

TUBITAK UME (National Metrology Institute of TURKEY)

Elements of Metrological Traceability for Laboratory Medicine



14:50 - 15:10	20 min.	Traceability in laboratory medicine and IVD directives Tomris Ozben, Akdeniz University, Turkey
15:10 - 15:30	20 min.	Introduction of the European Metrology Network on Traceability in Laboratory Medicine Muslum Akgoz, TUBITAK, Turkey
15:30 - 15:50	20 min.	Amino acid and organic acid CRMs for newborn screening Simay Gunduz, TUBITAK, Turkey
15:50 - 16:10	20 min.	ID-MS based reference measurement method for small analytes: vitamin D, creatinine, glucose, cholesterol, amino acids Mine Bilsel, TUBITAK, Turkey
16:10 - 16:30	20 min.	Reference methods for quantification of peptides & proteins: β -amyloid in CSF (ReMIND Project), human C-peptide, oxytocin, HbA1c, insulin, human growth hormone Merve Oztug Kilinc, TUBITAK, Turkey
16:30 - 17:00		Coffee Break
17:00 - 17:20	20 min.	Latest developments on NMR; reference method for purity determination of small analytes and peptides: 17β -estradiol, folic acid, human C-peptide, oxytocin, HbA1c Ilker Un, TUBITAK, Turkey
17:20 - 17:40	20 min.	Development of a reference method for transferrin quantification in serum F. Gonca Coskun, TUBITAK, Turkey
17:40 - 18:00	20 min.	A Reference method for genetic mutation quantification of KRAS Muslum Akgoz, TUBITAK, Turkey



WORKSHOP

Elements of Metrological Traceability for Laboratory Medicine




XXVII. XXX.

**Balkan Clinical Laboratory
Federation Meeting**

**National Congress of the
Turkish Biochemical Society**

BCLF 2019 TBS 2019

 **OCTOBER 27-31, 2019**

 **PAPILLON ZEUGMA CONVENTION CENTRE, BELEK ANTALYA - TURKEY**

Metrology?

**National Metrology Institute?
(TUBİTAK UME, Ulusal Metroloji Enstitüsü)**

Traceability?

CRM?

What is Metrology?

Metrology is the science of measurement

Metrology includes
all aspects both theoretical and practical reference measurements,
including their uncertainty,
in whatever the field of science or technology



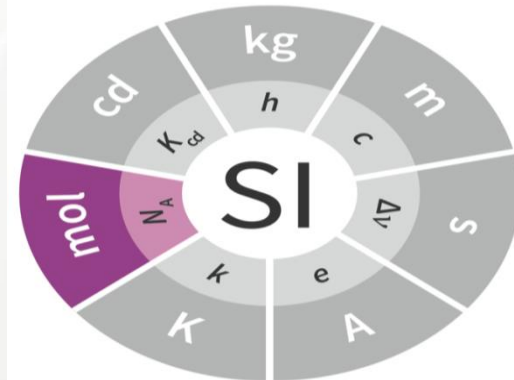
The Aim of Metrology

Main activities:

