Instituto Português da Qualidade

10,5 millions

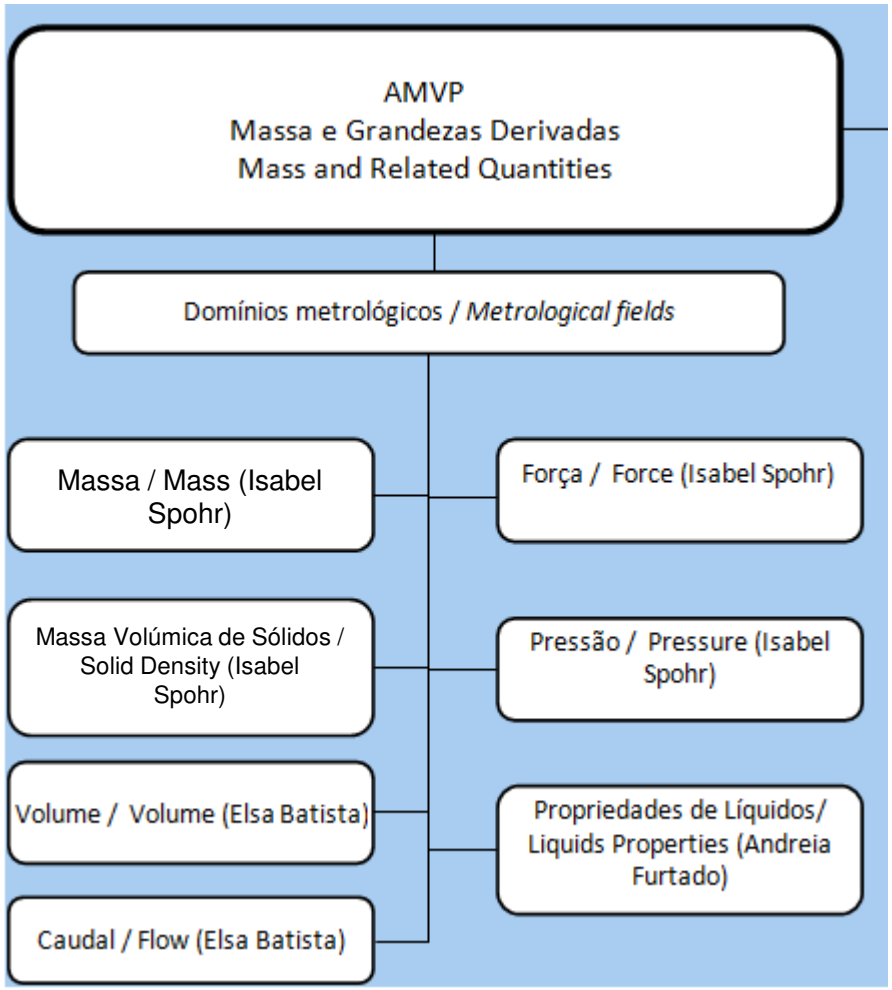
PORTUGUESE INSTITUTE FOR QUALITY

Isabel Spohr

17th meeting of the CCM

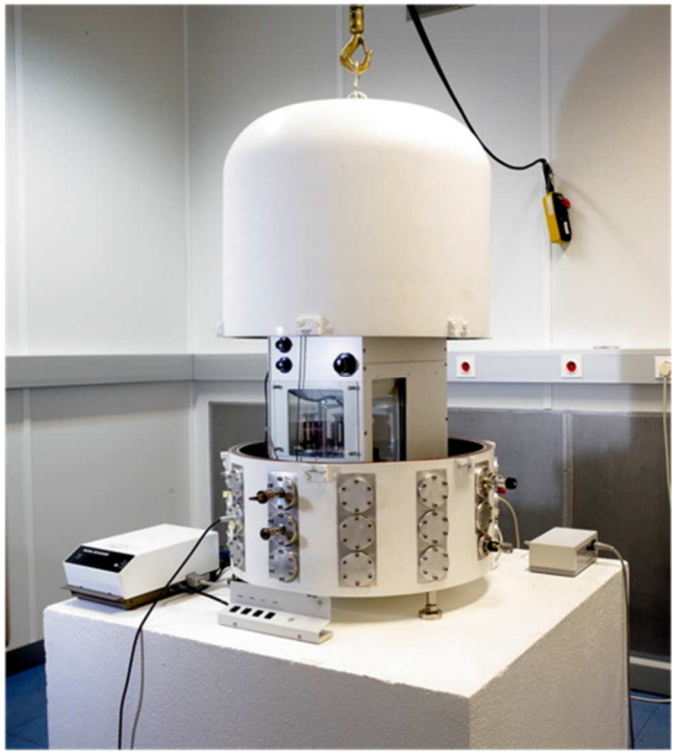
BIPM, Sèvres, 17th May 2019

Metrology Department – Mass and Related Quantities



Mass Laboratory

Prototype N.º 69

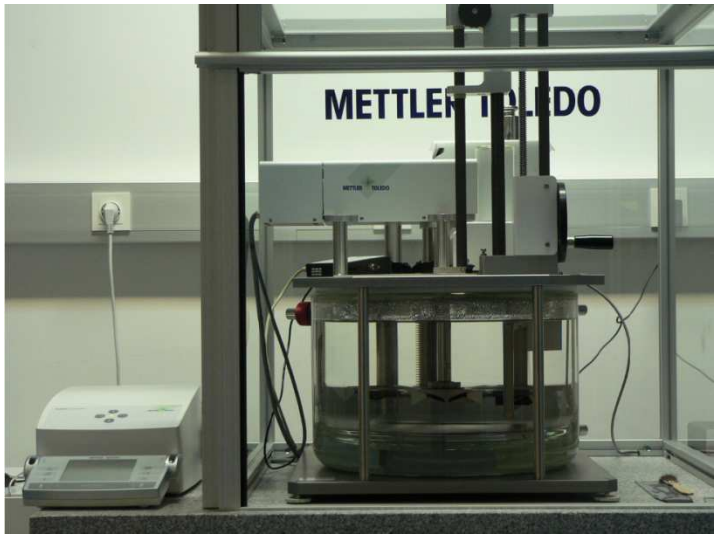


