measurement uncertainty of its test results", aims at producing a guide for classification and quantification of risks of false decisions on conformity of a multicomponent materials to specification or regulation limits of its chemical composition. The latter project intends to adapt the approach developed for multicomponent materials to those cases in which the component contents of a substance or material are linked by a mass balance constraint (i.e. when the sum of their mass fractions, molar fractions or any other positive quantity ratios is 100 % or 1). In such cases the test results of the substance or material are "compositional data" with a "spurious" correlation.

The researchers of the group are actively involved in European and International bodies, networks and associations, ranging from metrology (CCQM, EURAMET Technical Committee on Metrology in Chemistry, the European Metrology Networks "Climate and Ocean Observations" and "Mathematics and Statistics"), to chemistry (CITAC, Eurachem, IUPAC) and standardization (ISO/TC 69), also comprising cross-disciplinary topics (IMEKO, ENBIS – European Network for Business and Industrial Statistics).

REFERENCE MATERIALS R&D @ MERCK

Markus Obkircher // Merck / Sigma-Aldrich Production GmbH, Buchs, Switzerland

Reference materials are one of the most critical components of the analytical testing workflow. Through calibration of measurement systems, validation of methods, and quality control programs, reference materials ensure accuracy in testing.

Even before the acquisition of Sigma-Aldrich, Merck KGaA Darmstadt already had a very strong name as reference material supplier mainly in the field of inorganic calibration standards for ICP-MS or AAS applications, volumetric solutions, Karl Fischer testing kits or pH buffers. After the take-over of Sigma-Aldrich in 2015, several additional product lines were added to this portfolio. While some these, for example the *Trace*CERT® inorganic calibration standards, show an overlap with Merck's original Certipur® products, the focus especially of the newer reference materials are organic compounds. Most of these organic standards come out of the sites in Laramie (Wyoming, USA), Round Rock (Texas, USA) and Buchs (Switzerland). These three sites as well as Darmstadt hold the so-called double accreditation – the ISO 17034 for the manufacturing of reference materials and ISO/IEC 17025 for specific testing methods that are applied in accreditation workflows. In addition to the abovementioned accreditations, Merck's Laramie laboratories are ISO 17043 accredited as

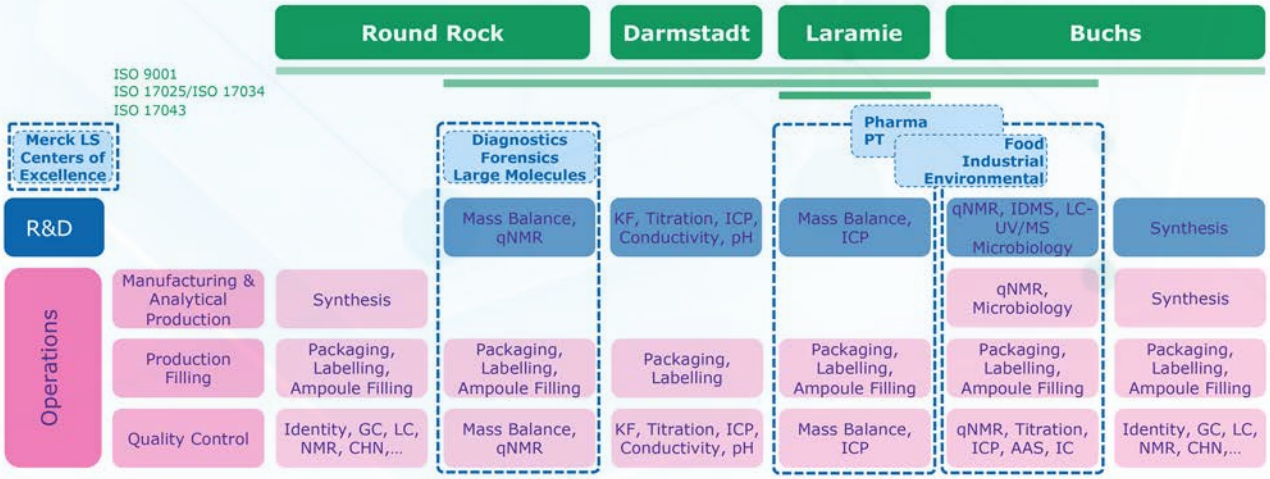


Figure 1: Core competences at the different sites within the Advanced Analytical Reference Materials network

Proficiency Testing provider.

DAkkS in Germany, SAS in Switzerland, and ANAB in the US are controlling the management system and even more important the quality of the work during yearly audits to ensure that ISO norms and guidelines are followed.

Each of the individual sites is specialized using certain of these ISO/IEC 17025 accredited testing methods to determine the content of a neat substance (sometimes also referred to as mass fraction or potency) or the concentration of solutions. Fig. 1 summarizes the techniques that are applied at the different locations in R&D and after a successful transfer in the supply chain organization.

Each of the R&D groups is developing new reference materials for specific market segments thereby creating centers of excellence in that field.

Round Rock (formerly known as Cerilliant) is specialized in the certification of larger molecules and brings highly regulated products to the market for an intended use in diagnostic and forensic testing laboratories. All the other sites are focusing with their new product developments on small molecules – Darmstadt for the industrial industry, Laramie for pharma customers and Buchs for food, industrial and environmental market segments. In addition to this, Buchs is also realizing Microbiology reference materials, where bacteria are immobilized in a matrix that lead to a certified number of colony-forming units (cfu) on defined media.

