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RMG1: BIM, Bulgaria (Employing organisation); LNE, France (Guestworking organisation)		

TABLE OF CONTENTS

1 Overview 3
2 Need 3
3 Objectives 4
4 Results 4
5 Impact 7
6 List of publications 9

1 Overview

Metrology in chemistry is a rapidly growing field, strongly driven by societal needs for reliable chemical measurements as well as legislation and international agreements. Metrological comparability of measurement results is a key requirement in many situations, such as cross border trade, laboratory medicine, and transnational implementation of environmental regulations. The project enhanced the research capabilities in the field of metrology in chemistry by developing analytical procedures, for emerging National Metrology Institutes (NMIs) and Designated Institutes (DIs). Furthermore, it demonstrated the uptake of the improved capabilities through the application of case studies. With support from the project, four NMIs /DIs also prepared roadmaps and defined their long-term strategies, for the implementation of national metrological infrastructure and effective collaboration with neighbouring countries.

2 Need

When performing routine chemical analysis, field laboratories need reliable tools such as reference materials and reference measurements in order to establish metrological traceability and to demonstrate their capabilities to meet the environmental EU Directives and food safety requirements in terms of low limit of quantification (LOQ) which are often close to, or even lower than, few nanograms per kilogram (ng/kg). Heavy metals such as cadmium (Cd), lead (Pb), mercury (Hg) and nickel (Ni), are among the inorganic pollutants regulated by the Water Framework Directive (WFD) 2000/60/EC with set Environmental Quality Standards (EQS) of 0.2 µg/l for Cd, 7.2 µg/l for Pb, 0.05 µg/l for Hg, and 20 µg/l for Ni. Moreover, pH is one of the most common routine analyses providing quick information about pollution and/or contamination risk. pH levels are typically measured by field laboratories with an uncertainty of 0.01 pH but in order to assess their performances and to calibrate the routine instruments, buffer solutions characterised with an uncertainty < 0.01 pH are needed. The metrological approach to calibration in chemistry is based upon Isotope Dilution Mass Spectrometry (IDMS). This method has the highest metrological standing and the potential of being a primary reference measurement procedure. Major advantages of the technique with respect to external calibration approaches is that, it can ensure direct traceability to SI units and that the analyte recovery does not need to be quantitative, providing that a good equilibration of the calibrant/sample blend has been achieved. In addition, the ratios can be reproducible and, thus, concentrations can be determined in a highly accurate way. Despite the relatively simple principle, the IDMS approach requires experienced operators, since many aspects (e.g. the selection of the proper isotopes, optimisation of the calibrant/sample blend equilibration), have to be carefully evaluated and considered for optimal results. Prior to the start of the project, few NMIs/DIs were sufficiently experienced in applying this methodology. The project addressed these needs by fulfilling Objectives 1, 2 and 3.'

In the field of environmental monitoring, EU Member States are required to implement the Water Framework Directive (WFD) 2000/60/EC, with a strong emphasis on Europe's waters achieving good ecological and chemical status to protect human health, water supply, natural ecosystems and biodiversity. In this respect, transnational research collaboration has been priority, particularly for members with shared interests. A typical case is the Black Sea area, which requires coordinated action at the regional level, in accordance with the Black Sea Convention. In order to implement EU Policies such as the WFD, project partners that were from countries in the Black Sea Region (Bulgaria, Romania, Turkey and Greece) needed to improve the quality of the routine analysis performed by field laboratories. These countries also needed to reinforce their synergies to enable a sharing of the analytical competencies and the services for end-users such as field laboratories and accreditation bodies. The capabilities developed in this project; in terms of measurement procedures, have aided direct traceability to SI units; and in terms of metrology in chemistry, have promoted sustainable approaches for the provision of reliable tools such as certified reference materials (CRMs) and proficiency testing (PT) schemes thus strengthening confidence in chemical analysis results. Furthermore, through its European Neighbourhood Policy (ENP), the EU works with its southern and eastern neighbours to achieve the closest possible political association and the greatest possible degree of economic integration. It indicated a need for Tunisia to dispose of reliable and acceptable data in compliance with the EU import requirements in order to improve the exchanges with the EU Countries. The project addressed these needs by addressing Objectives 4 and 5.