Mettler-Toledo HK 1000 MC

Mass and Solid Density Laboratories

1 mg to 10 kg Mass Comparators

Sauter 107 (20 kg; 50 kg)

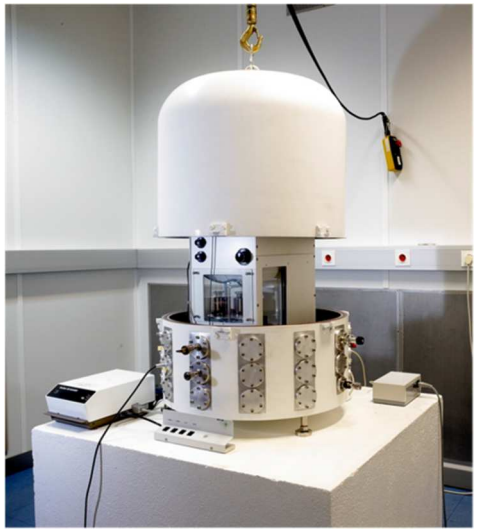


Mettler-Toledo VC1005 (1 g to 1 kg)

Mettler-Toledo A5 Comparator (1 mg to 5 g)

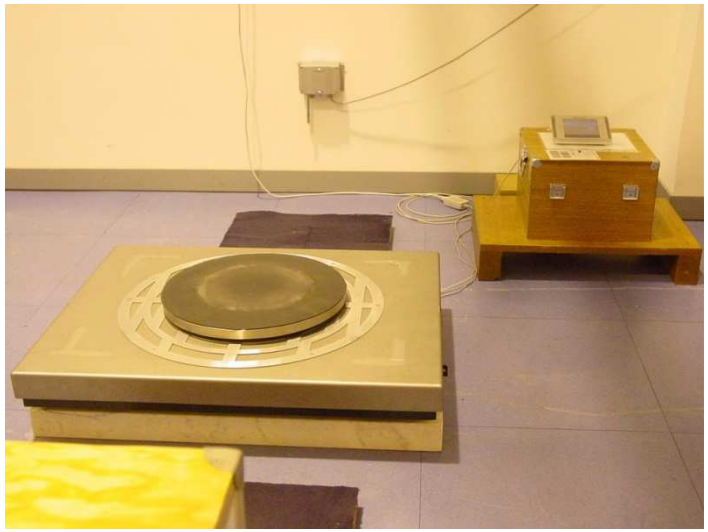
Participation in recent EURAMET Mass Comparisons