Merck's reference material hierarchy includes four major quality grades with a clear differentiation to research chemicals, as shown in Fig. 2. While national government organizations like National Metrology Institutes (NMIs, e.g. NIST, NRC) or Pharmacopeias (e.g. USP, EP, BP) provide standardization at the top level with traceable products to the SI or define primary substances, specific ISO norms give clear guidance for the realization of Certified Reference Materials (CRMs), Reference Materials (RMs), and Analytical Standards. The level of certification and traceability requirements increase with each higher level and reference material producers must meet the already mentioned ISO requirements as ISO 17034, ISO/IEC 17025, and ISO Guide 31 to manufacture CRMs or RMs.

In addition to purity and identity of the material, the certificates of analysis of these compounds must state a content, mass fraction or potency with its expanded uncertainty (typically k=2). This overall uncertainty not only includes the deviations of the measurements for the characterization, but also the uncertainties deriving from homogeneity and stability studies to assure that the 'true' value stays within the indicated uncertainty range over the entire shelf life of the product.

Over the last decades every Merck site working in the

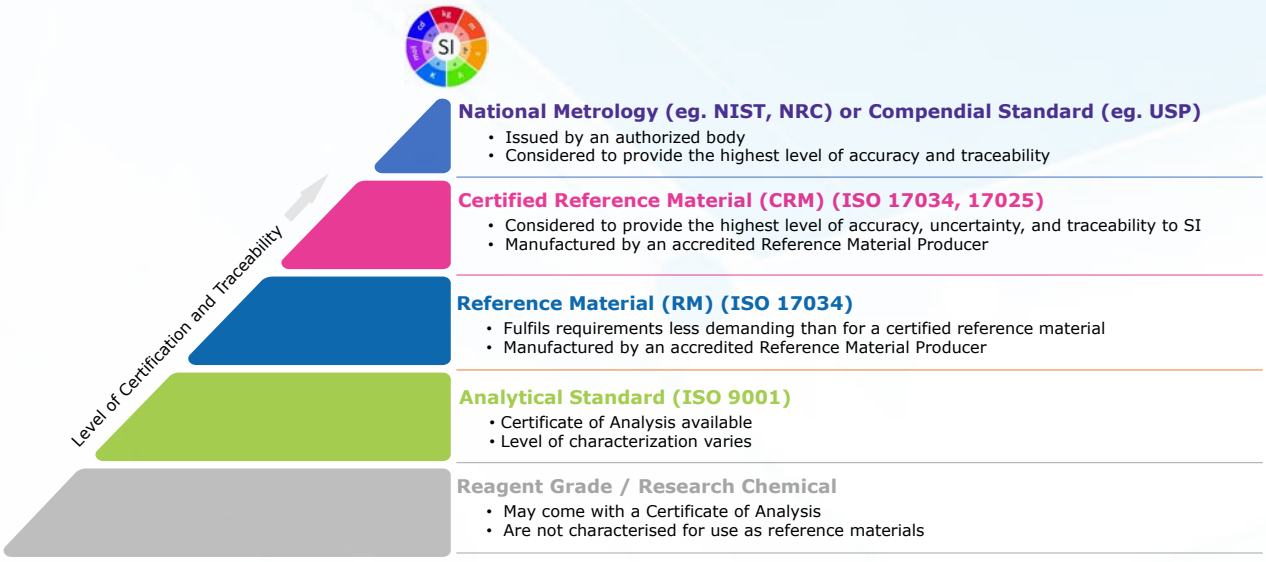


Figure 2: Merck's reference material hierarchy

field of reference materials not only focused on a well-defined customer market but also specialized in different analytical methods for the characterization of candidate molecules.

A technique often used in R&D Round Rock and Laramie is the mass balance approach, which begins with the measurement of a purity by different chromatographic methods as starting point for the certification. Subsequently, multiple organic and inorganic impurities are determined using a variety of trace analyses like Karl Fischer for residual water, GC headspace or Loss on Drying for residual solvent, and residue on ignition or ICP for residual inorganic content. All these traces are subtracted from the chromatographic purity to result in the mass fraction of the pure analyte in the sample. The biggest challenge in this approach is the careful evaluation of chromatographic methods in order to not create a bias by unseparated peaks or under- or overvaluation the response factors of present impurities. Therefore, an identical reference material of high purity for calibration purposes is a requirement.

Because such well-characterized primary materials of the same identity are not always available, quantitative Nuclear Magnetic Resonance (qNMR) is applied since more than a decade in R&D Buchs. As qNMR is a primary ratio method, in which the integrals of the peaks are directly proportional to the number of nuclei contributing to the peak, any substance can be used as internal reference as long as the signals for comparison do not overlap with each other or with other impurities. qNMR allows a direct traceability to the SI unit if this reference is a CRM or a primary material from an NMI. In order to close a long-existing gap in this traceability chain, Merck collaborated with NIST for the realization of Benzoic Acid PS1 as first high purity standard with specific intended use in qNMR measurements (Nelson M et al, Analytical Chemistry 2018, *90*(17), DOI: 10.1021/acs.analchem.8b02575). Merck's R&D division in Buchs is well-recognized for its competence in that field and publishes every few years new research results and application of this characterization technique, for example the extension from 1H-qNMR to 31P and 19F-qNMR measurements.

