

Organization Name: TUBITAK National Metrology Institute, TUBITAK UME

JCTLM Member status: National and Regional Member

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Period covered: 2024 – 2025

1. Major achievement(s) in support of standardization in laboratory medicine

➤ The production of reference materials:

The following reference materials are on sale from TUBITAK UME web site “https://rm.ume.tubitak.gov.tr/urun_listesi_en.aspx”.

- UME CRM 1301: Chloramphenicol
- UME CRM 1308: 25-Hydroxy Vitamin D2 and 25-Hydroxy Vitamin D3 in lyophilized serum
- UME CRM 1314: Amino Acids in Plasma, Lyophilized
- UME CRM 1315: Organic Acids in Urine, Lyophilized
- UME RM 2019: SARS-CoV-2 RNA
- UME RM 2020: SARS-CoV-2 RNA Lyophilized
- UME CRM 3022: Synthetic DNA fragments (80 bp and 240 bp)
- UME CRM 3024: Synthetic DNA fragments (80 bp, 120 bp, 160 bp and 240 bp)
- UME CRM 1008: C-Reactive Protein (CRP)

➤ Development of reference measurement methods

- Sensor Production for Different Virus Antigens or Antibody Proteins.
In this project, electrochemical biosensing platform for yellow fever NS1 antibody was developed, and real sample application in human serum samples was performed. The project was completed in August 2024.
- Primary measurement methods were developed for quantification of DNA methylation.
- Primary measurement methods were developed for quantification of TP53 R273C
- Primary measurement methods were developed for quantification of IDH2 R172K
- Reference measurement method was developed for quantification of Cardiac Troponin I in human serum.
- Reference measurement method was developed for quantification of GFAP in human serum.
- Reference measurement method was developed for quantification of GFAP in CSF.

- Primary measurement methods were developed for quantification amount-of-substance fraction of [HbA1c/(HbA1c+HbA0)] in Human Hemolysate.
- Primary measurement methods were developed for quantification of SARS-CoV-2 Monoclonal Antibody in Solution
- Primary measurement method was developed for quantification of mass fraction of Parathyroid hormone 1-84 in aqueous solution.
- Primary measurement method was developed for the quantification of total hemoglobin in blood.

➤ **Projects in the field of Laboratory Medicine:**

EURAMET projects:

Chemistry Group Laboratories have been collaborating in health related projects and contribute to the development of new measurements methods and production of new certified reference materials in Laboratory Medicine. TUBITAK UME Laboratories actively participated in the following EURAMET projects in the period of 2024-2025:

- JRP-h01- GenomeMET: Metrology for genomic profiling to support early cancer detection and precision medicine, 2023-2025
- JRP-h06- NEuroBioStand: Standardisation of measurements of neurodegenerative disease biomarkers, 2023-2025
- JNP: 18NET02- TraceLabMed: Support for a European Metrology Network on Traceability in Laboratory Medicine, 2019-2024
- JRP-f11 – ProMET: Fundamental protein metrology to support the definition of measurands, analytical targets, and their associated measurement uncertainty, 2024-2026
- JRP-i19 – COMET: Manufacturing of commutable calibrators and quality control materials for standardization and post-market surveillance of IVD tests, 2024-2026
- 22HLT04 - Metrology for Innovative Nanotherapeutics (MetrINo)

The following EURAMET project proposals were supported and they will start in 2026.

National projects:

- TUBITAK 223N176 2507 - Bilateral Cooperation Program with the German Research Council (DFG): TUBITAK UME- PTB GERMANY "The Impact of Biological Variables on Measurement of Cardiac Troponin in a Clinical Context". 2024-2027.
- TUBITAK 2218- National Post-Doc Scholarship Program "The production of reference material for cell-free DNA (cfDNA) measurements: The standardization of recovery efficiency of cfDNA isolation which is used as a biomarker in the diagnosis and treatment of diseases". 2022-2024.
- Development of Reference Materials to Enable SI-Traceable DNA Methylation Measurements in Pre-Analytical Workflows (2025-2027)

➤ **The establishment of calibration (reference) measurement services.**

The following reference measurement services were offered in 2023 and listed under TUBITAK UME measurement services (Table 1).

Table 1. TUBITAK UME primary level measurement services offered in 2023.