Comparison on Mass Standard
1 kg EURAMET.M.M-K4.2015



Mettler-Toledo HK 1000 MC

Comparison of 500 kg Mass Standard
EURAMET.M.M-S7



Mettler-Toledo XP 1003K Comparator

Force Laboratory

Dead Weight Force Machines:

- ✓ from 50 N to 5 kN (EUROMET M.F-K1)
- ✓ from 1 kN to 100 kN (EUROMET M.F-K2)

Dead Weight Force Machines + Lever Amplification:

- ➢ from 10 kN to 1 MN (EUROMET M.F-K3)

Pressure Laboratory

Gauge Pressure Balance – Oil Medium
0.2 MPa to 100 MPa
CMC: 29 Pa to 5.5 kPa

Gauge/Absolute - Pressure Balance
3.5 kPa to 170 kPa
CMC: 0.52 Pa to 6.4 Pa (Absolute)
0.11 Pa to 5.1 Pa (Gauge)

Gauge Pressure Balance – Gas Medium
40 kPa to 2 MPa
CMC: 1.2 Pa to 60 Pa

Participation in Recent EURAMET Pressure Comparisons

Comparison in the gas media in the range from 25 kPa to 200 kPa EURAMET.M.P-K8

Gauge/Absolute - Pressure Balance

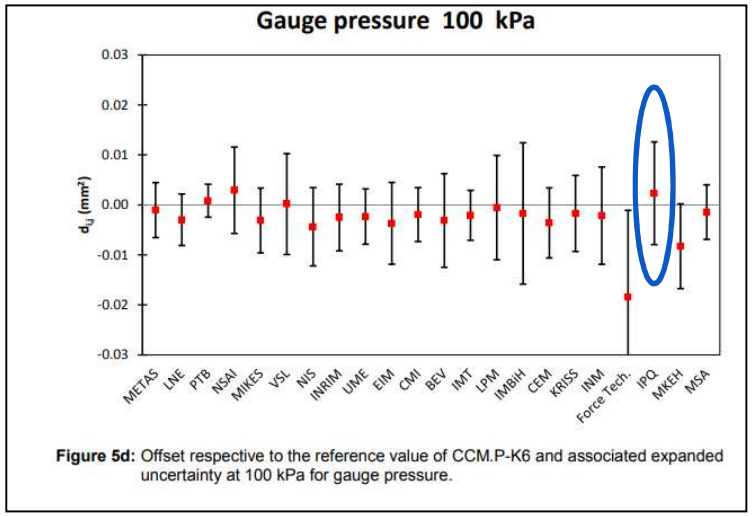


Figure 5d: Offset respective to the reference value of CCM.P-K6 and associated expanded uncertainty at 100 kPa for gauge pressure.