3 Objectives

The overall aim of the project was to improve the measurement capabilities of less experienced NMIs/DIs in the field of metrology in chemistry. This project focussed on the following scientific and technical objectives:

1. To develop traceable measurement capabilities for the analysis of heavy metals for concentrations at ppt and ppb levels (depending on the matrices) with uncertainties less than 10 % by developing isotope dilution mass spectrometry (ID-ICPMS) methodology as a primary procedure for elemental determination.
2. To develop a secondary method for pH measurement and to apply the method for the production and characterisation of reference pH buffer solutions with a target uncertainty of 0.008 pH for the calibration of pH-meters and as reference samples for inter-laboratory comparisons and proficiency testing.
3. To apply the methods developed (ID-ICPMS) to environmental and food samples to determine the heavy metals content in representative matrices, such as potable and natural waters, sediments, and different types of fish/biota samples.
4. To validate the developed methods (secondary pH procedures, ID-ICPMS) by participation in suitable international comparisons (organised by CCQM, EURAMET, another RMO, and/or bilateral – between the NMIs participating in the project) and hence to underpin the development of appropriate CMCs (Calibration and Measurement Capabilities) for submission to the BIPM Key Comparison Database.
5. To develop individual strategies for the long-term operation of the capacity developed, including regulatory support, research collaborations, quality schemes and accreditation. The involved NMIs/DIs will also develop strategies for offering calibration services from the established facilities to their own country and neighbouring countries.

4 Results

To develop traceable measurement capabilities for the analysis of heavy metals (Objective 1).

Measurement procedures were developed for elements (such as cadmium, lead, mercury, and nickel) in three representative matrices. These elements were selected as representatives of their analytical challenges, in terms of characterising the isotopic composition and the presence of different interferences which required different instrumental approaches to remove them (i.e. medium vs. high resolution, or collision cell).The representative matrices were of fresh water and fish samples. Water is relevant for both environmental studies and food safety (drinking water), it is a relatively easy matrix since it does not need digestion. However, the analyte natural concentrations are usually low and show relatively short stability for some analytes (high blank contamination risk). Fish is another relevant matrix for both environmental and food safety issues however it represents a more complex matrix due to the presence of fat components, usually high analyte concentrations along with a high risk of interferences. In like manner, other food and environmental matrices (such as sediments, seawater and estuarine water) were tested so the learned procedures could be implemented.

Additionally, the project provided knowledge transfer from the more experienced to the less experienced NMIs/DIs through organised training plans. LNE provided a one-month training course on ID-ICPMS to BIM and BRLM respectively. Two scientists from BIM and one scientist from BRLM studied the main concepts of the technique and practiced in the laboratory. At the beginning of the training course, a booklet containing information about the IDMS implementation (systematic analysis procedure, certificates of certified reference materials (CRMs), equations, calculations, etc.) was provided to the trainees, together with the necessary safety requirements. The principles and application of the IDMS method were shown and explained first by determination of mercury (Hg), nickel (Ni), lead (Pb) and cadmium (Cd) in a food sample (fish homogenate). Then the trainees applied what they have learned to analysis of sediment sample. The work was conducted on the following points:

- Matrix digestion of fish, rice and sediment samples,
- Evaluation of the matrix composition, choice of suitable isotopes and characterisation of the natural isotopic composition of the analyte (in particular for elements with an high variability such as Pb),
- Preparation of the standards (including the evaluation of its purity if not certified),
- Evaluation of the blanks,

- Application of the ID equations and estimation of the uncertainty budget following the GUM (Guide to the Expression of Uncertainty in Measurement) approach.

