Draft template for biennial activity report from JCTLM Member organizations

Organization: TUBITAK National Metrology Institute, TUBITAK UME

JCTLM Member status: National and Regional Member
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Period covered: 2018 – 2019

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

- **The production of certified reference materials:**

  - A certified reference material (CRM) preparation project that was supported by TUBITAK UME titled "25-Hydroxy Vitamin D2 and 25-Hydroxy Vitamin D3 in Lyophilized Serum" was completed and the CRM is on sale. The CRM is listed under JCTLM database for higher-order reference materials.

  - Project titled "Development and Production of Certified Reference Materials and Quality Control Materials for Newborn Screening and Measurements Routinely Performed by Clinical Biochemistry Labs for Amino Acids and Organic Acids" was financially supported by TUBITAK 1003 program. Zivak Technologies, a LC-MS based test and instrument producer company, was also an industrial partner in the project. The project has been completed and two different CRMs are on sale: UME CRM 1314 and UME CRM 1315 were certified for 32 amino acids in lyophilized plasma and 47 organic acids in lyophilized urine, respectively. These CRMs has been submitted for listing under JCTLM CRM database for higher-order reference materials.

  - HbA1c CRM project is expected to be completed in 2020 and the CRM will be on sale in 2021.

  - C-Reactive Protein CRM project has just started in 2018 and it is expected to be finished in 2021.

➢ **Development of reference measurement methods**

- **Mass fraction of amino acids in acidic aqueous solution.**
  Westwood, S., Josephs, R., Choteau, T., Daireaux, A., Wielgosz, R., Melanson, J., Thibeault, M., Meija, J., Quan, C., Li, H., Huang, T., Zhang, W., Song, D., Martos, G., Ohlendorf, R., Henrion, A., Kakoulides, E., Giannikopoulou, P., Alexopoulos , C., Yamazaki, T., **Goren, A.C., Gunduz, S., Un, I., Bilsel, G. Mass fraction assignment of Amino Acids in acidic aqueous solution (CCQM-K78.a), Metrologia , 56:1A, Technical Supplement. 2019, 08010**

- **Counting of cells.**
  Luisa Saraiva, Lili Wang, Martin Kammel, Andreas Kummrow, Eleanor Atkinson, Ji Youn Lee, Jana Höckner, Andreas Ruf, Andrea Engel, Yu-Zhong Zhang, Orla O'Shea, **Burhanettin Yalcinkaya, Muslum Akgoz,** Maria Paola Sassi, Carla Divieto, Tamara Lekishvili, Jonathan Campbell, Yingying Liu, Jing Wang, Richard Stebbings, Adolfas K. Gaigalas, Peter Rigsby, Jörg Neukammer and Sandrine Vessillier. **Comparison of Volumetric and Bead-Based Counting of CD34 Cells by Single Platform Flow Cytometry. Clinical Cytometry**, 2019, doi: 10.1002/cyto.b.21773

- **Mass fraction of folic acid in high purity material**
  Westwood, S., Josephs, R., Choteau, T., **Goren, A.C., Gunduz, S**., Yilmaz, H., **Un, I., Bilsel, G. Mass Fraction Assignment of Folic Acid in a High Purity Material, Metrologia,** 55, Technical Supplement, 2018, 08013

- **Digital PCR as a reference measurement procedure for DNA copy number quantification of KRAS mutation.**
  Alexandra S. Whale, Gerwyn M. Jones, Jernej Pavšič, Tanja Dreo, Nicholas Redshaw, **Sema Akyurek, M. Akgoz**, Carla Divieto, Maria Paola Sassi, Hua-Jun He, Kenneth D. Cole, Young-Kyung Bae, Liesbet Deprez, Philippe Corbisier, Sonia Garrigou, Valérie Taly, Raquel Larios, Simon Cowen, Denise M. O'Sullivan, Claire A. Bushell, Heidi Goenaga-Infante, Helen Parkes, Carole A. Foy, Alison J. Woolford, Jim F. Huggett, Alison S. Devonshire. **An assessment of digital PCR as a reference measurement procedure for DNA copy number quantification of point mutations to support advances in precision medicine. *Clinical Chemistry,*** 2018, 64, 9, 1296-1307. doi: 10.1373/clinchem.2017.285478

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

- **EMPIR projects:**

Chemistry Group Laboratories have been collaborating in health related EMPIR projects and contributes to the development of new measurements methods and production of new certified reference materials in Laboratory Medicine. Our laboratories were partners in the following EMPIR projects completed in the period of 2018-2019:

Completed projects:

- AntiMicroResist - Novel methods and materials for the detection, traceable monitoring and evaluation of antimicrobial resistance, 2016-2019.