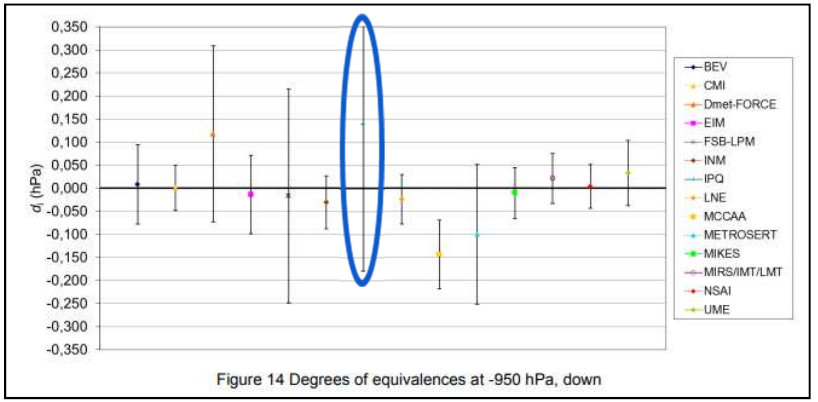


Figure 14 Degrees of equivalences at -950 hPa, down

Comparison in the negative gauge pressure range -950 hPa to 0 hPa EURAMET.M.P-S9

Negative Pressure Gauge - Pressure Balance + Pressure Divider

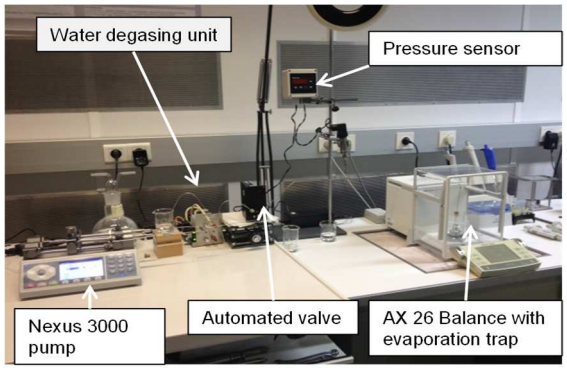
Volume and Flow Laboratory

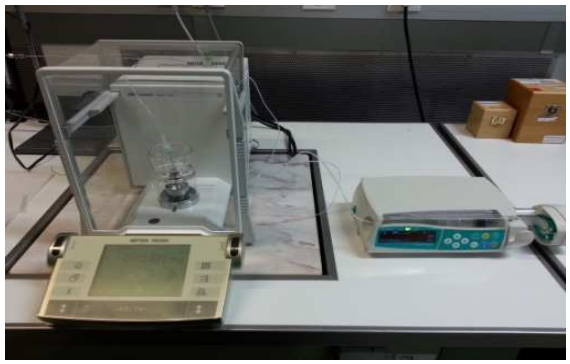
← Calibration of small volumes by gravimetry
1 µL to 10 L
CMC: 0.01 %

Primary volumetric standards →
1 L to 1500 L
CMC: 0.01 %

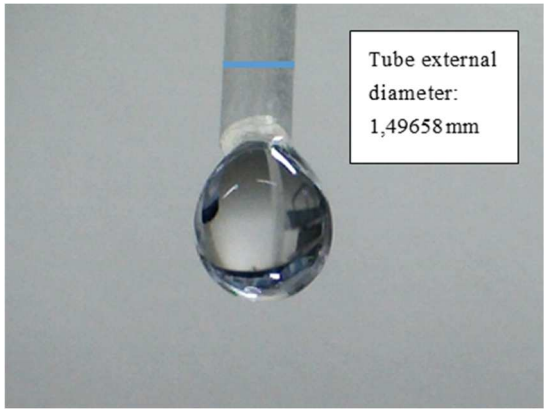
← Calibration of large volumes by volumetry
1 L – 10 000L
CMC: 0.02 %

Volume and **Flow** Laboratory





Microflow calibration, from 0.12 ml/h up to 600 ml/h, with 2.5 % to 0.3 %



New research - Microchips developments and measurements, new calibration method - optical

EMPIR Project – 18HLT08 MEDDII
Metrology for Drug Delivery

EMPIR

The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

Coordinator - Elsa Batista - IPQ, Portugal

Starts in June 2019

15 partners

Overview

This project aims to characterize and improve dosing accuracy of existing drug delivery devices and multi infusion systems and enable traceable measurements of their volume, flow rate, pressure and inline sensing operation at very low infusion rates:

- ✓ by the development of **new calibration methods**
- ✓ by **expanding the existing metrological infrastructure**

Additionally this project will investigate:

- ➢ the effects of **fast transient flows** on dosing response
- ➢ the **physical properties** of liquid mixtures used in infusion
- ➢ the **occlusion phenomena** in multi-infusion systems



Motivation

PATIENT SAFETY

- ➢ **Infusion therapy** → Main form of therapy in health care.
- ➢ **Deviations** in medication dose into the patient bloodstream have **dramatic effects.**
- ➢ Wide range of applications (vasoactive drugs, multi-infusion therapy, pre-term babies therapy, organ-on-a-chip technology, etc.).

NEEDS

Validated metrological infrastructure for traceable measurement and calibration

- volume
- ultra-low flow rates (<100 nL.min^{-1})
- pressure
- fast changing flow rates
- physical properties of mixtures
- occlusion phenomena

