BIPM Capacity Building & Knowledge Transfer Programme

2024 BIPM - TÜBİTAK UME Project Placement

REPORT

Project Name	Production and characterization of a reference material in wastewater
Description	This project focuses on training in the production and characterization of wastewater reference materials, as well as the development of proficiency testing schemes in line with ISO/IEC 17043. The program emphasizes methodologies for produce reference materials, operating specialized equipment, applying good laboratory practices, and conducting homogeneity and stability assessments, all in compliance with the ISO 17034 standard.
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Motivation & Introduction

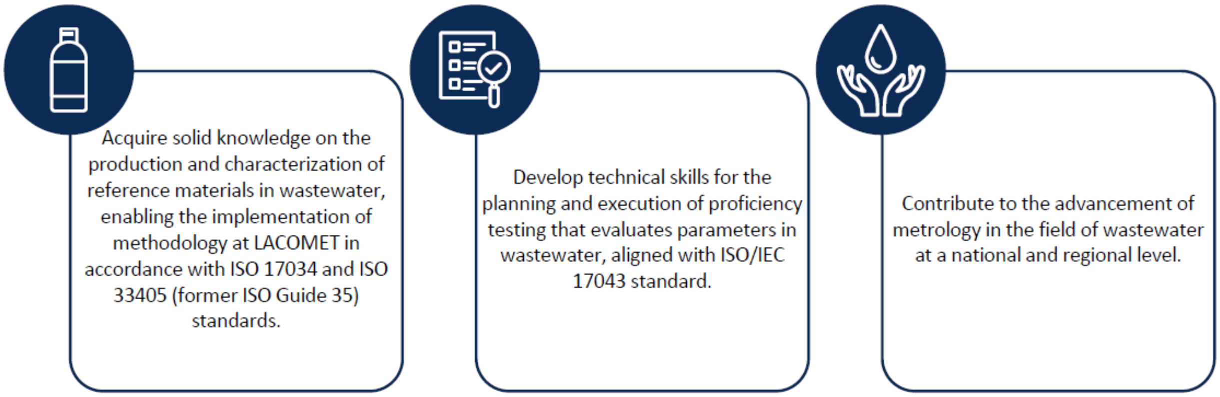
Ensuring the availability and sustainable management of water and sanitation is crucial for achieving the Sustainable Development Goals outlined by the United Nations. Within this framework, the proper management of sanitation, including the treatment of black and industrial waters, is essential for the well-being of communities. With approximately 3.5 million people lacking access to adequate sanitation facilities, it is imperative to invest in robust infrastructure, particularly in the field of metrology, to address this pressing need.[1]

In this context, the acquisition of reliable results in physicochemical analysis laboratories to determine contaminants in wastewater requires internal and external controls, specifically the use of reference materials. These reference materials are essential for verifying and validating analytical methods and also ensuring the quality of measurements conducted by environmental laboratories. In Costa Rica, Lacomet plays a crucial role as a National Institute of Metrology that provide reference materials for national needs. Currently, we are finalizing the production and certification of the first reference material in drinking water for metal quantification, a significant achievement that will ensure the reliability of measurements in testing laboratories.

However, clients' surveys have shown a growing demand for Lacomet to develop proficiency testing and reference materials in wastewater. In fact, 80 % of our clients are currently seeking a national provider that offers proficiency testing and reference materials covering parameters in both drinking water and wastewater, including major and trace elements, pH, electrolytic conductivity, biochemical oxygen demand (BOD), chemical oxygen demand (COD), among others.[2]

Therefore, our vision is to initiate a technical infrastructure that allows us to produce and characterize a specific reference material for wastewater, thus addressing a critical need in our country and strengthening confidence in measurements conducted by our clients. Hence, the knowledge transfer facilitated by this project holds significant potential to drive both national and international metrological advancements. Such progress is pivotal for fostering sustainable development within our country and the broader Central American region.