When products are being developed, which contain larger amounts of stable isotope labeled (SIL) fragments, qNMR reaches its limits for distinguishing between the different isotope forms. Because of this and since mass spectrometry applications in testing laboratories are becoming increasingly important, R&D Buchs also received the ISO/IEC 17025 accreditation for Isotope Dilution Mass Spectrometry (IDMS) measurements. Very similar to qNMR, HPLC-IDMS and GC-IDMS can be

applied for the determination of contents of SIL organic compounds. In this case, the ratio of MRM transitions between a native, non-labeled reference material (ideally a well characterized CRM) and its isotope labeled analog yields to the mass fraction of the analyte, whereby either single IDMS or double IDMS experiment are applied.

In contrast to the already described methods the certification of secondary pharmaceutical standards in R&D Laramie does not only establish traceability to the SI unit by mass balance but in addition to batches from Pharmacopeias. This approach follows the published monograph methods and compares the chromatographic purity of a material with the current lot from USP, EP or BP. The resulting secondary pharmaceutical standards give the customer the choice of either using this value from traceability assay against Pharmacopeia or applying the SI traceable certified value for their experiment.

The Microbiology CRMs that are realized in Buchs as Vitroids and Lenticule Discs also do not establish traceability to the SI unit, but to national culture collections like CECT, NCTC or NCPF. In this case the certified value stated on the certificate is the number of colony-forming units (cfu) that should be found by customers when applying the materials in their QC testing workflow.

Reference materials are used in different formats in testing laboratory, depending on product availability, price and method requirements. All these factors are already taken into account when a product is designed with a very specific intended use. Merck realized in general the three formats for reference materials, which are either a neat or powder form, a reference material in solution or in matrix. While reference materials in a powder form typically come with smaller uncertainties, CRMs in solutions and matrices provide time saving through ready-to-use concentrations and often allow more realistic comparisons. However, they pose challenges for the reference materials producer as characterizations, homogeneity and stability assessments as well as calculations of uncertainties are less straight forward than in the case of pure compounds.

In the past years, Merck was working on the development of several multicomponent mixtures in solutions and matrices. For this purpose, newly designed ISO 17034 workflows were established that typically start with complete characterizations of neat products followed by several gravimetric and dilution steps to the reference material in its final form. Especially the development of Matrix CRMs has many synergies with the preparation of samples for Proficiency Testing (PT). With the new Supelco® PT portal launched, MERCK has a tool available to offer new and innovative schemes to participants around the globe for educational purposes or for their ISO audit requirements.

To fulfill complex projects, the Reference Materials R&D team is collaborating with several partners around the world such as NMIs, research institutes, equipment manufacturers, commercial organizations and even competitors. The main goal of these collaborations is to utilize each individual knowledges and skills in a most effective way to provide solutions to the analytical community as efficient and time effective as possible. One example is the already mentioned work on high purity standards with NIST, another one the cooperation with Bruker for the realization of a quantitative Performance Qualification sample, with which users can control and monitor the system suitability of their NMR equipment. This product development could only be accomplished by combining the core competences of Bruker as NMR equipment manufacturer and Merck as reference material producer.

Either through partnerships and collaborations or by in-house development, Merck thrives to provide reference materials with highest accuracy and lot-to-lot consistency to help customers solve the toughest challenges in their testing laboratories.

CITAC
Cooperation on International Traceability in Analytical Chemistry

MESSAGE FROM THE NEW MEMBER

TANG LIN TEO

Health Sciences Authority (HSA), Singapore

Every bit about me is deeply rooted in Singapore. I was born, bred and educated here. In 2007, I was conferred the Doctor of Philosophy (Ph.D.) in Chemistry by the National University of Singapore. I joined the Health Sciences Authority (HSA) in 2008 as a novice in the field of Chemical Metrology since I worked on organic synthesis during my postgraduate study.

My 3.5-month stint at the National Measurement Institute of Australia (NMIA) provided me with invaluable experience that honed my current skills. At NMIA, I acquired the skills and knowledge in isotope dilution mass spectrometry, mass balance approach for purity assay and measurement uncertainty. When I returned to HSA, I led the Organic Chemistry Section from 2008-2016. I also had the opportunity to represent HSA in international fora such as the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM)'s Working Groups, Asia Pacific Metrology Programme (APMP)'s Technical Committee for Amount of Substance (TCQM) and its Focus Group, and to serve in the local standards and conformance committees as a member and technical assessor (for accredited laboratories that comply with ISO/IEC 17025 or ISO/IEC 17043). Prior to my current role in the management team, I also led a unit which organises proficiency testing programmes and oversees the production of certified reference materials from 2011-2019.

Last year, HSA's Chemical Metrology Laboratory celebrated its 10th anniversary. This year, I have undertaken the leadership role in Chemical Metrology Division. I am indebted to my predecessor and mentor, Dr Tong Kooi Lee, who started his forensic career in HSA 40 years ago and laid strong foundations for chemical metrology work in our Laboratory. I am humbled by the opportunity to lead the Chemical Metrology team and strive to stay relevant in the age of the Fourth Industrial Revolution (4IR).

The 4IR is characterised by the existence of disruptive technology and innovation. As chemical metrologists, we are challenged to ensure the traceability of new measurements. I am grateful and excited to be part of CITAC and look forward to contribute to the activities of this long-standing network.