Code	Measurement Service Name
G3OK-4600	Determination of 3-epi-25-Hydroxyvitamin D3 in Serum
G3OK-4610	Determination of Vitamin 25-OH D2
G3OK-4620	Determination of Vitamin 25-OH D3
G3OK-5600	Determination of Cholesterol in Serum
G3OK-5700	Determination of Glucose in Serum
G3OK-5800	Determination of Creatinine in Serum
G3OK-6900	Determination of Urea and Uric Acid in Biological Matrix
G3OK-10800	Determination of Amino acid in Plasma
G3IK-3301	Determination of As in Biological Materials
G3IK-3302	Determination of Pb in Biological Materials
G3IK-3303	Determination of Cr in Biological Materials
G3IK-3306	Determination of K in Human Serum
G3IK-3307	Determination of Ca in Human Serum
G3IK-3308	Determination of Mg in Human Serum
G3IK-3309	Determination of Fe in Human Serum
G3IK-3310	Determination of Selenomethionine in Human Serum
G3IK-3311	Determination of Cl in Serum
G3IK-3312	Determination of Cu in Serum
G3IK-3313	Determination of Na in Serum
G3IK-3314	Determination of P in Serum
G3IK-3315	Determination of Se in Serum
G3IK-3320	Determination of Hg in Biological Materials
G3IK-3321	Determination of Ni in Biological Materials
G3IK-3322	Determination of P in Biological Materials
G3IK-3323	Determination of Zn in Biological Materials
G3BA-2100	Determination of Relative Gene Expression Levels - Real Time PCR
G3BA-3100	Relative quantification of DNA methylation levels - RT PCR Melting Analysis
G3BA-4100	Absolute quantification of Plasmid DNA - Digital PCR instrument
G3BA-4210	Relative quantification of oncogenes (KRAS-G12D) - Digital PCR Instrument
G3BA-4220	Relative quantification of oncogenes (BRAF-V600E) - Digital PCR Instrument
G3BA-4230	Relative quantification of oncogenes (EGFR-?746-750) - Digital PCR Instrument
G3BA-4310	Absolute quantification of HIV virus - Digital PCR Instrument
G3BA-4320	Absolute quantification of SARS-CoV-2 virus - Digital PCR Instrument
G3BA-5100	Amino Acid Analysis For Pure Protein/Peptide - LC-ID-MS
G3BA-5300	Quantification of C-peptide/angiotensin - LC-ID-MS(n)
G3BA-5400	Quantification of Protein Concentration - HPLC
G3BA-5500	Quantification of Protein Concentration - ELISA
G3BA-5600	Quantification of Protein Concentration - PICAA
G3BA-5700	Relative Quantification of HbA1c Protein - HPLC
G3BA-5800	Relative Quantification of HbA1c Protein- LC-ID-MS
G3BA-5900	Determination of Amylase Enzyme Activity
G3BA-6000	Complex Proteome Analysis - Relative Quantification (LFQ-TMT)
G3BA-6100	Identification of Post Translational Modifications
G3BA-6200	Peptide Fragmentation (HCD)
G3BA-6300	LC-MS/MS Method based protein identification

➤ **Outline of the measurement area(s)/measurands covered:**

CCQM Measurement Comparison Studies

TUBITAK UME Chemistry Group Laboratories have participated to several international measurement comparison studies related to the field of Laboratory Medicine between 2024 and 2025 (Table 2). More resources will be devoted to the development of new reference measurement methods in this field.

Table 2. CCQM international measurement comparison studies organized and participated by TUBITAK UME between 2024 and 2025.