The main objectives of the project are:



Research

As part of the activities for the development of the project, an initial training session was conducted on key topics related to reference materials (RMs). The main stages of the production process were thoroughly discussed, including the required infrastructure to equip a laboratory specializing in RM production. Particular attention was given to the processes of homogeneity, stability, and characterization testing, primarily in collaboration with the Inorganic Chemistry Laboratory of TÜBİTAK UME, as the focus was on developing a reference material for wastewater analysis.

Simultaneously, a comprehensive methodology was applied to proficiency testing (PT). The entire process was addressed, according with the ISO/IEC 17043[3] standard, beginning with identifying customer needs and progressing to the delivery of results. Key steps included offering proficiency tests (via TÜBİTAK UME's platform), participant registration, protocol development, forming the working committee, producing and shipping test items, collecting results, evaluating participant performance, and preparing the final report. A practical exercise was conducted for a PT focused on pH and conductivity measurements in wastewater.

In the context of the wastewater reference material, important details about its production were discussed from the theoretical perspective, using the *UME CRM 1204 Elements in wastewater* certificate[4] and an explanation provided by UME's metrologists. The manufacturing process was analyzed in detail, highlighting raw material acquisition, acid treatment, and filtration techniques. Methodologies for homogeneity and stability testing were reviewed, with a focus on statistical approaches aligned with ISO 33405[5]. The characterization stage was examined, emphasizing two approaches: primary measurement methods and the use of two or more independent reference methods implemented by qualified laboratories. Detailed information on the UME CRM 1204 is accessible via its official certificate.

Practical training to observe the manufacturing process for UME CRM 1204 was not possible due to the absence of a production schedule during the internship period. However, participation in the production of other reference materials provided valuable insights into good manufacturing practices and real-world case studies. These included homogeneity and stability studies for various RMs, which are detailed in subsequent sections of this report.

Additional training activities were conducted to deepen knowledge on RM production and laboratory analytical capabilities. These included:

- Hands-on training on the Mettler Toledo V305 Karl Fischer VE Motion Autosampler.

- Participation in the Eurachem/CITAC webinar on the production of qualitative reference materials.
- Training on the technical requirements of ISO 17034, focusing on the competence of RM producers.

Lastly, the internship included an in-person seminar organized by the BIPM. The seminar covered critical international aspects of metrology, such as participation in the CIPM MRA mechanisms, interlaboratory comparisons, quality management systems, calibration and measurement capabilities (CMC), peer review processes for CMCs, and ensuring metrological traceability.

ACTIVITIES CONDUCTED DURING THE INTERNSHIP

1. **Familiarization with the Reference Materials Laboratory and Production Stages**

A comprehensive tour of the Reference Materials Laboratory was conducted to provide an in-depth understanding of its operations. During the visit, each equipment was thoroughly explained, including its function and role within the reference materials (RM) production process. The stages of RM production (Figure 1) were outlined, highlighting the specific equipment used at each stage. This hands-on introduction facilitated a clearer understanding of the laboratory's workflow and its alignment with best practices for RM production.

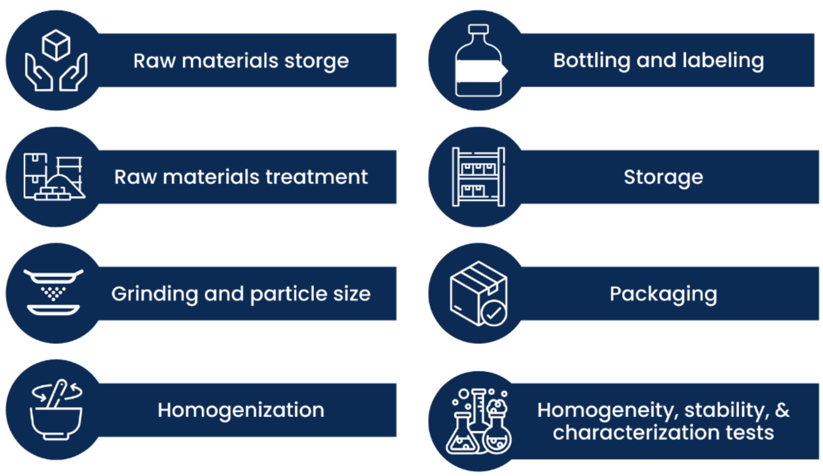


Figure 1. Main stages of the reference materials production process.