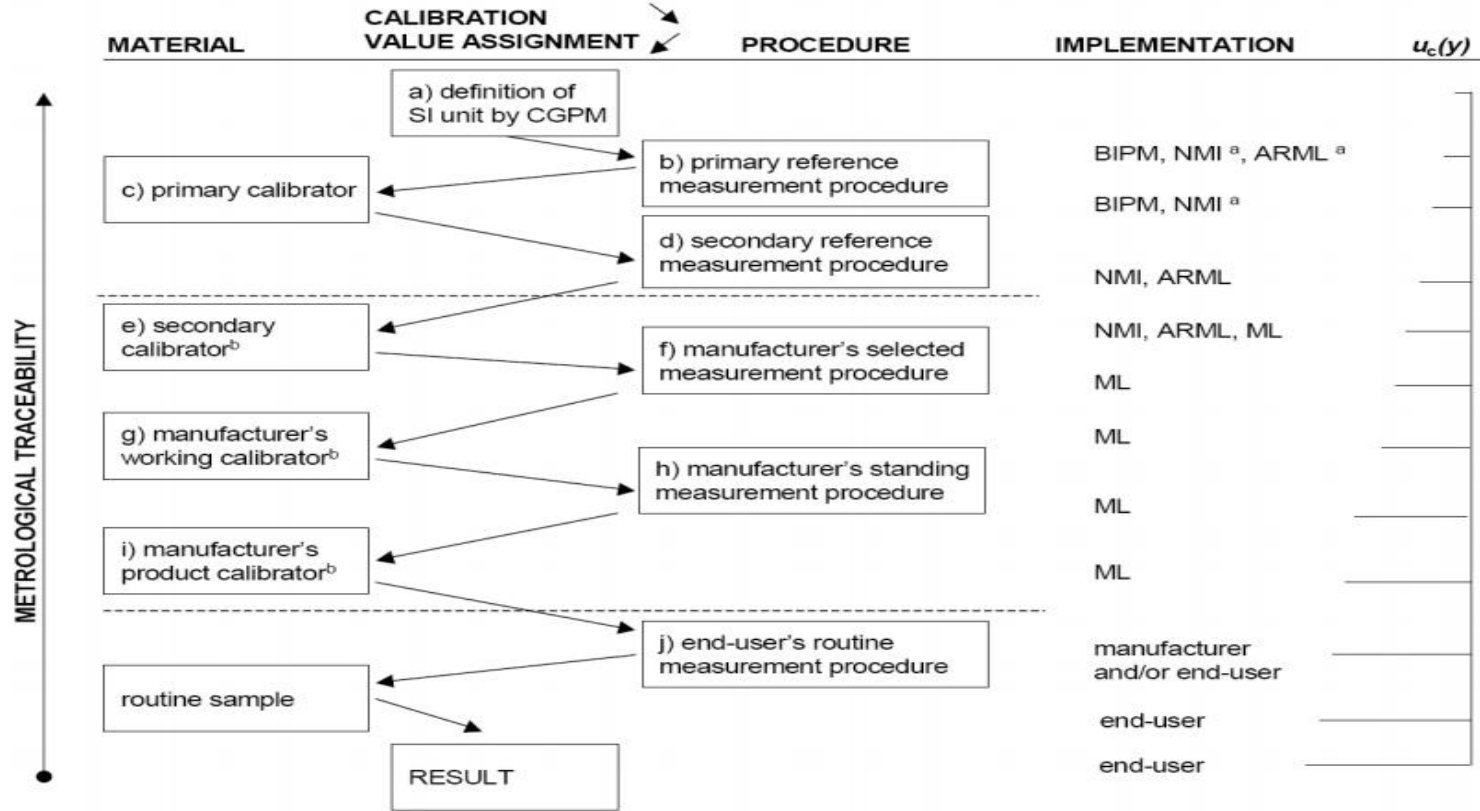
- ✓ Definition of internationally accepted units of measurement (SI units)
- ✓ Realization of primary references according to SI and derived units by scientific methods
- ✓ **Establishment of traceability chain** by determining and documenting the value and **uncertainty** of a measurement and disseminating that knowledge

Duties:

- ✓ Basic research on measurement
- ✓ Refining state-of-the-art measurement methods
- ✓ Production and certification of reference materials



Elements of Traceability Chain



Abbreviations: ARML - Accredited reference measurement laboratory (such a laboratory may be an independent or manufacturer's laboratory); BIPM - International Bureau of Weights and Measures; CGMP - General Conference on Weights and Measures; ML - Manufacturer's laboratory; NMI - National Metrology Institute.

The symbol $u_c(y)$ stands for combined standard uncertainty of measurement.

Elements of Traceability Chain

MATERIAL CALIBRATION VALUE ASSIGNMENT PROCEDURE IMPLEMENTATION $u_c(y)$

a) definition of SI unit by CGPM

c) primary calibrator

b) primary reference measurement procedure

BIPM, NMI^a, ARML^a
BIPM, NMI^a

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

25-OH Vitamin D2, D3 in Lyophilized Serum listed under JCTLM database
poster #: P-008