- ReMiND - Role of metals and metal containing biomolecules in neurodegenerative diseases such as Alzheimer's disease, 2016-2019.

Ongoing projects:

Our laboratories are also collaborating in the following health related EMPIR projects:

- CardioMet - Improvement and metrological underpinning of quantitative diagnostic methods for biomarkers of coronary heart diseases, 2019 - 2022.

- JNP: TraceLabMed - Support for a European Metrology Network on Traceability in Laboratory Medicine, 2019 - 2024.

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

- ALCOREF - Development and certification of forensic alcohol reference materials for the law enforcement of drinking/driving regulation, 2017 - 2020.

- QUIERO - Quantitative MR-based imaging of physical biomarkers, 2019 - 2022.

- **Dual Collaboration Project:**

A dual collaboration project, "Korea-Turkey collaboration project on the development of an international standard system for the measurement of gene methylation" has been completed in 2018. A new measurement method for genomic DNA methylation measurement, which is a critical marker on the diagnosis of several diseases including cancer, will be suggested. The results of the project will be presented by Dr. Sema AKTUREK at JCTLM Members' and Stakeholders' meeting, on 2-3 December 2019, BIPM.

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

  The following reference measurement services were offered in 2019 and listed under TUBITAK UME services (Table 1).

Table 1. TUBITAK UME measurement services offered in 2019.

Code	Measurement Service Name
G3OK-4600	Determination of Vitamin 3-epi-25-Hydroxyvitamin D3
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
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-4100	Absolute quantification of Plasmid DNA - Digital PCR instrument
G3BA-4200	Relative quantification of oncogenes - Digital PCR Instrument
G3BA-5100	Amino Acid Analysis For Pure Protein/Peptide - LC-ID-MS
G3BA-5200	Protein Identification - Peptide Mass Fingerprinting Method, LC-MS/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-8100	Cell counting - Flow Cytometer instrument

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

- **CCQM and EURAMET Measurement Comparison Studies**
  TUBITAK UME Chemistry Group Laboratories have participated to several international measurement comparison studies in the field of Laboratory Medicine between 2018 and 2019 (Table 2). More resources will be devoted to the development of new reference measurement methods in this field.

Table 2. CCQM and EURAMET international measurement comparison studies participated by TUBITAK UME between 2018 and 2019.

Comparison #	**Comparison Name**
EURAMET 1185	Determination of Selenomethionine in Human Serum
CCQM-K107	Total Elements and Selenomethionine in Human Serum
CCQM-K139*	Elements in Human Serum
CCQM-P164	Mass fraction of human growth hormone in serum
CCQM-K151	Determination of the amount content of a purity-assessed recombinant protein in an aqueous calibration solution- Insulin
CCQM-K115b	Peptide purity - synthetic oxytocin (OXT)
CCQM-P184	Copy Number Concentration and Fractional Abundance of a Mutation (SNV or INDEL) Mixed with Wild-type DNA
CCQM-P199	Capability in low level detection/identification of specific (pathogen) sequence: Measurement of HIV-1 RNA copy number concentration
CCQM-K115c* CCQM-P55.2C*	Peptide purity - synthetic glycated hexapeptide of HbA1c (GE)
CCQM-K115.2018* CCQM-P55.2*	Peptide purity - synthetic hexapeptide of HbA0 (VE)

*In progress

- **Calibration and Measurement Capabilities:**
  By using its expertise and providing services in clinical measurements, TUBITAK UME Chemistry Group Laboratories applied for calibration and measurement capabilities (CMC) and qualified for several measurement capabilities (Table 3).

Table 3. TUBITAK UME Calibration and Measurement Capabilities gained between 2018 and 2019.