The production process for reference materials involves several critical stages, each requiring specialized equipment to ensure quality and reliability. Below is a description of these stages and the equipment used in each:

- **Raw materials storage:** The process begins with the acquisition and secure storage of raw materials under controlled conditions to preserve their properties. The raw materials are stored in specially designed cold rooms that protect them against heat, light and contamination. These rooms are equipped with automated systems that continuously monitor environmental parameters such as temperature and humidity, generating alarms if deviations are detected. For this stage, storage rooms maintained at -20 °C and 4 °C are used to ensure proper material preservation.

- **Raw material treatment:** At this stage, raw materials are conditioned according to their specific characteristics. In many cases, for materials such as food, water removal is necessary to improve stability. This is achieved using ovens, as well as freeze-dryers in two scales: a pilot-scale and a production-scale.

- **Grinding and particle size analysis:** Grinding is essential for solid materials to achieve the appropriate particle size, which contributes to homogeneity, physical and chemical stability, and representativeness of the material in laboratories. This stage employs specialized mills, including cryogenic, roller, variable-speed rotary, jaw crushers, disk mills, planetary ball mills, mortar grinders, and universal cutting mills. Additionally, a particle size analyzer equipped with laser diffraction and an air jet sieve are used alongside a vibratory sieve to analyze and ensure uniformity.

- **Homogenization:** Homogenization ensures that any portion of the material is representative of the entire batch, a critical requirement for consistent and reliable analytical results. For this purpose, V-type mixers, three-dimensional mixers with different capacities, high-speed homogenizers and vacuum mixers are used to ensure a uniform blend.

- **Filling and labeling:** Filling and labeling are carried out under controlled conditions to prevent contamination and ensure traceability. In line with ISO 33401[6], labels include essential information, such as unique identifier number, name of the material, unit number (to trace the filling order) and recommended storage conditions. This stage uses automatic machines for liquid filling, capping, and labeling, as well as semi-automatic systems for viscous liquids with heating and mixing capabilities. Additional equipment includes ampoule filling and labeling machines, sealing machines, vacuum packaging machine.

- **Storage of RM:** Finished reference materials are stored under specific temperature, humidity, and protection conditions to maintain their stability throughout their shelf life. Automated monitoring systems ensure environmental conditions are controlled. Storage equipment includes cold rooms, freezers set at -70 °C and -40 °C and refrigerators maintained at 4 °C.

- **Packaging:** Packaging ensures that reference materials reach their destination in optimal conditions. Primary packaging is carefully selected based on the characteristics of the material to protect its integrity, while secondary packaging provides additional protection during transportation. The laboratory has a dedicated room for the packaging process, equipped with large worktables, various packing materials, and tools necessary to ensure proper handling and secure packaging.

- **Homogeneity, stability, or characterization testing:** These tests ensure the quality and reliability of reference materials, ensuring uniformity and stability over time. The tests are conducted in collaboration with specialized laboratories in inorganic chemistry, organic chemistry, electrochemistry, gas, and bioanalysis.

The Reference Materials Laboratory is equipped with infrastructure designed to support each stage of the production process. Dedicated areas ensure optimal conditions for raw material storage, treatment, grinding, homogenization, bottling, labeling, and storage of final products. Figure 2 provides an overview of this infrastructure, highlighting key areas and equipment essential for producing high-quality reference materials.

Figure 2. Infrastructure of the Reference Materials Laboratory visited.