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

pH CRM: 1401, 1402, 1403
pH: 4, 7, 10

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

HbA1c CRM project to be completed in 2020
Dr. Pinar EKER poster #: P-063

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

CRP CRM project to be completed in 2021

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

EA

RESULT

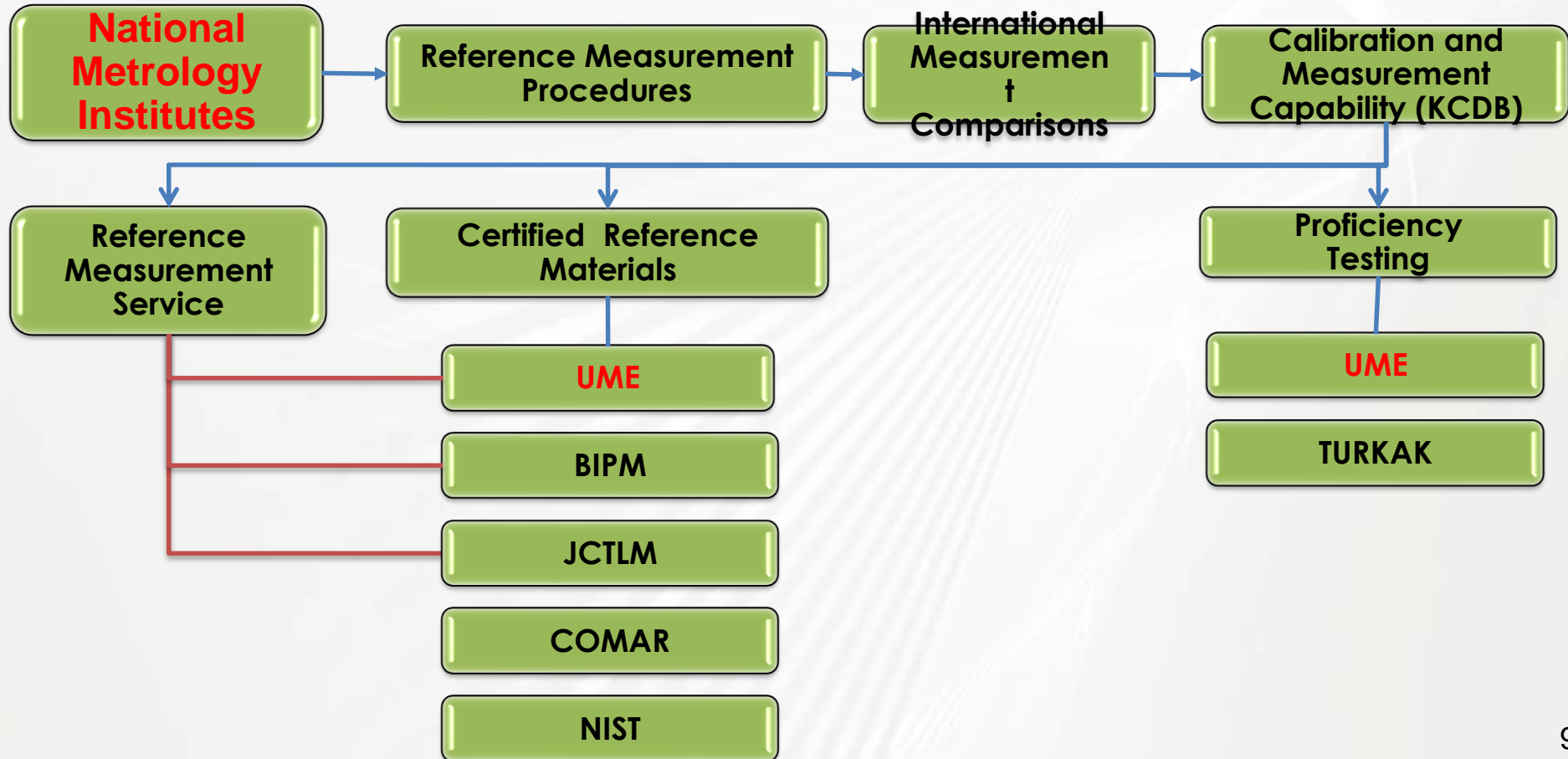
and reference measur
IP - International Bu
manufacturer's labora
combined standard unc

The National Metrology Institute of Turkey



- Establishes and maintains national measurement reference standards of Turkey
- Assures traceability of measurements in trade and industry to SI units through calibration services
- Training, consulting, contracting R&D, measurement equipment production based on expertise in measurement science
- Fundamental public infrastructure for quality assurance in industrial production, trade, research and human services