Four elements were chosen to be determined in this study due to their different features: Hg – instability when the concentration is low (stabilization is very often required); Ni – strong spectral interferences (high peak resolution required); Pb – variable natural isotope ratio (determination of the natural isotope ratio required); Cd – spectral interferences (mathematical correction required).The IDMS methodology was applied by the trainees (with support from the trainer when needed) in a second study. The elements Pb, Cd and Hg were determined in the sediment certified reference material.

LNE also provided a two-day training course to IAPR, on the improvements of the use of the high resolution ICPMS. Different settings of the instrument were tested and the impact on the results were evaluated. TUBITAK provided two training courses to INRAP, one on ID-ICPMS and the second on the production of certified reference materials. The training on ID-ICPMS was applied to the determination of the amount of Cu and Cd in seawater samples using High Resolution ICPMS and Quadrupole-ICP-MS/MS. The one on the production of the reference materials was conducted on the characterisation of a fish sample and the determination of the amount of Hg.

In addition to the objective of developing primary procedures for elemental analysis, procedures for the quantification of total Hg and its speciation in seawater and fish were developed by a Research Mobility Grant (RMG)researcher. Mercury analysis is regularly done with Advanced Mercury Analyzer (AMA). However, the establishment of SI traceability for AMA analyses needs further study. Therefore, one of the first steps of the RMG researcher was to evaluate how to reach metrological SI traceability and establish a complete uncertainty budget for AMA analyses. This was done using different Certified Reference Materials (CRM) and careful identifying and estimating all individual uncertainty contributions such as the standard deviation of measurements of CRM or sample, the standard uncertainty of the CRM and the standard uncertainty from recovery factor correction. At the same time, measuring mercury in very low concentrations (as is the case of seawater), requires to ensure the stability of the instrument and method performance in order to avoid different difficulties such as contaminations, analyte losses or strong matrix effect. For these reasons, a study of AMA and ICP-MS performances and methods optimization by using different CRM from fishery products (NIST 2976 - Mussel tissue, NIST 1566b - Oyster tissue and IAEA 452 - Scallop tissue) containing mercury at higher concentrations than ppt were performed. A comparative study on determination of total mercury (THg), methylmercury (CH_3Hg^+) and inorganic mercury (Hg^{2+}) in fishery products by AMA and three different mass spectrometry techniques was conducted: high resolution ICP-MS technique (ICP-HR MS), classical quadrupole ICP-MS technique (ICP-QMS) and Gas Chromatography coupled with ICP-HR MS (GC-ICP-HR MS). The results were obtained with double isotope dilution (ID) and species-specific double isotope dilution (SS ID). The studied methods were finally applied for analysis of THg and CH_3Hg^+ in real samples, i.e. Gammarus, Sea Bass and seawater.

Objective 1 was fully achieved, since all the less experienced NMIs/DIs had never performed ID-ICPMS analysis before the project and are able to conduct this measurement approach to exemplar elements in representative food and environmental matrices, with an uncertainty of about 10%.

To develop a secondary method for pH measurement and to apply the method for the production and characterisation of reference pH buffer solutions with a target uncertainty of 0.008 (Objective 2)

Prior to the start of the project, BIM applied only the primary method for their production and characterisation of reference pH buffer solutions. Although this method can provide pH values of buffer solutions that are directly traceable to the SI, in most applications it's expensive use is not justified. Particularly when a traceable secondary standard of sufficient accuracy is available. The secondary method for pH measurements is internationally recognised and provides traceability to the SI through primary reference buffer solutions. This procedure is simpler and faster and requires lower cost equipment. The quality of the produced secondary buffer solutions is sufficient for the requirements of the customers - laboratories dealing with routine pH measurements.

In order to realise the secondary method for pH measurement, a secondary measurement standard is required in which the most critical component is the secondary cell. The project partners reviewed the available literature on several types of secondary cells and considered their respective pros and cons. Based on the literature review, the researchers from BIM and LNE chose the differential potentiometric cell with a single junction, without a salt bridge. The parameters of the secondary cell (such as the sizing of the cell structure and the porosity of sintered-glass disk) were specified by the researchers and a producer of the cell was found. Then, the produced secondary cell prototype was tested with respect to the parameters mostly affecting the accuracy

of secondary pH values: stability of the signal in time and reproducibility of junction potential. Both the velocity of the hydrogen flow and the approach for cleaning the sintered-glass disk; between the two half-cells; were also optimised.