2. Overview of the Inorganic Chemistry Laboratory

The visit to the Inorganic Chemistry Laboratory offered an in-depth understanding of the processes and equipment utilized for sample preparation, treatment, and measurement within the field of inorganic analysis. Key areas and specialized equipment were observed, with a particular focus on the ICP-MS (Inductively Coupled Plasma Mass Spectrometry) technique, renowned for its precision and sensitivity in detecting and quantifying trace elements. Below is an overview of the key areas and techniques observed:

- **Sample Preparation and Treatment**: Proper sample preparation and treatment are essential for ensuring reliable results in chemical analyses. During the visit, the processes for cleaning, dissolution, and filtration of samples prior to analysis were observed. Equipment such as microwave ovens for sample digestion, filtration and decantation systems for separating impurities or undesired phases, and systems for water and acid purification were highlighted. The laboratory is also equipped with laminar flow hoods to maintain contamination-free conditions during sample handling.

- **Measurement Rooms and Clean Room**: The measurement rooms (figure 3), specifically designed to maintain controlled conditions of temperature, humidity, and cleanliness, are essential for achieving the precision and accuracy required in inorganic analyses. One of the primary techniques utilized in this area is ICP-MS (Inductively Coupled Plasma Mass Spectrometry). This highly sensitive and precise method detects metals and trace elements in samples, offering the capability to perform multielement analysis and quantify inorganic elements at trace levels. During the internship, it was possible to work on the measurement of trace metals in acids used for the extraction of analytes, as well as in a candidate reference material for seawater. These activities provided hands-on experience with the analytical techniques and processes involved in detecting and quantifying trace elements in complex matrices.

  The clean room, another vital facility, provides a strictly controlled environment to prevent external contamination of samples during sample preparation and analysis. Equipped with specialized tools and adhering to rigorous protocols, this space ensures the integrity and reliability of measurements conducted within.

Figure 3. Infrastructure of the Inorganic Chemistry Laboratory visited.

3. Practical Work on the Production and Testing of Reference Materials (RMs)

As part of the training, practical sessions were conducted to apply theoretical knowledge to the production and testing of reference materials (RMs). These sessions included work on homogeneity and stability studies for various RMs. The materials covered in this work included pure ethanol for the production of ethanol CRM in water, aflatoxins in hazelnuts, fatty acid composition in olive oil, and a rare earth candidate RM in soil. The tasks performed for each material are described below:

- **Primary standard ethanol bottling:** Participation in bottling a primary standard of pure ethanol was conducted using the Ampulmatic-10 vial filling and sealing machine (figure 4). This ethanol, traceable to the International System of Units (SI), was previously characterized using techniques such as q-NMR (Quantitative Nuclear Magnetic Resonance Spectroscpy) and its purity was determined. This primary standard is used for the production of UME CRM 1320 (Ethanol in Water), commonly used to calibrate breath simulators.

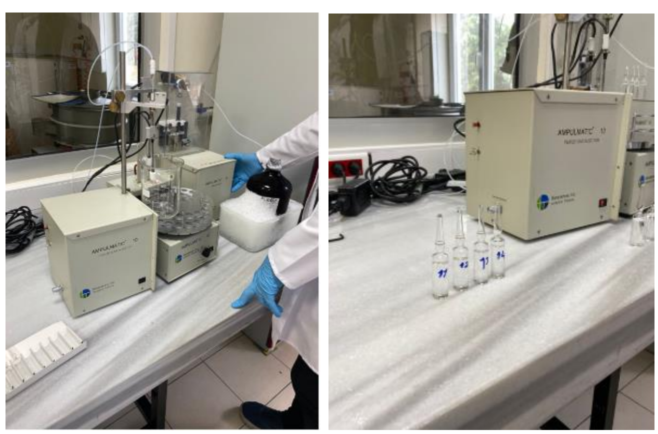


Figure 4. Bottling process of a primary standard of pure ethanol.