CITAC
Cooperation on International Traceability in Analytical Chemistry

MEETING REPORTS

*it*ENBIS/INRIM WORKSHOP "MATHEMATICAL & STATISTICAL METHODS FOR METROLOGY" (MSMM 2019)

Torino, Italy, 30-31 May 2019

Francesca R. Pennecchi // INRIM, Italy

A first edition of the Workshop "Mathematical and Statistical Methods for Metrology" (MSMM 2019, http://www.msmm2019.polito.it/) was held in Torino, Italy, hosted by the INRIM, the National Institute of Metrological Research. It was a joint *it*ENBIS/INRIM workshop, co-organized by the Politecnico di Torino (https://www.polito.it/) and the INRIM (https://www.inrim.it), with the co-chairing of Prof. Grazia Vicario (PoliTo) and myself, Dr. Francesca Pennecchi (INRIM). *it*ENBIS (https://enbis.org/about/ln/itenbis/index) is the Italian local network of ENBIS, the European Network for Business and Industrial Statistics (https://enbis.org/), whose main aim is to foster and facilitate the dissemination and the understanding of statistical methodologies to benefit and profit businesses and industries, nurturing interactions between academic statisticians and statistical practitioners.

Recognizing the increasing need of ad hoc and innovative mathematical and statistical tools for current and emerging metrological applications, the Workshop was aimed at presenting recent developments in Mathematics and Statistics applied to the several areas of the Science of Measurements. Researchers and practitioners from the international metrology community and the mathematical/statistical community, including experts from Academy, Industry and Standardization, were encouraged to join the workshop, in order to strengthen connections and collaborations and to provide benefit for the fields of interest.

The workshop availed itself of an international Scientific Committee of 24 members, mainly from National Metrology Institutes (NMIs) and Academies, and took advantage of the support of several sponsors (INRIM, Politecnico di Torino, *it*ENBIS, Department of Mathematical Sciences of the Politecnico di Torino - DISMA, Hexagon Manufacturing Intelligence). Participants were about 60 (73 % Italian and the rest from other European countries), mainly coming from NMIs and Universities, but also from

industries, accreditation bodies and other realms. The scientific programme included 2 invited lectures and 41 presentations, articulated in 6 plenary sessions and 8 parallel sessions, according to the following scheme:

The program at a glance

			Room key	
			Conference Hall	
			Seminar room	
			Expo room	
			The courtyard	
30th May				
08:00	09:00	**Registration**		
09:00	09:30		**Introduction**	
09:30	10:20		**Invited speaker 1: Anthony O'Hagan - Chair: Maurice Cox**	
10:20	10:50	**Coffee break**		
10:50	11:50		JCGM Working Group on the Expression of Uncertainty in Measurement (GUM) (3) - Chair: Anthony O'Hagan	
11:50	12:50		Machine Learning and Predictive models (3) - Chair: Luca Zilberti	
12:50	14:00	**Lunch**		
14:00	15:00		Uncertainty evaluation 1 (3) - Chair: João Alves e Sousa	Conformity assessment and Process/Quality control 1 (3) - Chair: Alistair Forbes
15:00	16:00		Uncertainty evaluation 2 (3) - Chair: Adriaan van der Veen	Conformity assessment and Process/Quality control 2 (3) - Chair: Maria Sole Pellegrino
16:00	16:30	**Coffee break**		
16:30	17:30		Coordinate metrology (3) - Chair: Grazia Vicario	Time and frequency metrology (3) - Chair: Alen Bosnjakovic
17:30	18:10		Chemometric methods (2) - Chair: Stephen L. R. Ellison	Optimization algorithms (2) - Chair: Oriano Bottauscio
18:15	20:30	**Welcome party**		
31st May				
08:30	09:00	**Registration**		
09:00	09:50		**Invited speaker 2: Giulio D'Agostini - Chair: Walter Bich**	
09:50	10:30		Statistical indices (2) - Chair: Grazia Vicario	
10:30	11:00	**Coffee break**		
11:00	12:20		Simulated experiments and numerical modelling (4) - Chair: Alessandra Manzin	
12:20	13:30	**Lunch**		
13:30	15:00		EMPIR EMUE Project "Advancing measurement uncertainty - comprehensive examples for key international standards" (4) - Chair: Francesca Pennecchi	
15:00	16:00		Bayesian methods (3) - Chair: Giulio D'Agostini	
16:00	16:15		**Conclusions**	

The invited speakers were Anthony O'Hagan – Emeritus Professor of Statistics, School of Mathematics and Statistics, The University of Sheffield (UK), providing the presentation "Measurement or Estimation?", and Giulio D'Agostini – Professor of the Physics Department of the University of Rome "La Sapienza", Roma (Italy) and INFN Roma 1, providing the presentation "*p*-values: meaning, misconceptions and dangers, but also their practical utility if used *cum grano salis*".