The secondary pH cell contained two identical Pt/H2 electrodes interconnected by a semipermeable membrane (sintered-glass disk) which is at the origin of a liquid junction (diffusion) potential. In order to minimise this residual potential, the chemical composition of the buffer solutions into the two half-cells had to be identical. The sintered membrane that separates the two half-cells is a critical point in secondary pH cell design and can directly affect quality of the measurement taken. It was also important to have equal measurement conditions in both parts of the cell (the two half-cells) to ensure each half-cell had the same depth of immersion and temperature, as well as, identical hydrogen flow. This developed secondary pH measurement standard was validated using phthalate, phosphate and borate certified reference materials which were produced by BIM and characterized by their primary pH measurement standard. The uncertainty achieved is lower than the target of 0.008 pH for all three buffer solutions. The developed secondary pH measurement standard will be used for production of secondary buffer solutions, which will be at lower cost but with similar quality compared to the primary ones.

Objective 2 was fully achieved since a secondary measurement standard for pH was validated with an uncertainty of 0.008 pH. This secondary standard was successfully applied for the characterisation of pH buffer solutions for calibration of pH meters of field laboratories and used by BIM as reference samples for interlaboratory comparisons and proficiency testing schemes.

To apply the methods developed (ID ICPMS) to environmental and food samples to determine the heavy metals content in representative matrices (Objective 3)

As a result of the training courses organised under Objective 1, each NMI/DI began implementing the ID-ICPMS method in their own laboratories. TUBITAK distributed two reference materials (a river water and a fish) to be used for the implementation of the methods. The river water was a previously certified TUBITAK reference material for Cd and Pb and the fish reference materials was prepared during the project. Furthermore, samples of six different fish species obtained from a local market (e.g. alosa, engraulis encrasicolus, mullus barbatus, belone, merlangius merlangus, dicentrarchus labrax) were studied to identify the natural level of elements. Among these samples, dicentrarchus labrax (seabass) was selected and approximately 10 kilograms of it was purchased, processed and bottled. 85 bottles have been filled with 10 g of processed fish material. Between unit homogeneity test was carried out for the elements As, Cu, Fe, Hg, Se and Zn and the results were evaluated according to the requirements of ISO Guide 35. Short term stability studies were carried out with the simulation of transport conditions in the laboratory, considering environmental conditions that may occur during shipment to the end users and storage conditions and carried out by using an isochronous design. All the participating NMIs/DIs performed the analysis on a set of elements (depending on their instrument capabilities) in the two reference materials and sent the results to LNE, which collected and treated the data.

Another part of the work was dedicated to providing a demonstration on the services that NMIs/DIs can provide to disseminate metrological traceability. This was done via the organisation of a Proficiency testing for field laboratories. IAPR prepared the material, i.e. a tuna fish enriched with the elements relevant for the project. The project partners circulated the invitation to the routine laboratories in their respective countries. 45 laboratories (mainly from Bulgaria, Romania, Serbia, Tunisia and Greece) participated in the PT. the project partners provided their results applying the ID-ICPMS procedure. IAPR calculated a consensus value from the laboratories results and a reference value from the NMIs/DIs results. The results from the field laboratories were compared with the results from project partners. The final report (SCHEMA 62 08 Report), with the assessment of laboratories' performance, was issued by IAPR.

Objective 3 was achieved, since the NMIs/DIs were able to implement in their own institutes and autonomously the ID-ICPMS procedure. The results have shown that most NMIs have improved their measurement capabilities due to the training provided, particularly in analysing the element concentration ranges suitable for addressing the WFD Directive 2000/60/EC. During this exercise, there has been a knowledge transfer between the most experienced NMIs and the emerging NMIs/DIs. Difficulties encountered by the less experienced NMIs/DIs have been addressed by providing a better understanding on the source of their discrepancies and how best to overcome the most critical steps of analysis. Moreover, the PT organised was a case study to show how the measurement capabilities of the NMIs can be used to provide regular services for field laboratories.