Comparison #	Comparison Name
CCQM-K115c	Peptide Purity - Synthetic Glycated Hexapeptide of HbA1c (GE)
CCQM-K115.2018	Peptide Purity - Synthetic Hexapeptide of HbA0 (VE)
CCQM-K148.b	Mass fraction of oxytetracycline in oxytetracycline hydrochloride material
CCQM-K176	Breast Cancer Biomarker HER2 Copy Number Variation (CNV) Measurement
CCQM-K179	Mass fraction of oxytetracycline hydrochloride salt
CCQM-K180	Metranidazole in porcine muscle
CCQM-K181	SARS-CoV-2 RNA Copy number quantification
CCQM- P94.3:	Quantitative analysis of DNA methylation of a defined human genomic DNA region*
CCQM-P216	Quantification of SARS-CoV-2 Monoclonal Antibody in Solution
CCQM-P199	Measurement of HIV-1 RNA Copy Number Concentration
CCQM-P199.b	SARS-CoV-2 RNA Copy Number Quantification
CCQM-P219	Determination of the Amount-of-Substance Fraction of [HbA1c/(HbA1c+HbA0)] in Human Hemolysate
CCQM-P232	Fire Drill Influenza RNA copy number quantification
CCQM-K186	Quantification of total hemoglobin in blood
CCQM-K115.d	Mass fraction of Parathyroid hormone 1-84 in aqueous solution
CCQM-K189	Measurement of Single Nucleotide Variation (SNV) and Small Deletion in Cancer Biomarker of PIK3CA and EGFR
CCQM-P231	The species specific meat composition determination of DNA extracted from meat
CCQM-K148.c	Mass fraction of digitoxin (DGT) in a solid organic material
CCQM-K192	17β-Estradiol in Human Serum

➤ **Listing of the relevant technical/scientific publications:**

- Dong, L., Wang, X., Devonshire, A., Huggett, J., Ellison, S., Gonzalez, A. F., ... Yalçinkaya B. & Akgoz, M. (2024). CCQM-K176 breast cancer biomarker HER2 copy number variation (CNV) measurement. *Metrologia*, 61(1A), 08017.
- Tiryaki,S. “Development of a locus-specific HRM assay for DNA methylation analysis of the SHANK3 gene” DOI:10.1101/2025.09.03.673955

- Aytan B, Oztug M, Ozturk HU, Kazan D, Ari S. Efficient Cloning and Expression of IsPETase in the E. coli SHuffle Cells; Activity Analysis using HR-LC/MS. *Appl Biochem Microbiol* 2025;61:302–11. <https://doi.org/10.1134/S0003683824605353/FIGURES/5>
- Öztuğ M, Kiliç E, Öztuğ Durer ZA, Baloğlu E. Proteomic investigation of acute and chronic hypoxia/reoxygenation responsive proteins and pathways in H9C2 cardiomyoblasts. *Turkish J Biol* 2024;48:192–202. <https://doi.org/10.55730/1300-0152.2695>.
- Ascioglu M, Swart C, Saban E, Yurek E, Karaguler NG, Oztug M. Comparative evaluation of peptide vs. protein-based calibration for quantification of cardiac troponin I using ID-LC-MS/MS. *Clin Chem Lab Med* 2025;63:1016–30. <https://doi.org/10.1515/CCLM-2024-0999/MACHINEREADABLECITATION/RIS>.
- Uçar B, Öztuğ M, Tör M, Çelik-Öztürk N, Vardar F, Cevher-Keskin B. Comparative Analysis of Protein Extraction Protocols for Olive Leaf Proteomics: Insights into Differential Protein Abundance and Isoelectric Point Distribution. *ACS Agric Sci Technol* 2025;5:739–49. https://doi.org/10.1021/ACSAGSCITECH.4C00642/ASSET/IMAGES/LARGE/AS4C00642_0009.JPEG.
- Oztug M. Bioactive Peptide Profiling in Collagen Hydrolysates: Comparative Analysis Using Targeted and Untargeted Liquid Chromatography–Tandem Mass Spectrometry Quantification. *Molecules* 2024;29. <https://doi.org/10.3390/molecules29112592>.
- Oztug M, Saban E, Ascioglu M, Isleyen A, Akgoz M. Development of UME CRM 1008: certified reference material for C-reactive protein. *Accredit Qual Assur* 2024;29:19–29. <https://doi.org/10.1007/s00769-023-01563-w>.
- Demircan Çeker D, Baysungur V, Evman S, Kolbaş İ, Gördebil A, Nalbantoğlu SM, Oztug M, Saban E, et al. LUNGBANK: a novel biorepository strategy tailored for comprehensive multiomics analysis and P-medicine applications in lung cancer. *Turkish J Biol* 2024;48:203–17. <https://doi.org/10.55730/1300-0152.2696>.
- Oztug M, Vatanserver B, Altin G, Akgoz M, Can SZ. An LC-MS/MS-based platform for the quantification of multiple amyloid beta peptides in surrogate cerebrospinal fluid. *J Mass Spectrom Adv Clin Lab* 2024;31:40–8. <https://doi.org/10.1016/j.jmsacl.2024.01.002>.
- Karaböce, B., Hamid, R., Saban, E., Sözeri, H., Danacı, E., Büyük, A.A., Durmuş, H., Dorosinskiy, L., Kızılbey, O., Bilecik, S., Yazgan, T., Hatipzade, R., Battal, H., Baş, A. Comparison of Disinfection of Phi6 Virus Bacteriophage on Fomites by Various Methods and a Prototype for IR Application. *Thermal Science and Engineering Progress*, 2025, 61, 103477. <https://doi.org/10.1016/j.tsep.2025.103477>
- Yalçinkaya B, Eskin Z. Optimizing qPCR Annealing Temperatures for Cancer-Related lncRNAs. *Clinical and Experimental Health Sciences*. June 2025;15(2):387-391. doi:10.33808/clinexphhealthsci.1596074
- Yalçinkaya, B., Sağlam, K. A., Terali, K., Tekin, E., Taslak, H., & Türkyılmaz, A. (2024). Biallelic Deletion of PEX26 Exon 4 in a Boy with Phenotypic Features of both Zellweger Syndrome and Infantile Refsum Disease. *Molecular Syndromology*, 15(5), 380-388.
- Taslak, H., Yalçinkaya, B., Eskin, Z., Aydoğan, H. Y., & Öztürk, O. (2025). The Role of Liposomal Delivery Systems in the Treatment of Triple Negative Breast Cancer. *Sakarya University Journal of Holistic Health*, 8(2), 99-112.