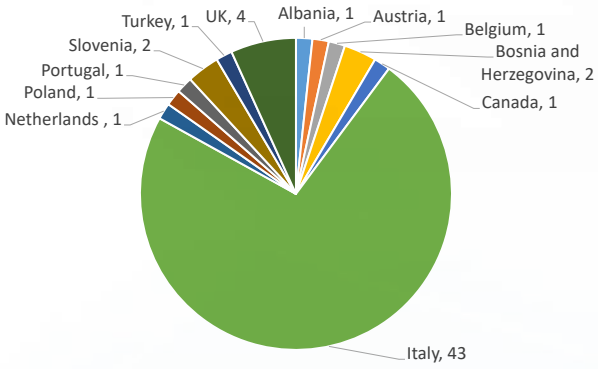
Several topics were treated, from uncertainty evaluation (with dedicated sessions on activities of the JCGM Working Group on the Expression of Uncertainty in Measurement and the European Joint Research Project "EMUE - Examples of Measurement Uncertainty Evaluation") to conformity assessment and quality control, from machine Learning and Bayesian methods to simulated experiments, from optimization algorithms to statistical indices, from coordinate metrology to time and frequency applications. A whole session was dedicated to chemometric methods and several presentations were focused on chemistry applications, such as: "Effective validation of chromatographic analytical methods", "Chemometrics handling of Raman spectra for live systems monitoring and susceptibility tests", "On the detection of anomalous values of Radioxenon in IMS stations of CTBTO", "The evaluation of chronic alcohol abuse biomarkers in hair samples: the interpretation of cut-off values", "Assessment and management of occupational exposure to airborne dust in a quality approach". In the framework of the IUPAC/CITAC Project n. 2019-012-1-500 "Influence of a mass balance constraint on uncertainty of test results of a substance or material and risks in its conformity assessment" (https://iupac.org/projects/project-details/?project_nr=2019-012-1-500), I gave the presentation "Conformity assessment of multicomponent materials or objects using compositional data", showing the preliminary results of the relevant project. All the abstracts and the

presentations of the workshop are available at http://www.msmm2019.polito.it/programme.

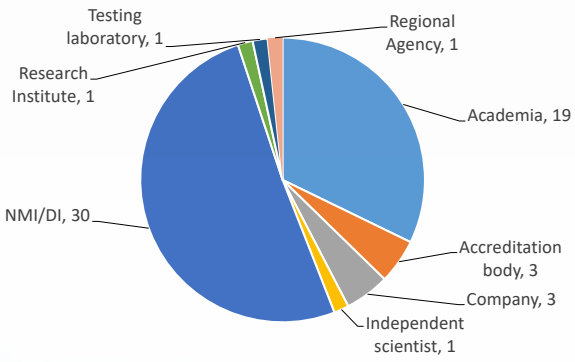
Two journals have agreed on organizing a special issue dedicated to MSMM 2019, namely Measurement Science and Technology (MST) and Accreditation and Quality Assurance (ACQUAL): the deadline for the paper submission expired in October 2019 and the two issues are now under completion.

A second edition of the workshop is foreseen in spring 2021, this time under the auspices of the European Metrology Network "Mathematics and Statistics", of which INRIM is a Member.

THE FLAG OF THE MSMM 2019 WORKSHOP AND DISTRIBUTIONS OF ITS PARTICIPANTS:



Distribution of participants by country



Distribution of participants by affiliation

IV INTERNATIONAL SCIENTIFIC AND TECHNICAL CONFERENCE "METROLOGY OF PHYSICOCHEMICAL MEASUREMENTS"

Suzdal, Russia, 17-19 September 2019

N.G. Oganyan // VNIIFTRI, Russia

Natalia Justus, VNIIFTRI, Russia, invites participants to the conference hall

The IV International Scientific and Technical Conference "Metrology on Physicochemical Measurements" was held 17-19 September 2019 in Suzdal, Russia.

It was organized by the All-Russian Scientific Research Institute for Physical-Engineering and Radiotechnical Measurements (VNIIFTRI) with participation of the Cooperation on International Traceability in Analytical Chemistry (CITAC) under the slogan "Let's speak about measurement uncertainty" and with the technical and organizational support of LLC STC "NAVITEST". Conference sponsors were: VNIIFTRI (General Sponsor) and Endress+Houser Company "AnalytikJena" (Sponsor).

About 100 participants from metrological, academic and high-education institutes, metrology service centers and other organizations of Belarus, Bulgaria, China, Israel, Germany, Switzerland and Russia took part in the Conference. There were 44 oral presentations, some posters and a small exhibition.

The Conference program included scientific and technical topics from the fields of electrochemistry, spectrometry, chromatography and other instrumental methods of physicochemical analysis; reference materials; measurements of dispersed parameters of particles in heterogeneous media, including aerosols and suspensions and air ions; applied and legal metrology and others.

Sergey Donchenko, VNIIFTRI, Russia

The conference was opened with welcoming remarks by Prof. Dr. Sergey Donchenko, General Director of VNIIFTRI.

Alfred Wiedensohler, Leibniz Institute for Tropospheric Research, Germany

A lecture auditory

On the first day, the most number of the reports was related to measurements of dispersed parameters of particles in gases and liquids. The conference work in particles area was started with the lectures by Prof. Dr. Alfred Wiedensohler, Head of Experimental Aerosol and Cloud Microphysics Department, Leibniz Institute for Tropospheric Research, Germany - "Mobility particle size spectrometers: calibration procedures and measurement uncertainties", and by Dr. Lucia Bustin, TSI GmbH, Germany - "CEN standard "Harmonized counting of atmospheric ultrafine particles and UFP monitoring initiatives in Europe". This day the speakers talked about the current state of metrological support in this area, monitoring intensity of dust deposits in coal mines, leading to disasters, early warning emergency and pre-emergency situations by monitoring aerosols (arising in air as results of physical and chemical processes, as well as of vital functions of microorganisms), measuring instruments for automatic monitoring atmospheric air and emissions of enterprises, importance of gas-dynamic protection of processes and microelectronics objects from external contamination.