Measurement Service Sub-Category	**Matrix**	**Analyte or Component**
Biological fluids and materials	Blood serum	Sodium
Biological fluids and materials	Blood serum	Chlorine
Biological fluids and materials	Blood serum	Copper
Biological fluids and materials	Blood serum	Selenium
Biological fluids and materials	Blood serum	Phosphorus
Biological fluids and materials	Blood serum	Transferrin
Other	Pure DNA sequence in buffered matrix	Linearized plasmid DNA between 3 kbp and 6 kbp

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

- Ralf D Josephs, Gustavo Martos, Ming Li, Liqing Wu, Jeremy E Melanson, Milena Quaglia, Paulo J Beltrão, Désirée Prevoo-Franzsen, Amandine Boeuf, Vincent Delatour, **Merve Öztug,** André Henrion, Ji-Seon Jeong and Sang-Ryoul Park. **Establishment of measurement traceability for peptide and protein quantification through rigorous purity assessment, Metrologia**, 2019, 56, 4, 1-29

- Westwood, S., Josephs, R., Choteau, T., Daireaux, A., Wielgosz, R., Melanson, J., Thibeault, M., Meija, J., Quan, C., Li, H., Huang, T., Zhang, W., Song, D., Martos, G., Ohlendorf, R., Henrion, A., Kakoulides, E., Giannikopoulou, P., Alexopoulos , C., Yamazaki, T., **Goren, A.C., Gunduz, S., Un, I., Bilsel, G. Mass fraction assignment of Amino Acids in acidic aqueous solution (CCQM-K78.a), Metrologia , 56:1A, Technical Supplement. 2019, 08010**

- Abdurrahman Coşkun, Ahmet Tarik Baykal, **Merve Oztug**, Dilek Kazan, Ekrem Kaya, Remzi Emiroğlu, Sezai Yılmaz, Halit Z. Dundar, **Muslum Akgoz**, Ibrahim Berber, Hikmet Aktas, Gokhan Bilsel, Kubra Karaosmanoğlu, Banu Çetiner, Cansu Arslan, Ilknur Yurtsever and Cevat Yazıcı. **Proteomic Analysis of Liver Preservation Solutions Prior to Liver Transplantation. Current Proteomics,** 2019, 16, 2, 119 - 135

- **Mozioğlu, E., Akyürek S., Gündüz, S., Akgoz, M., Gören, A.C., Kocagöz T. Oligomer based real-time detection of microorganisms producing nuclease enzymes. Analyst,** 2019, 144, 4, 1379-1385. doi: 10.1039/c8an02129e

- Luisa Saraiva, Lili Wang, Martin Kammel, Andreas Kummrow, Eleanor Atkinson, Ji Youn Lee, Jana Höckner, Andreas Ruf, Andrea Engel, Yu-Zhong Zhang, Orla O'Shea, **Burhanettin Yalcinkaya, Muslum Akgoz,** Maria Paola Sassi, Carla Divieto, Tamara Lekishvili, Jonathan Campbell, Yingying Liu, Jing Wang, Richard Stebbings, Adolfas K. Gaigalas, Peter Rigsby, Jörg Neukammer and Sandrine Vessillier. **Comparison of Volumetric and Bead-Based Counting of CD34 Cells by Single Platform Flow Cytometry. Clinical Cytometry**, 2019, doi: 10.1002/cyto.b.21773

- Westwood, S., Josephs, R., Choteau, T., **Goren, A.C., Gunduz, S**., Yilmaz, H., **Un, I., Bilsel, G. Mass Fraction Assignment of Folic Acid in a High Purity Material, Metrologia,** 55, Technical Supplement, 2018, 08013

- Alexandra S. Whale, Gerwyn M. Jones, Jernej Pavšič, Tanja Dreo, Nicholas Redshaw, **Sema Akyurek, M. Akgoz**, Carla Divieto, Maria Paola Sassi, Hua-Jun He, Kenneth D. Cole, Young-Kyung Bae, Liesbet Deprez, Philippe Corbisier, Sonia Garrigou, Valérie Taly, Raquel Larios, Simon Cowen, Denise M. O'Sullivan, Claire A. Bushell, Heidi Goenaga-Infante, Helen Parkes, Carole A. Foy, Alison J. Woolford, Jim F. Huggett, Alison S. Devonshire. **An assessment of digital PCR as a reference measurement procedure for DNA copy number quantification of point mutations to support advances in precision medicine.** ***Clinical Chemistry,*** 2018, 64, 9, 1296-1307. doi: 10.1373/clinchem.2017.285478