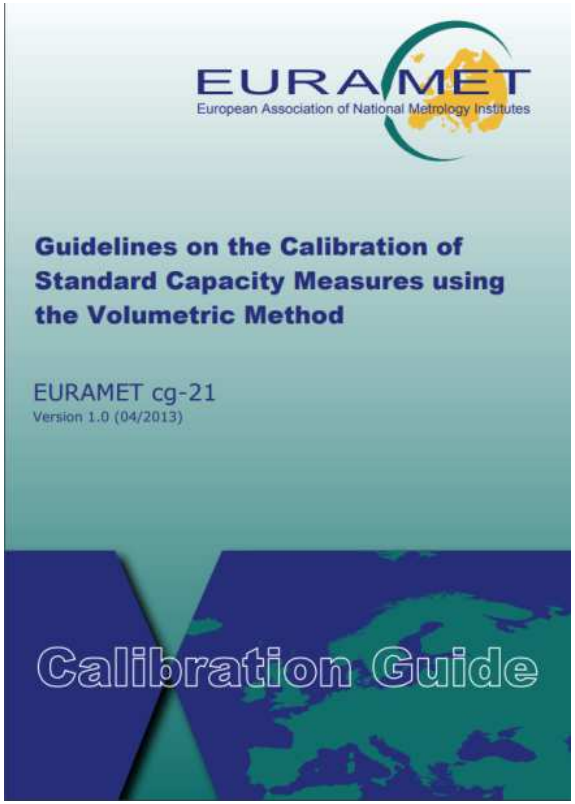
Crucial for patient safety and to advances in:

- ✓ microfluidics and organ-on-a-chip faithfull reproduction of multi-organ functions
- ✓ reproducibility and accuracy of multi-infusion therapies
- ✓ reliability of drug delivery devices

Volume and Flow Laboratory

Guide development or revision

Coordination of development and revision of EURAMET- Calibration Guide No. 19 | Guidelines on the Determination of Uncertainty in Gravimetric Volume Calibration | TC-F | Version 3.0, 09/2018



Coordination of development of EURAMET- Calibration Guide No. 21 | Guidelines on the Calibration of Standard Capacity Measures using the Volumetric Method | TC-F | Version 1.0, 04/2013

Volume and Flow Laboratory

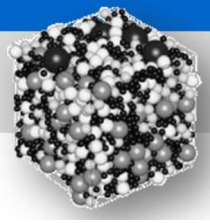
Delivering training

Metrology in Volume at NIM (China) in the calibration of micropipettes in 2013

Participation in international comparisons – LVC

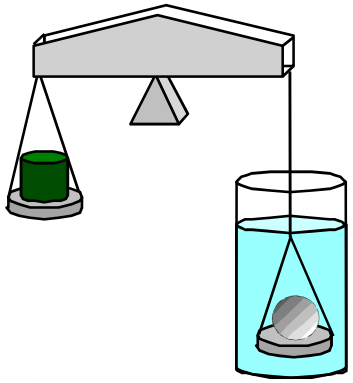
2018/2019

- SIM.M.FF-S11 (**coordinator**) - Calibration of micropipettes;
- AFRIMETS.FF-K4.2.2015 (**coordinator**) - Volume comparison at 100 mL – Calibration of micropipettes;
- EURAMET.M.FF-K4.2.2014 (EURAMET 1322) (**coordinator**) - Calibration of micropipettes;
- EURAMET 1353 (**coordinator**) - Calibration of micropipettes by the gravimetric and photometric method;
- EURAMET.M.FF-K4.1.2016 – Calibration of a 20 L volume standards;
- EURAMET 1425 (**coordinator**) - Calibration of micropipettes by the gravimetric and photometric method – pilot study;
- EURAMET.M.FF.S8 (EURAMET 1297) - Comparison of a 50 mL pycnometer and a 500 mL flask;
- 767/GE/18 – COOMET (**coordinator**)- Calibration of micropipettes and digital burette