Samuel Wunderli, "atomolmetron" GmbH, Switzerland

The second conference day started with presentations of CITAC members: Dr. Samuel Wunderli, CEO, "atomolmetron" GmbH, Switzerland - "Uncertainty evaluation in general and Monte Carlo uncertainty evaluation"; Dr. Narine Oganyan, Deputy Head of Physico-Chemical and Electrical Measurements Department of VNIIFTRI, Russia - "Measurement uncertainty and corresponding risk of false decisions", and Dr. Ilya Kuselman, Independent Consultant on Metrology, Editor of CITAC News and Chair of the IUPAC Interdivisional Working Party for Harmonization of Metrology and Quality Guidelines, Israel - "How many shades of grey are in conformity assessment due to measurement uncertainty?". A short booklet about CITAC, developed by Dr. Narine Oganyan and approved by Dr. Michela Sega, CITAC Chair, was issued by VNIIFTRI in Russian and English and distributed among the conference participants.

Then, other speakers talked about instrumental methods, reference procedures and problems in physicochemical measurements, necessity to improve relevant national standards (in particular, in Russia) using international activities of metrological institutes, including key and pilot comparisons, reference materials and developed measures.

The third day was devoted to reference materials, electrochemistry and achievements in the development of measuring equipment in this field.

The conference participants were very active, heat discussions were also continued during the breaks. The practical output of the conference was formulated

as recommendations for improving applied research and exchange of experience in the field of physical and chemical measurements.

Ilya Kuselman, Independent Consultant on Metrology, Israel

The participants noted the high scientific, practical and organizational level of the conference, the wide list of the topics and geography of the presented specialists. After the conference, they had an opportunity to enjoy the beauty of Suzdal and to buy souvenirs from Russia.

A book "Abstracts of the Conference" in Russian and English was published before the Conference. In addition, the abstracts of the conference in English will be published as an open access volume of the Journal of Physics: Conference Series, on the website: http://conferenceseries.iop.org/.

Narine Oganyan, VNIIFTRI, Russia

The next such conference is planned by VNIIFTRI for 14-16 September 2021 in historical place, Park-Hotel "MOROZOVKA", Moscow region, Mendeleevo, Russia.

Participants of the conference "Metrology of physicochemical measurements", Suzdal, Russia, 17-19 Sep 2019

EURACHEM WORKSHOP ON 'UNCERTAINTY FROM SAMPLING AND ANALYSIS FOR ACCREDITED LABORATORIES'

BAM, Berlin, 19-20 November 2019

Michael H. Ramsey // University of Sussex, UK

Eurachem Workshop on 'Uncertainty from sampling and analysis for accredited laboratories', was held in conjunction with Eurolab-Germany and CITAC, at BAM in Berlin on November 19th-20th 2019.

This two-day Workshop attracted over 140 participants from 27 counties, who made 30 presentation, both orally and as posters. One of its objectives was to launch the Second Edition of the Eurachem/CITAC Guide on Measurement Uncertainty arising from Sampling (UfS) (reviewed on page 60 of this Newsletter). The first day was therefore mainly focused on UfS and several of the new ideas in this area that have been incorporated into the revised Guide. For example, the Uncertainty Factor was explained as a better way to express measurement uncertainty (U) when the values are large (e.g. U > 20%), and when the frequency distribution of the uncertainty is shown to be log-normal, rather than the Gaussian that is usually assumed. Some examples where given where this asymmetry in the uncertainty was seen to arise from the sampling process, but other examples arose from purely analytical sources, such as the determination of genetically modified organisms (GMOs) in soya.

Another general objective of the Workshop was to understand how UfS relates to the accreditation of sampling, that has an increased role in the latest version of ISO/IEC 17025, explained in contributions from ILAC and UKAS. Another interesting presentation reviewed over 100 published applications of UfS estimation, since the publication of the First Edition of the UfS Guide in 2007. These ranged across many application sectors, mainly environmental (70%, of which 40% on water, and 30% on soil and sediment), but also on food safety (22%) and industrial processes (8%). This review set the scene for discussion of the way forward for research and applications in UfS. Suggestions for new areas of application included estimating uncertainty of *in situ* measurements (e.g. sensors), were the sample is not removed but left undisturbed and therefore unmixed. The uncertainty of *in situ* measurements needs, therefore, to include the UfS caused by the heterogeneity of the analyte in most test materials in nature. Also recognized was the need to find better ways of allowing for high values of UfS in compliance assessment. The first review and meta-analysis of UfS estimates across a whole application sectors, has been published for food (Ellison *et al.*, 2017, Analytical Methods, 9, 5989-5996). Two potential benefits of applying this type of approach to other applications sectors were identified. The results may help to substantiate the general applicability of the mathematical model between UfS and analyte concentration that was found across the food sector. Secondly, such models may allow regulators to predict approximate values of UfS that can be incorporated into new regulatory guidelines.

On the second day, the earlier discussion of the uncertainty factor for UfS on particular, lead on to discussions of the more general topic of expressing high levels of uncertainty and its asymmetric distribution, regardless of its origins. There were some differences between what presenters considered the limits to be for various levels of uncertainty. Low levels of uncertainty were generally considered to be when the relative standard uncertainty (u') is below either 10 or 15% (i.e. expanded U' below 20 or 30%), with high levels classified as being over either u' = 40% or 50%, and a medium level in between these two limits. There was also a range of

views on how uncertainty should be expressed at each level. Most speaker suggested that at low levels of uncertainty, uncertainty should be expressed as relative expanded uncertainty, unless the analyte concentration was close to the detection limit (e.g. s < 2 x limit of quantitation), when the expanded uncertainty should be used. For medium and high levels of uncertainty, use of the expanded uncertainty factor (^{F}U) was generally recommended. Although ^{F}U is usually calculated by taking logarithms to the base '*e*' of the measured analyte concentration, the same values are obtained if logarithms taken to the base 10. It was recognized that the microbiological sector has been expressing uncertainty using logarithms taken to the base 10, but not expressed as ^{F}U.