To validate the developed methods by participation in suitable international comparisons and hence to underpin the development of appropriate CMCs for submission to the BIPM Key Comparison Database. (Objective 4)

During the project, no EURAMET or CCQM key comparison was organised for food or environmental matrices. Therefore, it was not possible for the project partners to participate in a comparison able to underpin CMC submission. However, the comparison conducted on the TUBITAK reference materials showed that the emerging NMIs/DIs have acquired the necessary measurement capabilities.

Although this objective was partially met, the project partners will continue to pursue this beyond the lifetime of the project. A suitable key comparison has already been identified within the Inorganic Analysis Working Group of CCQM, the CCQM-K158 elements in rice. For pH, BIM has registered to participate in CCQM-K19.2018 key comparison that focuses on pH determination of borate buffer solution, in order to validate the secondary cell that was developed during the project.

To develop individual strategies for the long-term operation of the capacity developed (Objective 5).

This was done by sharing the LNE experience in two national networks in France for both air and water quality monitoring (Central Laboratory for Air Quality monitoring – LCSQA and Reference National Laboratory for Aquatic Media Monitoring – AQUAREF), in which LNE is member. These networks gather expert national laboratories in a way that each of them brings its complementary expertise within the consortia. Among the aims, ensuring the quality of the information produced by the national system via standardisation, technical guides, audits, as well as developing rules for measurement, sampling and analysis in order to foster the production of reliable data for monitoring programmes, are those where LNE plays his main role. LNE organised a workshop for the project partners in order to initiate the reflection in the respective countries on the implementation of similar infrastructures based upon the individual national needs.

BIM, BRLM, IAPR and INRAP have also consulted their national stakeholders (such as environmental agencies, accreditation bodies, proficiency testing providers, to define a strategy able to address the national needs). As a result of the consultation, INRAP have started preparing for accreditation according to ISO 17034:2016 by developing capabilities in the production of calibration solutions (Hg) with the improved method development during the training and knowledge acquired during this project.

In conclusion, this objective has been achieved since the long-term strategies have been developed, with indicators that can be followed in the next years to benchmark the progress.

5 Impact

The project has produced 3 peer-reviewed publications, 8 training courses (6 internal, 2 external), 7 oral presentations and 3 posters; which were presented at International and European conferences. The project's results have been disseminated further through the organisation of a proficiency testing scheme, the contribution to the certification of 2 reference materials, the organisation of 2 stakeholder surveys. In addition, the results of the project have been presented to 2 sub-committees of the EURAMET TC-MC and another standardisation committee. During the lifetime of the project regular progress updates announced on the project website and circulated in newsletters on the NMIs websites.

Impact on industrial and other user communities

The reference values provisioned for proficiency testing schemes and reference materials were key project outputs which will directly benefit field laboratories. The production of reference samples with assigned reference values using a primary method of measurement, along with pH secondary reference materials in the participating countries, will help reduce the cost of purchasing imported reference materials for calibration as well as the costs of participation in PT schemes for competence demonstration abroad. During the project, a case study on a PT scheme was organised by IAPR. The materials and the samples were prepared and dispatched to the participating laboratories for analysis. The partners of the project assigned independent reference values obtained by IDMS methodology, as developed during the project. This led to more precise and reliable evaluation since the accuracy of the individual results obtained by the laboratories was better than what could have been achieved when comparing with a consensus value.

Furthermore, the less experienced NMIs/DIs have developed individual roadmaps for national strategies to promote long-term uptake of the developed capacities, based on meetings with their main stakeholders and surveys; that were organised by the project partners; to collate and prioritise national needs. This was an important output of the project which will also benefit accreditation bodies, since it provided them with the

necessary metrology tools to establish national traceability chains, i.e. reference methods, reference materials and proficiency testing schemes.