- Gary John, Emma English, Rajiv T Erasmus, David Barry Sacks, Cas Weykamp, Christoph Buchta, Mathias M. Mueller, Yolande Lenga, Marek Budina, Josef Kratochvila, Bedrich Friedecky, Jean-Pascal Siest, Patricia Kaiser, Alexander Haliassos, Otto Panagiotakis, Konstantinos Makris, Hazel Graham, Anne Kane, Thomas P Smith, Ned Barrett, Laura Sciacovelli, Mario Plebani, Ana Andrade Faria, Ana Cardoso, Helena Correia, Montserrat Ventura Alemany, carmen perich, Carmen Gonzalez Gomez, Gunnar Nordin, Carita Krook Persson, Roman Fried, **Fatma Akcadag, Muslum Akgoz,** Diler Aslan, Samantha Jones, Annette Thomas, Philippe Gillery, Stephane Jaisson, Andrea Mosca, Reneta Paleari, Robbert J Slingerland, Janine Slootstra, Sanne Leppink, Anders Elmgren, Randie R. Little, Shawn M Connolly, Vicky Makky, Maren Nowicki, Carla Siebelder, Liesbeth Schröer-Janssen, Marieke te Winkel, Irene de Graaf, and Erna Lenters-Westra. **EurA1c: the European HbA1cTrial**

to investigate the performance of HbA1c assays in 2166 laboratories across 17 contries and 24 manufacturers using the IFFC Model for Quality Targets. Clinical Chemistry, 2018, 64 (8)

- Ozgen, U., Sener, S.O., Badem, M., Secinti, H., Cakmar, S.D., **Goren, A.C.,** Kazaz, C., Palaska, E. **Evaluation of HPLC, Phytochemical, Anticholinesterase and Antioxidant Profiles of the Aerial Parts of Asperula Taurina Subsp. Caucasica. Journal of Faculty of Pharmacy of Ankara University,** 2018, 42, 1-13

- Kirmizibekmez, H., Inan, Y., Reis, R., Sipahi, H., **Goren, A.C**., Yesilada, E. **Phenolic Compounds from the Aerial Parts of Clematis Viticella L. and Their in Vitro Anti-Inflammatory Activities, Natural Product Research,** 2018, 1-4

- Atay Balkan, I., Dogan, H., Zengin, G., Colak, N., Ayaz, F., **Goren, A.C.,** Kirmizibekmez, H., Yesilada, E. **Enzyme Inhibitory and Antioxidant Activities of Nerium Oleander L. Flower Extracts and Activity Guided Isolation of the Active Components. Industrial Crops and Products,** 112, 2018, 24-31

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. Different genomic mutations will be measured and new measurement methods will be developed.

For measurement of DNA methylation, a new CCQM measurement study will be offered in collaboration with KRISS.

New peptide/proteins based CRM projects, HbA1c and CRP will be finalized.

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 started and it will be extended to other analytes in the field of Laboratory Medicine.

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 4).

Table 4. Certified Reference Materials Preparation Planning at TUBITAK UME, 2020-2021.

Date of Release	**Description of CRM or RM**
On sale	25-OH Vitamin D2 and D3 in serum (2012-2014)
On sale	Amino acids for neonatal screening (2014-2018)
On sale	Organic acids for neonatal screening (2014-2018)
Will be on sale 2021	HbA1c CRM (2016-2020)
Will be on sale 2021	CRP CRM (2019-2021)
	Elements in serum (2020-2022)
	Elements in whole blood (2023-2026)
	Elements in urine (2023-2026)

➢ **EMPIR projects:**

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

- CardioMet - Improvement and metrological underpinning of quantitative diagnostic methods for biomarkers of coronary heart diseases, 2019 - 2022
- JNP: TraceLabMed - Support for a European Metrology Network on Traceability in Laboratory Medicine, 2019 - 2024
- EMN: TraceLabMed - European Metrology Network - Traceability in Laboratory Medicine, 2019 -
- ALCOREF - Development and certification of forensic alcohol reference materials for the law enforcement of drinking/driving regulation, 2017 – 2020
- QUIERO - Quantitative MR-based imaging of physical biomarkers, 2019 – 2022

New EMPIR health call will be advertised in 2021, Chemistry Group Laboratories plan to be involved in these health related projects.

➢ **Measurement Comparison Studies:**

TUBITAK UME Chemistry Group Laboratories have been planning to attend to the following measurement comparison studies (Table 5).

Table 5. CCQM international measurement comparison studies planned between 2020 and 2021.

Comparison #	**Comparison Name**
CCQM-K162	Selenoproteins in serum
CCQM-K159	Free Amino Acids in Plasma
CCQM-XX	Quantification of DNA Methylation (Planning to organize collaboration with KRISS)
CCQM-XX	HER2 Genetic Mutation Quantification
CCQM-XX	ProCalcitonin in Serum
CCQM-XX	Brain Natriuretic Peptide (BNP)

- **Calibration and Measurement Capabilities:**

Participating to the new measurement comparisons in clinical area, it is aimed to develop new measurement methods and new reference measurement materials, to broaden our services in the field of Laboratory Medicine (Table 6) leading to new CMC entries in the area.