There was increasing appreciation of Monte Carlo (MC) simulation is studies of uncertainty. In one presentation MC simulation was used to show that at low uncertainty levels (u' < 15%) there was no significant discrepancy between normal, log-normal and MC distributions. Above this level (u' > 15%), the prediction from the normal distribution progressively diverged from those of both the log-normal and the Monte Carlo simulation, which were virtually identical. The conclusion was that the distribution of the values attributable to the measurand was lognormal rather than normal.

One innovative presentation described how to calculate the confidence interval of an uncertainty estimate. The equations used to make these calculations for classical ANOVA applied to a normal distributed data have been published earlier, but not previously incorporated into packages for uncertainty estimation. The innovation here was to extend this procedure to deal with data sets with up to 10% of outlying values, requiring the application of robust ANOVA. The boot-strapping approach was applied to calculate the 95% confidence interval of the estimates of uncertainty arising from both the chemical analysis and the sampling. These intervals can then be used to compare estimated of uncertainty made by difference approaches, to test whether the apparent differences are statistically significant.

The case for using more empirical information from quality control schemes to improve the reliability of uncertainty estimates, was made by several speakers. There was also discussion the best software both for the estimation of uncertainty, and for research into improving such methods. For the estimation of *U* and UfS various packages in Microsoft Excel were described (e.g. RANOVA2, and @Risk for MC), but for research purposes, the more flexible packages in the language 'R' were often recommended.

The substantial number of participants and presentations at this Workshop indicate that research into uncertainty estimation, and its applications, are topics of sustained interest and relevance. The many discussions within the Workshop raised numerous new and emerging issues that will ensure that further research into uncertainty and UfS estimation will continue to develop over the coming years. The abstracts and slides from all of the presentations made in the Workshop are available at: https://www.eurachem.org/index.php/events/workshops/277-wks-mu2019#plenaryDay1

A proportion of the participants at the Uncertainty Workshop in Berlin in November 2019, are shown below.

CITAC
Cooperation on International Traceability in Analytical Chemistry

ANNOUNCEMENTS

10TH WORKSHOP ON PROFICIENCY TESTING IN ANALYTICAL CHEMISTRY, MICROBIOLOGY AND LABORATORY MEDICINE

WINDSOR (UK), 12TH–15TH OCTOBER 2020

Brian Brookman // LGC Ltd., UK

The EURACHEM Proficiency Testing Working Group (www.eurachem.org), in co-operation with CITAC (www.citac.cc) and EQALM (www.eqalm.org), is organising the 10th event of a series of Workshops addressing current practice and future directions of proficiency testing (PT) and external quality assessment (EQA) in analytical chemistry, microbiology and laboratory medicine.

VENUE

The workshop will take place at the De Vere Beaumont hotel in Windsor, a town on the River Thames in southeast England, just west of London. It is home to Windsor Castle, a residence of the British Royal Family, built by William The Conqueror in the 11th century. The story of De Vere Beaumont Estate in Old Windsor is a very British one; a tale of democracy, royalty, education and religion. At its heart, sits an 18th-century mansion, a chapel, 75 event spaces and a Georgian white house in 40 acres of parkland grounds. The original house was built for Lord Weymouth but it was during its time as a public school, from 1854 - 1967, that saw most of the estate's architectural developments.

TECHNICAL PROGRAMME

The workshop will be structured to include training sessions, keynote lectures, short presentations, working group discussions and poster sessions, to enable interactive participation and cross-fertilisation of ideas. The official language of the workshop will be in English. Invited lectures and accepted presentations/posters will be considered, through peer-review, for publication as full papers as a topical focus in an issue of Accreditation and Quality Assurance (Springer Verlag).

TRAINING SESSIONS

Four training sessions, which are open to workshop delegates, will be held on the following topics:

- Basic statistics

- Further statistics
- PT scheme design
- Test item QC testing

LECTURES AND WORKING GROUP TOPICS

- Revision of ISO/IEC 17043
- Guidance on different methods for setting the standard deviation for proficiency assessment
- Collusion or falsification of results in PT – why does it happen and how can it be prevented
- Comparisons of synthetic vs real PT items
- Emerging trends in PT
- Risk analysis approach for PT participation

WHO SHOULD ATTEND?

The workshop will provide an excellent opportunity for PT/EQA scheme organisers, and end-users of PT/EQA (laboratories, accreditation bodies, regulators and the laboratories' customers) to come together and share their views.

REGISTRATION

Visit the workshop website to register.

WORKSHOP SECRETARIAT

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IUPAC/CITAC WORKSHOP "METROLOGY, QUALITY AND CHEMOMETRICS - CORRELATION OF TEST RESULTS AND MASS BALANCE INFLUENCE ON CONFORMITY ASSESSMENT"

19-20 JAN 2021, TEL AVIV, ISRAEL

Ilya Kuselman // Independent Consultant on Metrology, Israel

Dear Colleagues,

On behalf of the International Advisory Committee it is my pleasure to invite you to participate in this Workshop, in conjunction with the 24th Isranalytica Conference and Exhibition, 19-20 Jan 2021, Tel Aviv, Israel, www.isranalytica.com.

