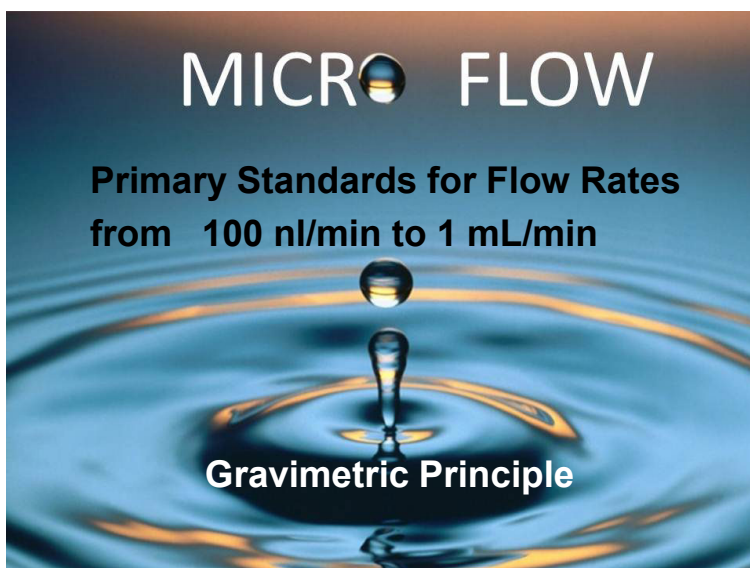




Hugo Bissig METAS, Elsa Batista IPQ, Peter Lucas VSL,
Harm Tido Petter VSL, Anders Koustrup Niemann DTI,
Benoit Savanier CETIAT, Florestan Ogheard CETIAT

EMRP HLT07 – Metrology for Drug Delivery

This project is carried out with funding by the European Union under the EMRP. The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union.

EMRP

European Metrology Research Programme
■ Programme of EURAMET

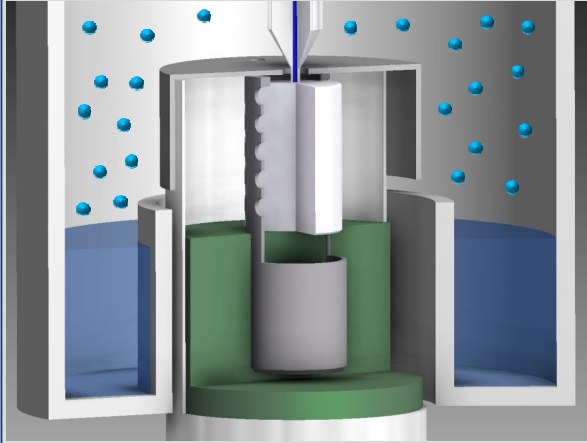
The EMRP is jointly funded by the EMRP participating countries within EURAMET and the European Union



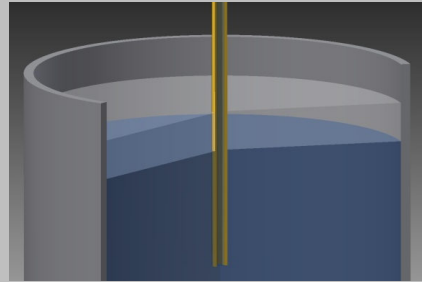
www.drugmetrology.com

2 types of collecting water in beaker to avoid droplet formation

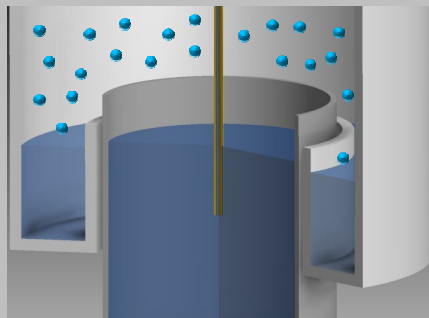
Water Bridge to waterabsorbing materials in saturated air



Needle immersed into water
• with oil cover



• in saturated air

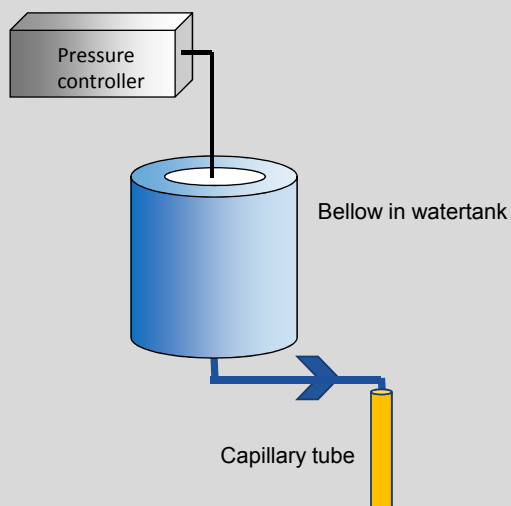


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Flow Generator: 2 principles