METROLOGY SYSTEM





- CIPM Mutual Recognition Arrangement was signed in 1999
- CIPM – MRA



- CMC - calibration and measurement capabilities
<http://www.bipm.org/kcdb>



- Member of EURAMET
European Association of National Measurement Institutes



- JCTLM Member since 2012
<https://www.bipm.org/jctlm/>

- the first reference material producer in Turkey
- accredited according to the ISO 17034



Chemistry Group of TUBITAK UME

- state-of-the-art facilities on material processing and storage
- well-equipped infrastructure on all kinds of chemical and biological analyses
- produces and certifies reference materials

Laboratory Infrastructure

Material Processing

- Vacuum Blender
- Sieving Systems
- Various Mixers
- (V-Type (150 L), 3-Dimensional (2, 20 and 350 L capacity))
- Vibratory Feeder and Sample Divider
- **Lyophilizers: Large scale [3.9 m² shelf area] and Pilot scale**
- Powder Filling Machine
- **Liquid Filling, Capping and Labeling Machine**
- Vacuum Sachet Machine



Certified Reference Materials

ISO 17034:2016



- **UME CRM 1301: Pure Primary Calibrant for Chloramphenicol**
- **UME CRM 1401: pH CRMs, pH: 4, 7 & 10**
- **UME CRM 1308: 25-OH Vitamin D2, D3 in Lyophilized Serum**
 - listed under JCTLM database
 - poster #: P-008
- **UME CRM 1314: Certified for 32 aminoacids in lyophilized plazma &**
- **UME CRM 1315: Certified for 47 organic acids in lyophilized urine**
 - was submitted for listing JCTLM CRM database

Ongoing projects:

- **UME CRM 1318: Hemoglobin A1c (HbA1c) CRM project**
 - poster #: P-063
- **UME CRM 1008: C-Reactive Protein (CRP) CRM project**

Full list of all updated CRM and RM are in the following link:

https://rm.ume.tubitak.gov.tr/urun_en.aspx?u=7

<http://www.ume.tubitak.gov.tr/en/laboratuvarlarimiz/reference-materials-laboratory>

- Determination of 25-OH Vitamin D2, D3 and 3-epi-25-OH D3 in Serum
- Determination of Cholesterol, Glucose and Creatinine in Serum
- Determination of Urea and Uric Acid in Biological Matrix
- Determination of As, Pb, Cr, Hg, Ni, P and Zn in Biological Materials
- Determination of K, Ca, Mg, Fe, Cl, Cu, Na, P, Se and Se-Met in Serum
- Determination of Relative Gene Expression, Real Time PCR
- Absolute Quantification of Plasmid DNA, Digital PCR
- Relative Quantification of Oncogenes, Digital PCR
- **Amino Acid Analysis For Pure Protein/Peptide, LC-ID-MS**
- **Proteomic Analysis, HR-LC-MS/MS**
- Absolute Quantification of C-Peptide / Angiotensin, LC-ID-MS(n)
- Absolute Quantification of Protein Concentration, HPLC, PICA
- Relative Quantification of HbA1c Protein, HPLC, LC-ID-MS



EurA1c (HbA1c)




EurA1c projects are organized by

- IFCC; C-EUBD, Committee Education in the use of Biomarkers in Diabetes
- to harmonize HbA1c measurement results in Europe
- Coordinators:
 - TUBITAK UME, Dr. Fatma AKÇADAĞ
 - Prof. Diler ASLAN (Pamukkale University)
- 2016 - 2019
- fresh and lyophilized samples - to 50 clinical laboratories in Turkey

EurAAA1c 2019:

- first set of samples were send to labs
- second set will be send in November

CHANGE THROUGH **MEASUREMENTS!**



The central graphic features four large, black, stylized icons arranged horizontally. From left to right: a gauge with a needle and scale; a Euro symbol (€) inside a circle; a thermometer with a bulb and a scale; and a molecular structure with three atoms connected by bonds, all contained within a circle. The text 'CHANGE THROUGH' is positioned above the icons, and 'MEASUREMENTS!' is positioned below them. The word 'CHANGE' is in red, while 'THROUGH' and 'MEASUREMENTS!' are in black.