Table 6. New Calibration and Measurement Capabilities applications planned between 2020 and 2021.

Measurement Service Sub-Category	**Matrix**	**Analyte or Component**
Peptides	Lyophilized or mQ-H_2O 20 mM Phosphate or other buffers with similar level of complexity	pure peptide primary reference material
Biological Fluids and materials	Blood Serum, Plasma	Amino Acids

3. Promoting traceability in laboratory medicine

- **EMN: TraceLabMed - European Metrology Network - Traceability in Laboratory Medicine,**
  Under this EMN, a workshop has been organized titled "Elements of Metrological Traceability for Laboratory Medicine" on 27th Balkan Clinical Laboratory Federation Meeting and 30th National Turkish Biochemical Society Meeting on 27-31 October 2019 in Antalya, Turkey. The Congress was supported by mother organizations, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM).

  During the workshop, the following oral presentations were given on 29th October 2019.

  - Traceability in laboratory medicine and IVD directives
    Tomris Ozben, Akdeniz University, Turkey

  - Introduction of the European Metrology Network on Traceability in Laboratory Medicine
    Muslum Akgoz, TUBITAK, Turkey

  - Amino acid and organic acid CRMs for newborn screening
    Dr. Simay Gunduz, TUBITAK, Turkey

  - ID-MS based reference measurement method for small analytes: vitamin D, creatinine, glucose, cholesterol, amino acids
    Mine Bilsel, TUBITAK, Turkey

  - Reference methods for quantification of peptides & proteins: β-amyloid in CSF (ReMIND Project), human C-peptide, oxytocin, HbA1c, insulin, human growth hormone
    Merve Oztug Kılınç, TUBITAK, Turkey

  - Latest developments on NMR; reference method for purity determination of small analytes and peptides: 17β-estradiol, folic acid, human C-peptide, oxytocin, HbA1c
    Dr. Ilker Un, TUBITAK, Turkey

  - Development of a reference method for transferrin quantification in serum
    Dr.F. Gonca Coskun, TUBITAK, Turkey

  - A Reference method for genetic mutation quantification of KRAS
    Dr. Muslum Akgoz, TUBITAK, Turkey

  The following poster presentations were also submitted.

  - 25-OH Vitamin D2, D3 in Lyophilized Serum
    Gökhan Bilsel, TUBITAK, Turkey

  - HbA1c CRM project
    Dr. Gonca Altın Yılmazer, TUBITAK, Turkey

- **A workshop titled "1st Biometrology and Molecular Biology Workshop" has been organized by TUBITAK Chemistry Group personnel at TUBITAK UME on 16 Jan 2018.**

  During the workshop, the following oral presentations were given.

  - Metrology in Biological Measurements
    Assoc.Prof.Dr. Müslüm AKGÖZ, TÜBİTAK UME

  - Turkey-South Korea Bilateral Cooperation Project: Development of Gene Methylation Measurement Method
    Sema AKYÜREK, TÜBİTAK UME

  - DNA Defective RASSF1A Gene Methylation Detection in Plasma
    Prof. Dr. Hülya YAZICI, Istanbul University

  - Effect of Circadian Clock Disruption on DNA Methylation
    Meltem AŞICIOĞLU, Gebze Technical University - TÜBİTAK UME

  - Antibiotic War Microorganisms or People Will Win?
    Prof. Dr. Tanıl KOCAGÖZ, Acıbadem University

  - Aging Without Getting Old
    Prof. Dr. Ali Demir TİRYAKİ, İstanbul Yeni Yüzyıl University

  - Importance of Internal Quality Control in Clinical Biochemical Measurements
    Prof. Dr. Abdurrahman COŞKUN, Acıbadem University

  - From Peptides to Proteins: Traceability to SI
    Merve ÖZTUĞ KILINÇ, TÜBİTAK UME

➢ **Congress Posters:**

- Mine Bilsel, Hasibe Yılmaz, Gökhan Bilsel, Ahmet Ceyhan Gören, Determination of Vitamin D Metabolites in Human Serum by LC-MS/MS, Medical Measurement Application, 26-28 Jun 2019, Istanbul, Turkey

- Sema AKYUREK, Development of dPCR Method for Rapid Screening of Carbapenem-Resistant Enterobacteriaceae, 13-16 Apr 2019, Amsterdam