The main aim of the Workshop is discussion of the experience of chemists-analysts, metrologists and quality specialists in method validation, quantifying measurement uncertainty, risks in conformity assessment due to measurement uncertainty, proficiency testing, reference materials, and treatment of laboratory data in pharmaceutical industry, food analysis, environmental analysis, forensic science and other fields. This discussion will include also the following topics:

- correlation of chemical analytical/test/measurement results;
- influence of mass balance or another constraint on uncertainty of test results of a substance or material and risks in its conformity assessment;
- risk management in a chemical analytical laboratory under accreditation.

The workshop is organized by the Israel Analytical Chemistry Society (IACS) with participation of the Israel Laboratory Accreditation Authority (ISRAC), in cooperation with International Union of Pure and Applied Chemistry (IUPAC) and Cooperation on International Traceability in Analytical Chemistry (CITAC), arranged by Bioforum Ltd. The workshop website page will be available at www.isranalytica.com (see also https://iupac.org/event/metrology-quality-and-chemometrics/).

Abstracts of your contributions, lectures or posters (up to 300 words), and a short CV (up to 100 words) please send till 15 Sep 2020 to Dr. Ilya Kuselman, ilya.kuselman@gmail.com. Requests concerning the Workshop organization, site, accommodation, participation, etc., please send to Ms. Reut Lazar, reutl@bioforum.co.il.

"REFERENCE MATERIALS IN MEASUREMENT AND TECHNOLOGY": IV INTERNATIONAL SCIENTIFIC CONFERENCE ON REFERENCE MATERIALS

15-17 SEP 2020, EKATERINBURG, RUSSIA

Olga Kremleva, Natalia Taraeva // Ural Scientific Research Institute for Metrology (UNIIM), Russia

IV International Scientific Conference on Reference Materials will be held in Ekaterinburg (Russia) from 15 to 17 September 2020. It is a unique opportunity for scientists and practitioners in the field of chemistry, technical physics, metrologists, as well as for specialists in analytical laboratories, working for companies and organizations, involved in the production, distribution and use of reference materials, to interact with the conference key participants from around the world, with the aim to promoting international cooperation, the exchange of experience and the relevant information on the latest achievements and technologies in the field of reference materials.

The next conference "Reference Materials in Measurement and Technology", continues the series of events, which began in 2013 and since then was held on a regular basis.

The conference will cover all areas where reference materials (RMs) play a certain role. The following issues will be discussed at the conference:

- Academic and practice-based aspects of development, production, distribution and use of reference materials;
- Metrological assurance of measurements in the field of biological RMs, multi-element RMs, pharmaceuticals, quality control, food safety, environmental monitoring, ferrous and non-ferrous industry, nuclear industry etc.;
- Measurement result processing, measurement traceability, commutability;
- Modern methods for analysis of substances and materials (chemical and physico-chemical methods, atomic and molecular spectroscopy, chromatography, X-ray spectroscopy, mass spectrometry, nuclear-physical methods of analysis, etc.);
- Interlaboratory comparison testing.

The conference will address the specifics of the creation and use of reference materials, intended for the needs of the pharmaceutical industry. It is planned to consider advanced practical experience in creation and use of pharmaceutical reference materials in the international community.

The conference will include plenary and poster sessions, demonstrations of measurement capabilities of RM and analytical equipment producers.

Conference materials will be published in a special issue of the journal "Reference Materials in Measurement and Technology: 2020".

Scientists and experts in the field of chemistry, metrologists, specialists from analytical laboratories and companies and organizations, engaged in RM development, distribution and use as well as other interested persons are invited to participate in the IV International Scientific Conference "Reference Materials in Measurement and Technology".

The conference will be held in Ekaterinburg, one of the major centers in science and industry in Russia. Ekaterinburg is a city with rich historical and cultural heritage, having unique historical monuments, museums, churches. Ekaterinburg is a scientific and business center of the Ural region of Russia.

More detailed information is available at www.conference.gsso.ru.

CITAC
Cooperation on International Traceability in Analytical Chemistry

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ABOUT CITAC

CITAC - Cooperation on International Traceability in Analytical Chemistry - arose out of an international workshop held in association with the Pittsburgh Conference in Atlanta in March 1993. The aim of this workshop was to discuss how analytical activities could be developed to meet the needs of the 21st century, and it identified a wide variety of issues to be addressed to ensure that analytical measurements made in different countries or at different times are comparable. These range from the development of traceable reference materials and methods to the harmonisation of analytical quality practices.

The CITAC Initiative aims to foster collaboration between existing organisation to improve the international comparability of chemical measurement. A Working Group takes matters forward and its initial activities have centred on a few specific high priority activities. The first tasks included the compilation of a directory of certified reference materials under development; preparation of quality system guidelines for the production of reference materials; preparation of a directory of international chemical metrology activities; defining criteria for establishing traceability to the mole; and the preparation of an international guide to quality in analytical chemistry.

Many of these activities are of a strategic nature, laying the ground for the improvement of international analytical measurement. This reflects the added geographical complexities associated with a world-wide organisation, such as greater diversity in culture and in technical approach, and frequently long timescales associated with its activities. Nevertheless, if the full benefits of improved analytical measurement are to be realised internationally, a truly global approach is needed, and there is a clear role for CITAC to play in this respect.

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