Density IPQ - Laboratory of Properties of Liquids

Hydrostatic Weighing Apparatus



1 Silicon sphere *m* ~233 g

Balance: 0.1 mg to 400 g

Mass standards OIML Class E1

Temperature interval: [-40; 100] °C

U (k=2.00) = 0.006 kg/m^3 to 0.02 kg/m^3

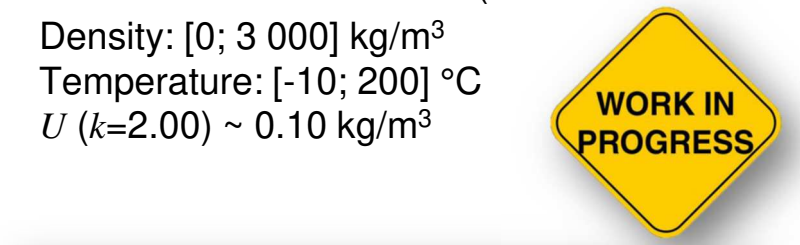
Oscillation-Type Density meters

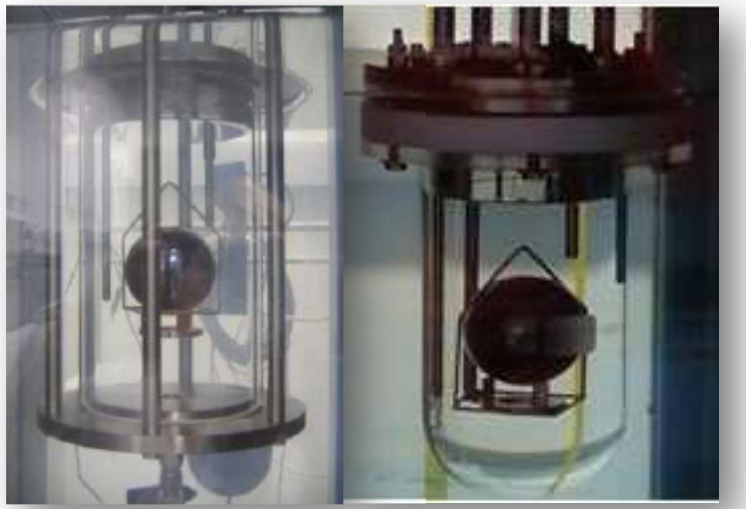
At atmospheric *p* (Anton Paar DMA 5000)

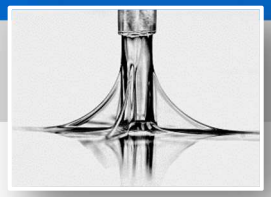
Density: [0; 2 000] kg/m^3
Temperature: [0; 90] °C
U (k=2.00) = 0.030 kg/m^3 to 0.010 kg/m^3

From 0.1 MPa to 70 MPa (Anton Paar DMA HP)

Density: [0; 3 000] kg/m^3
Temperature: [-10; 200] °C
U (k=2.00) ~ 0.10 kg/m^3







Viscosity

Surface tension

Capillary Glass Viscometer

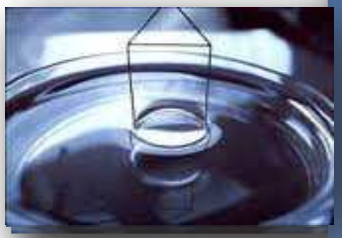
Ubbelohde type

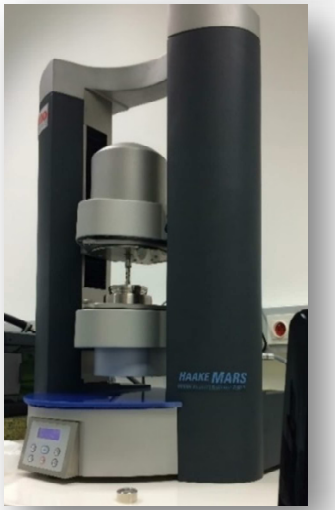
Kinematic viscosity

[1.2 to 17 000] mm^2/s

U (k = 2.00) = 0.60 % to 0.45 %

Temperature : [-40; 100] °C





Rotational viscometer

HAAKE

Viscotester 550

Rheometer

HAAKE Mars III

Thermo Scientific

U (k = 2.00) = 10 % to 2 %

Tensiometer

Kruss K100 MK2

Ring and Plate Method

Surface tension: [1; 1000] mN/m

Temperature: [-10; 130] °C

U (k=2.00) = 0.50 mN/m to 0.01 mN/m

Participation in international comparisons – LPL

Density

Hydrostatic Weighing

- EURAMET Project 858 - Hydrostatic weighing – exchange of experiences
- EURAMET Project 1019 - Comparison of density determinations of liquid samples

Oscillation-type density meters

- EURAMET Project 1214 – Density measurement of viscous oils (using vibrating tube density meters)
- EURAMET Supplementary Comparison EURAMET.M.D-S1 (1240) - Comparison of density determination of liquid samples by density meters

Hydrometers

- EURAMET Project 702 (EUROMET.M.D-K4) - Comparison of the calibrations of high-resolution hydrometers for liquid density determinations