Impact on the metrology and scientific communities

The project established reliable capabilities for traceable measurements in chemistry (in particular for elemental inorganic analysis and pH) which created significant impact within the metrology community. Based on the measurement methods developed and validated during the project, the less experienced NMIs/DIs have enhanced specific procedures within their internal quality system. Thus, ensuring easy and effective transfer of knowledge acquired during the project, to other operators within the NIMs/DIs. To further support these efforts after the project has ended, the NMIs/DIs involved have also identified relevant CCQM key comparisons which will be used to validate the ID-ICPMS procedures and the secondary pH system developed within the project.

It is anticipated that the project partners will be able to adapt the measurement procedures developed in the project, to different samples of a similar complexity. Overall, the project has supported emerging NMIs/DIs of the countries involved through the knowledge sharing activities undertaken, which has led to improved capabilities and exposure to delivering research projects (i.e. access to research funding, creation of research consortia, writing of scientific papers). This will enable emerging NMIs/DIs to participate in more future research programmes of EURAMET and other EU research initiatives.

Impact on relevant standards

The project has encouraged active participation in key European chemistry related committees such as the EURAMET TC MC, as well as knowledge transfer and exchange with international metrology in chemistry community such as BIPM CCQM. A presentation was given at the EURAMET TCMC meetings on the elemental analysis activities and another presentation on the secondary pH activities. BIM also presented the project results to the Bulgarian standardisation committee TC 28/ Metrology. In addition, the project partners regularly informed technical committees about the results of this project and endeavour to ensure they are incorporated in any futures updates to the relevant standards and guidelines beyond the lifetime of the project.

Longer-term economic, social and environmental impacts

Each emerging NMI/DI has started to develop a strategy for the implementation of the acquired capabilities in national traceability infrastructures. These national traceability infrastructures will include relevant national representatives in the field of chemical analyses for environmental monitoring and food safety. Collaborations will be established with the national accreditation bodies, environmental agencies and academic laboratories. Less experienced NMIs/DIs have launched discussions in their countries to collect and prioritize the needs of their internal stakeholders and end-users.

The example of two French networks for air and water quality monitoring (Central Laboratory for Air Quality monitoring – LCSQA; and Reference National Laboratory for Aquatic Media Monitoring – AQUAREF) has been illustrated with the aim of adapting the approach to the specific needs of each participant's country. These networks gather expert national laboratories in a way that each of them brings its complementary expertise within the consortia. One of the aims is ensuring the quality of the information produced by the national system via standardisation, technical guides, audits, as well as developing rules for measurement, sampling and analysis in order to foster the production of reliable data for monitoring programmes, are those where the NMI plays its main role. The impact of such collaborations will therefore be the enhancement of the quality of measurements performed by field laboratories, though the provision of reference values for materials and Proficiency testing schemes, tools for method validation and uncertainty evaluation as well as support for accreditation plans. The wider impact of the project will be the acquisition by emerging NMIs/DIs of the required knowledge and practice in research projects allowing them to rapidly adapt their measurement capabilities to emerging needs and new analyte/matrix combinations. Moreover, the growing participation of the NMIs/DIs in future research programmes of EURAMET and other EU research programmes will contribute to strengthen the link with the scientific community, bringing to an improved awareness of the scientific community about the need for coherent and quality data.

6 List of publications

1. "*Recent progress in chemical measuring capabilities in INM as a result of EMRP/EMPIR Programme*", Mirella Buzoianu, Mihail Radu, George Victor Ionescu, published in *19th International Congress of Metrology, 20004 (2019)*, https://doi.org/10.1051/metrology/201920004
2. "*Work at the INM to Develop Measurement Capabilities to Assign Reference Values in Proficiency Testing Schemes*", M.Buzoianu, published in Proceedings of *PT CONF 2019,* http://www.pt-conf.org/2019/wp-content/uploads/2019/09/Proceedings-PT-Conf-2019.pdf