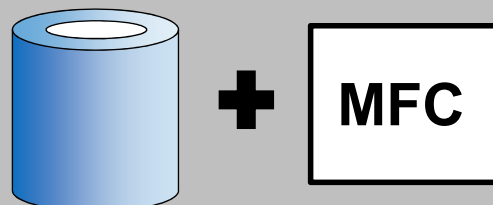
Constant pressure drop over capillary tube setting the flow rate



Syringe pump setting the flow rate



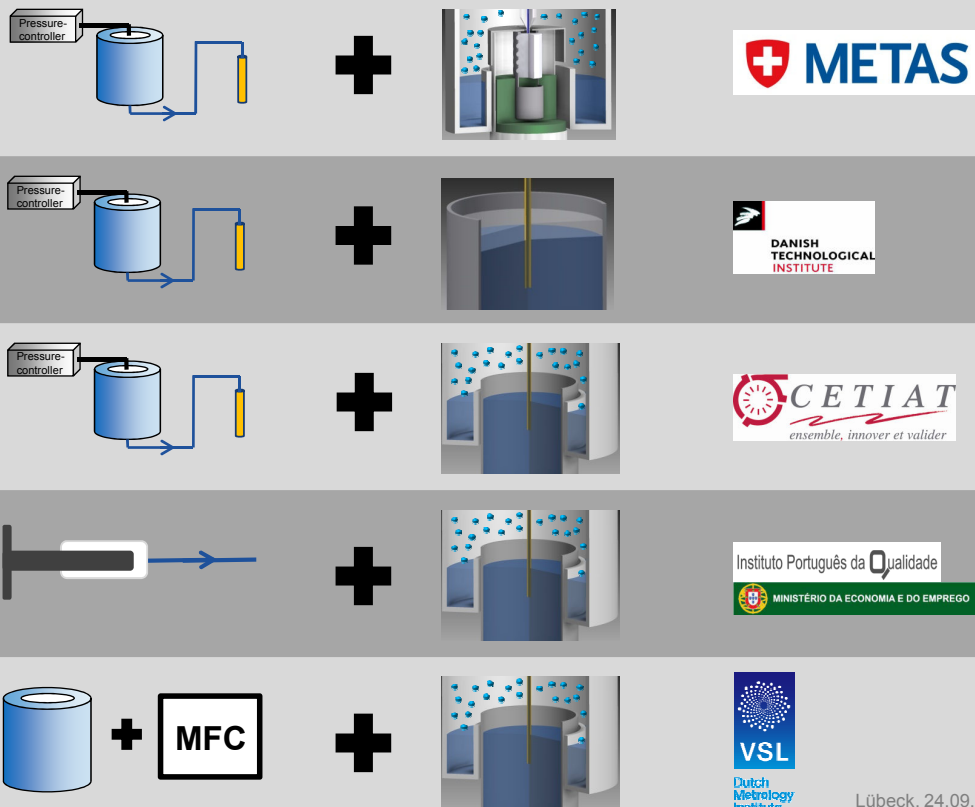
MFC setting the flow rate



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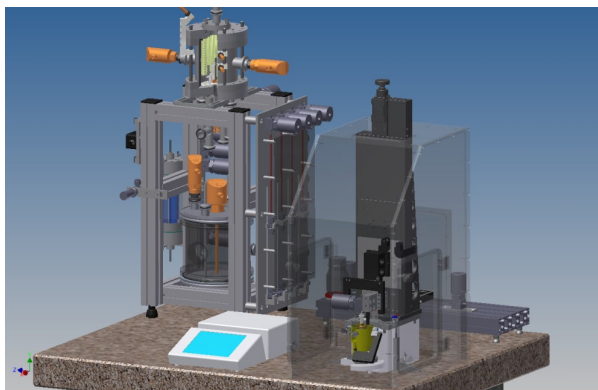
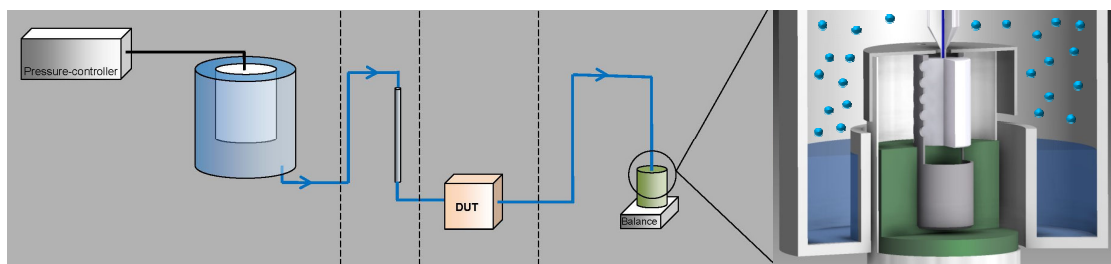
Flow generator and water collection method