- Gunduz, S., Yilmaz, H., Bilsel, G., Goren, A.C. Determination of Urea and Uric Acid in Human Serum (İnsan Serumunda Üre ve Ürik asidin LC-MS Yöntemi ile Belirlenmesi), 7th International Drug Chemistry Conference, Antalya, 14-17 Mar 2019, 1

- Yalçinkaya B., Çevik M., Aydin E., Comparison of miRNA Extraction Method From Blood Plasma, 7th Drug Chemistry Conference, March 2019

- Cakmar, S.D., Celik, M., Gunduz, S., Gunay, G., Isleyen, A., Un, I., Sadak, A.E., Zorlu, N., Aktas, G., Goren, A.C. Two New Certified Reference Materials for Newborn Screening for the Diagnosis of Metabolic Disorders: UME CRM 1314 Amino Acids in Lyophilized Plasma and UME CRM 1315 Organic Acids in Lyophilized Urine, 2019 IEEE International Symposium on Medical Measurements and Applications (MeMea), İstanbul, 26-28 Jun 2019, 1

- Sahin Un, S., Un, I., Unlu, A. "A Green Chemistry Approach For The Biosynthesis And Characterization Of Palladium Nanoparticles", 1. Euroasia Biochemical Approaches & Technologies Congress, Antalya, 27-30 Oct 2018, 1

- Un, I., Coskun, K., Yalcinkaya, B. "Profilling and Determination of Extracted DNA Solution Impurities by qNMR, 1st Euroasia Biochemical Approaches & Technologies Congress, Antalya, 27-30 Oct 2018, 105

- Burhanettin Yalcinkaya, Kubra Coskun, Engin Aydin, Muslum Akgoz, Sadrettin Pence. A simple silica based method for cell free DNA isolation from blood plasma. International IVEK Biotechnology Congress, 26-28 Nov 2018, Istanbul

- Burhanettin Yalcinkaya, Sadrettin Pence. Optimization of primers and probes that can be used in the diagnosis of mitochondrial diseases. International IVEK Biotechnology Congress, 26-28 Nov 2018 Istanbul

➢ **Congress Oral Presentations:**

- AKGOZ, M. Digital PCR and Applications. 29th National Biochemistry Congress. 26-30 Oct 2018, Bodrum, Turkey

- Un, I. Purity determination of Oxytosin Hormone by qNMR and TFA impurity (Oksitosin Hormonunun qNMR ile Saflık Tayini ve TFA Safsızlığının Belirlenmesi), 7th International Drug Chemistry Conference, Antalya, 14-17 Mar 2019, 1 p

- Un, I. Determination of Organic Acids by qNMR in Human Urine: Rapid Diagnosis of Metabolic Disorders, 6th Drug Chemistry: Design, Synthesis, Production and Standardization of Pharmaceutical Active Substances (6.İlaç Kimyası: İlaç Etkin Maddesi Tasarımı, Sentezi, Üretimi ve Standardizasyonu Kongresi), Antalya, 25 Mar 2018

- Gunduz, S., Hatipoğlu, S., D., Gören, A.C., Determination of amino acids in plasma by LC-MS/MS Method (Plazmada Aminoasitlerin LC-MS/MS Yöntemi ile Belirlenmesi). 6th Drug Chemistry: Design, Synthesis, Production and Standardization of Pharmaceutical Active Substances (6. İlaç Kimyası: İlaç Etkin Maddesi Tasarımı, Sentezi, Üretimi ve Standardizasyonu Kongresi), Antalya, 25 Mar 2018

- Evren Kilinç, Merve Oztug, Emel Timuçin. Modeling and dynamics of the full-length structure of the factor XII protein: Insights into the mechanism of activation through Zinc binding, 30th Biophysics Congress, Bodrum, Turkey, 10-13 Oct 2018

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

- **JCTLM Activities**

  TUBITAK UME become a member of JCTLM in 2012 and has actively participated to the JCTLM Members' and Stakeholders' Meetings since then. Biennial report was also submitted to JCTLM Executive Committee in 2018.

- **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 2018 and 2019.

  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).

- **EurA1c: The European HbA1c Trial "EQA Program"**

  In 2016 - 2019 several EQA organizers decided to participate in the "EurA1c" projects which are organized by The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Committee Education in the Use of Biomarkers in Diabetes (C-EUBD). TUBITAK UME was also involved in these trials as a partner and submitted the measurement results of Turkish clinical laboratories in 2016, 2017 and 2018. In 2019, TUBITAK UME also participated to the new study and new samples are being also distributed to the clinical laboratories.

5. Open questions and suggestions to be addressed by JCTLM