- **Aflatoxin measurement for stability studies of the CRM:** Measurements of aflatoxins were performed using the HPLC-FLD method (High-Performance Liquid Chromatography with Fluorescence Detection). This task provided practical insights into the analytical technique, as well as the processes for sampling, storage, and conducting long-term stability studies, critical to ensuring the integrity of the CRM over time.

- **Production of the candidate UME CRM 1335 Fatty acid composition in olive oil:** This project involved working with treated and filtered olive oil (free from additives and antioxidants). The oil was divided into 2 mL portions and bottled in amber vials using the Ampulmatic-10 vial filling and sealing machine (figure 5). During this process, compliance with ISO 17034[7] requirements was emphasized, covering documentation, stability and homogeneity studies, material characterization, and the statistical methodologies necessary for sampling studies. Additionally, subcontracting requirements were reviewed for the analysis to ensure that the production process aligns with international quality standards.

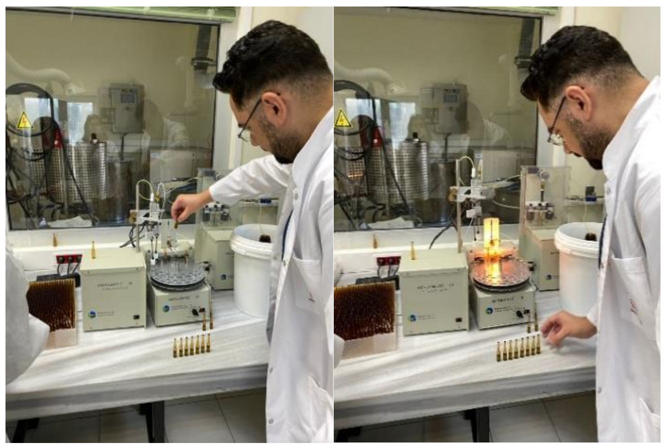


Figure 5. Bottling process of the UME CRM 1335.

- **Reference material candidate of rare earth elements in soil:** Homogenization of soil samples was carried out using a 3D mixer. These samples were subsequently bottled, sealed, and labeled to create a candidate reference material. The process underscored the importance of homogenization, adherence to good manufacturing practices, and safety protocols, including the proper use of personal protective equipment (PPE), as shown in figure 6.

Figure 6. Personal protective equipment used to produce a candidate RM of soil.

Conclusions and Future Work

The training activities made a significant contribution to achieving the project's objectives. Solid knowledge was acquired in the production and characterization of reference materials following ISO 17034 and ISO 33405. Technical skills were also developed for planning and executing proficiency testing, in compliance with ISO/IEC 17043. While the primary focus was on wastewater, participating in diverse RM production processes provided a comprehensive understanding of the procedures needed to ensure the quality and traceability of these materials. The training also enabled practical application of stability and homogeneity studies for RMs, aligned with ISO 17034 requirements.

For future work, knowledge transfer activities will be prioritized to benefit the staff of Lacomet's Chemical Metrology Department and, when feasible, extended to regional teams. These efforts will focus on RM production in environmental areas like wastewater and soils, with potential expansion to other sectors, such as food.

Additionally, Lacomet aims to strengthen its technical capabilities to implement methodologies for producing a CRM in wastewater. The acquired knowledge will support the planning and development of the first national proficiency testing scheme for wastewater parameter evaluation, in compliance with ISO/IEC 17043. This initiative will improve infrastructure and enhance the quality of environmental metrology services at both national and regional levels.

Acknowledgements

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I extend my sincere thanks to the BIPM for the opportunity to contribute to a project that will advance metrology in my country and region, and to my team at the Chemical Metrology Department of Lacomet for their continuous support, which enabled me to fully engage in this internship.

Finally, I thank everyone who enriched this experience with their time and expertise, and for the chance to immerse myself in Türkiye's vibrant culture. This country will always hold a special place in my heart.

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