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Micro Flow Facility – Gravimetric setup



Flow rates: 1 ml/min – 100 nl/min

Uncertainties: 0.1 % - 0.6 %

Pressure range: 0 bar – 2.5 bar

Temperature: ambient (22 °C)

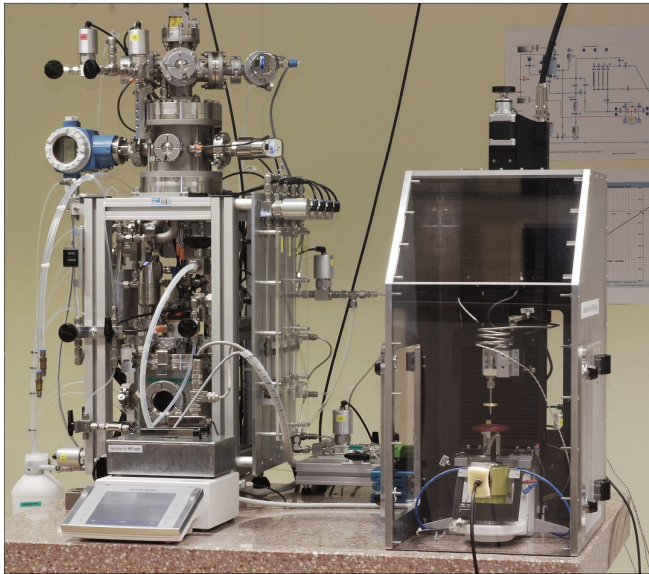
Contact: Hugo.Bissig@metas.ch

Lübeck, 24.09.2014

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**METAS**

Micro Flow Facility – Gravimetric setup



Flow rates: 1 ml/min – 100 nl/min

Uncertainties: 0.1 % - 0.6 %

Pressure range: 0 bar – 2.5 bar

Temperature: ambient (22 °C)

Contact: Hugo.Bissig@metas.ch

Lübeck, 24.09.2014

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Micro Flow Facility – Gravimetric setup



Flow rates: 133 ml/min – 16 µl/min

Uncertainties: 0.04 % - 1.0 %

Pressure range: 0 bar – 10 bar

Temperature: 10 °C – 50 °C

Left: flowmeter under test

Right: bellow to generate water pressure

Contacts:

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Lübeck, 24.09.2014

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Micro Flow Facility – Gravimetric setup



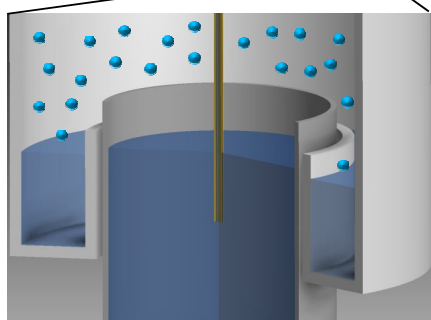
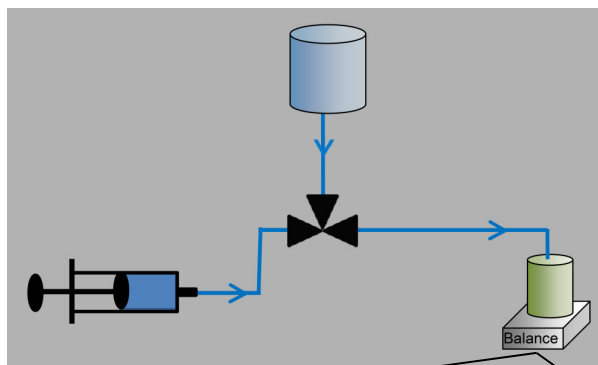
Four high precision scales
Weighting masses
from 0.5g to 500g

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Micro Flow Facility – Gravimetric setup



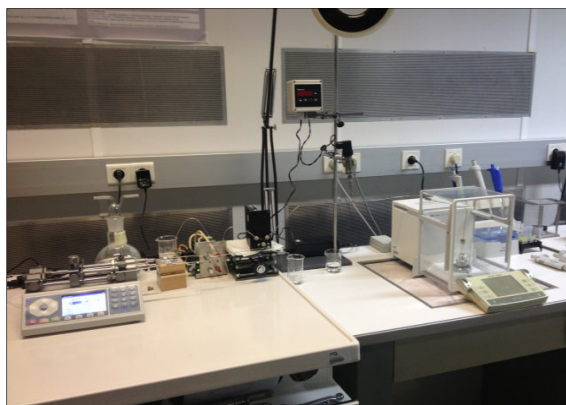
Flow rates: 10 ml/min – 50 nl/min
Uncertainties: 0.15 % - 6.0 %
Pressure range: 0 bar – 2 bar
Temperature: ambient