Viscosity

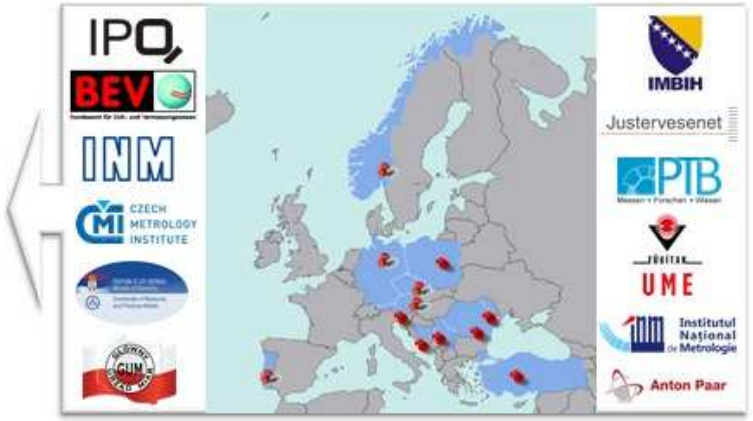
- CCM Key Comparison of the Viscosity CCM.V – K1
- CCM Key Comparison of the Viscosity CCM.V – K2
- CCM Key Comparison of the Viscosity CCM.V – K3
- CCM Key Comparison of the Viscosity CCM.V – K4

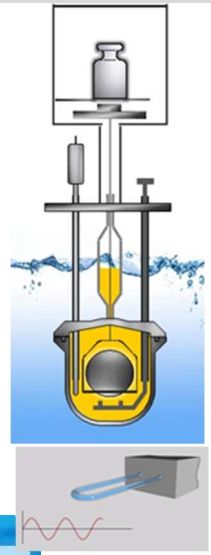
EMPIR Project - 17RPT02 rhoLiq

Establishing traceability for liquid density measurements

EMPIR
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

Coordinator
Andreia Furtado
IPQ, Portugal





WP5 Management & Coordination — IPQ, 11.3 PM

WP2 — UME, 32.0 PM
Hydrostatic weighing & Reference liquids
- Comparisons (diagnostic & consolidation)
- Robustness studies (effect of: surface tension, viscosity and viscoelasticity)

WP1 — PTB, 33.1 PM
Improving liquid density measurement capabilities
- Training
- Implementation of gained knowledge
- Selection and provision of RM
- Development of individual long-term strategies

WP3 — 31.5 PM
Oscillation-type density meters
- Comparisons (diagnostic & consolidation)
- Robustness studies (effect of: viscosity, temperature and viscoelasticity)
- Robustness studies at high pressure (up to 600 bar)

WP4 — IPQ, 12.0 PM

Early Impact
- Capacity to extend/improve liquid density mesurement capabilities
- Provide support to policy makers with reliable data
- Enhance of community and international confidence regarding economical transactions

Wider Impact
- Creation of a cohesive network of European NMIs able to share experiences concerning liquids density measurements
- Stronger involvement of the emerging NMIs in BIPM-CCM and EURAMET TC-M
- Definition of roadmaps for individual strategies of the emerging NMIs, describing the uptake of the developed capacities

EMPIR Projects

EMRP – European Metrology Research Programme

2011	HLT07 MeDD - *Metrology for drug delivery*	IPQ
2013	ENG59 NNL - *Sensor development and calibration method for inline detection of viscosity and solids content of non-Newtonian fluids*	IPQ

EMPIR – European Metrology Programme for Innovation and Research

2014	14IND-06 Pres2Vac – *Industrial standards in the intermediate pressure-to-vacuum range*	IPQ + FCT-UNL
2015	*15SIP-03 InfusionUptake – Standards and e-learning course to maximise the uptake of infusion and calibration best practices*	IPQ
2017	17RPT-02 *rhoLiq – Establishing traceability for liquid density measurements*	IPQ
2018	*18RPT-02 adOSSIG – Developing an Infrastructure for improved and harmonized metrological checks of blood-pressure measurements in Europe*	IPQ
2018	*18SRT-02 MeddII – Metrology for drug delivery*	IPQ

EURAMET Project 1123 - On site peer review CEM, INRIM and IPQ

QMS – ISO/IEC 17025

On site peer review (IPQ - Mass and Related Quantities Area)

Domain	First round	Second round	Third round
Mass	2010 Nieves Medina (CEM)	2016 Ángel Lumbreras (CEM)	
Force	2012 Nieves Medina (CEM)	2016 Alessandro Germak (INRIM)	
Pressure	2010 Mercede Bergoglio (INRIM)	2015 Salustiano Ruiz (CEM)	2019
Volume & Flow	2011 Nieves Medina (CEM)	2016 Pier Giorgio Spazzini (INRIM)	
Density & Viscosity	2013 Nieves Medina (CEM)	2018 Andrea Malengo (INRIM)	

Thank you for your attention!