2. Planned activity(ies) in support of standardization in laboratory medicine

➤ R&D project(s) and/or programme(s)

TUBITAK UME Chemistry Group Laboratories collaborate with public and private institutions to develop measurement procedures in the field scientific metrology.

In Bioanalysis Laboratory, the levels of biological molecules such as bacterial or eukaryotic genomic DNA and genomic mutations are measured with digital PCR systems considered as reference measurement system. In case of new infectious diseases or other variants of SAR-CoV-2 emerges, new measurement methods and reference materials will be developed for measuring these viruses.

For quantitative measurement of DNA methylation, a new CCQM measurement comparison was organized in collaboration with KRISS under NAWG.

The measurements of small biological molecules such as amino acids, organic acids, hormones, lipids, antibiotics, pesticides and other metabolites are carried out by Organic Chemistry Laboratory which utilizes the quantification power of qNMR as a new reference measurement system in addition to the classical primary reference measurement methods.

Inorganic Chemistry Laboratory develops new measurement methods with the use of a new clean laboratory and new state-of-the-art instruments.

HbA1c proficiency testing (EurA1c) has been carried out by IFCC since 2016 and we will continue to contribute to this study in the following years.

After establishing measurement capabilities further, priority will be given to the preparation of more certified reference materials according to the needs of clinical laboratories in Turkey (Table 3).

Table 3. Certified Reference Materials Preparation Planning at TUBITAK UME, 2024-2025.

Date of Release	Description of CRM or RM
2026	HbA1c CRM
2024	C-Reactive Protein CRM
Planning	DNA methylation CRMs
Planning	Elements in serum (2026-2027)
Planning	Elements in whole blood (2026-2027)
Planning	Elements in urine (2026-2027)

➤ **EURAMET projects:**

The following EURAMET projects will be completed or continued as outlined in the project proposals and new measurement methods and/or new CRMs/RMs will be produced.

- JRP-f11 – ProMET: Fundamental protein metrology to support the definition of measurands, analytical targets, and their associated measurement uncertainty, 2024-2026
- JRP-i19 – COMET - Manufacturing of commutable calibrators and quality control materials for standardization and post-market surveillance of IVD tests, 2024-2026
- JRP-h01- GenomeMET: Metrology for genomic profiling to support early cancer detection and precision medicine, 2023-2025
- JRP-h06-NEuroBioStand - Standardisation of measurements of neurodegenerative disease biomarkers, 2023-2025
- 18NET02 TraceLabMed - Support for a European Metrology Network on Traceability in Laboratory Medicine, 2019-2024

➤ **CCQM Measurement Comparison Studies:**

TUBITAK UME Chemistry Group Laboratories have been planning to attend to the following CCQM measurement comparison studies (Table 4).

Table 4. CCQM international measurement comparison studies planned between 2024 and 2025.

Comparison #	Comparison Name
CCQM-K159	Free Amino Acids in Plasma
CCQM-K/P	Purity assessment of primary reference materials for Parathyroid Hormone
CCQM- K/P	Purity assessment of primary reference materials for Cyclosporine
CCQM- K/P	Purity assessment of primary reference materials for hCMV
CCQM-K186/P238	Quantification of Total Haemoglobin in Blood Key Comparison and Pilot Study on
CCQM-K196	Determination of the Amount-of-substance Fraction of [HbA1c/(HbA1c+HbA0)] in Human Hemolysate
CCQM-K/P	Human Serum Albumin
CCQM-K/P	Sirolimus in Blood

3. Promoting traceability in laboratory medicine

➤ Congress Presentations:

- Şanal Demirci, S.N., Tiryaki, S., Akgöz, M. “Development of Certified Reference Materials for Standardization of cfDNA Isolation in Liquid Biopsy” AMP 2025 Annual Meeting & Expo, Boston, USA
- Yılmaz, S., Ascioglu, M., Tinaz, B., & Oztug, M. (2025, July). Quantification of glial fibrillary acidic protein in serum using ID-LC-MS/MS. In *FEBS OPEN BIO* (Vol. 15, pp. 172-172). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.
- Tinaz, B., Ascioglu, M., Yılmaz, S., Usluer, G. D., & Oztug, M. (2025, July). Expression, purification, and characterization of recombinant glial fibrillary acidic protein (GFAP) for ID-LC-MS/MS quantification in cerebrospinal fluid. In *FEBS OPEN BIO* (Vol. 15, pp. 172-172). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.
- Ascioglu, M., Swart, C., Kuhfuß, D., Karaguler, N. G., & Oztug, M. (2025, July). A comparison of peptide and protein based calibration strategies for LC-MS/MS quantification of cardiac troponin I. In *FEBS OPEN BIO* (Vol. 15, pp. 171-172). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.
- Kilinc, E., E. Sagdilek, Z. A. Durer, F. Ozer, O. Gurel, F. S. Elbeyoglu, B. G. Irez, M. Oztug, and R. Ariens. "Impact of SARS-CoV-2 spike protein on hemostasis: insights from platelet aggregation, coagulation, and fibrin polymerization assays." In *FEBS OPEN BIO*, vol. 15, pp. 511-511. 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY, 2025.
- Eskin, Z., Yalçınkaya, B., Taslak, H. D., Öztürk, O., & Yılmaz Aydoğan, H., (2025). Investigation of lncRNA modulation by apigenin in breast cancer therapy. . 49th FEBS Congress (pp.128). İstanbul, Turkey
- Taslak, H., Yalcinkaya, B., Yilmaz-Aydogan, H., & Ozturk, O. (2025, July). Optimization of liposomal formulations for targeted therapy in breast cancer. In *FEBS OPEN BIO* (Vol. 15, pp. 206-206). 111 RIVER ST, HOBOKEN 07030-5774, NJ USA: WILEY.

4. Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems

➤ JCTLM Activities

TUBITAK UME become a member to JCTLM in 2012 and has actively participated to the JCTLM Members’ and Stakeholders’ Meetings since 2012. Biennial report was also submitted to JCTLM Executive Committee in 2023.

➤ CCQM Activities

As a member of CCQM, TUBITAK UME Chemistry Group scientists attended and actively contributed to OAWG, IAWG, NAWG, PAWG, CAWG, EAWG and SAWG meetings in 2024 and 2025.

Merve OZTUĞ is also a member of PAWG Focus Group 1 (SI Value Assignment of Purity) and PAWG Focus Group 2 (SI-traceable determination of peptides and proteins in complex matrices).

➤ EMN: TraceLabMed: European Metrology Network - Traceability in Laboratory Medicine, 2019 - 2024

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➤ **EurA1c: The European HbA1c Trial “EQA Program”**

In 2016, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Committee Education in the Use of Biomarkers in Diabetes (C-EUBD) started a proficiency testing program for standardization of HbA1c measurements (EurA1c) throughout Europe. TUBITAK UME has also attended to these proficiency tests in 2024 and 2025.

5. Open questions and suggestions to be addressed by JCTLM