Contact:
Elsa Batista, ebatista@ipq.pt

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Micro Flow Facility – Gravimetric setup



Mettler Toledo AX 26



Mettler Toledo XP205

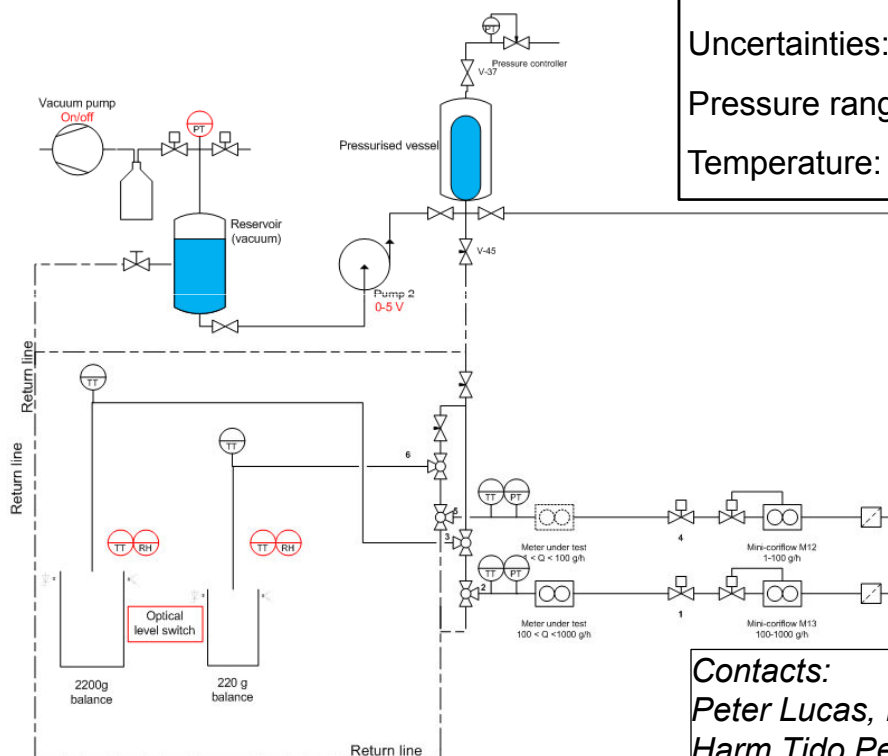
Contact:
Elsa Batista, ebatista@ipq.pt

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Micro Flow Facility – Gravimetric setup

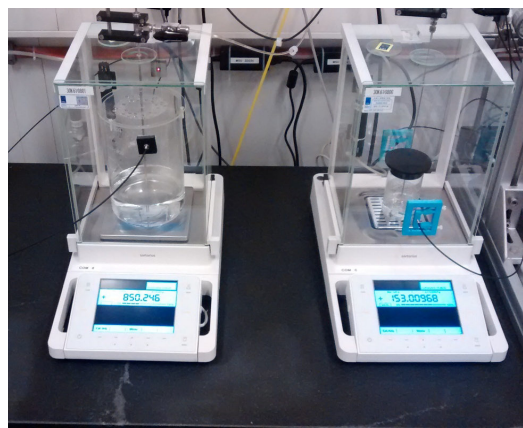
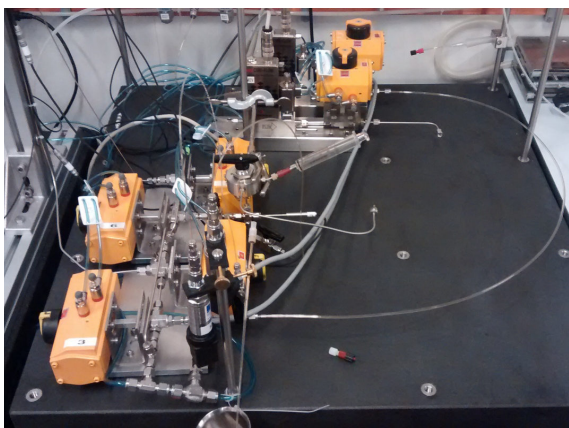


Flow rates: 16 ml/min – 4.2 μ l/min
Uncertainties: 0.06 % - 1.4 %
Pressure range: 0 bar – 5 bar
Temperature: ambient (20 °C)

Contacts:
Peter Lucas, PLucas@vsl.nl
Harm Tido Petter, HPetter@vsl.nl

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Micro Flow Facility – Gravimetric setup



Flow rates: 16 ml/min – 4.2 μ l/min

Uncertainties: 0.06 % - 1.4 %

Pressure range: 0 bar – 5 bar

Temperature: ambient (20 °C)

Contacts:

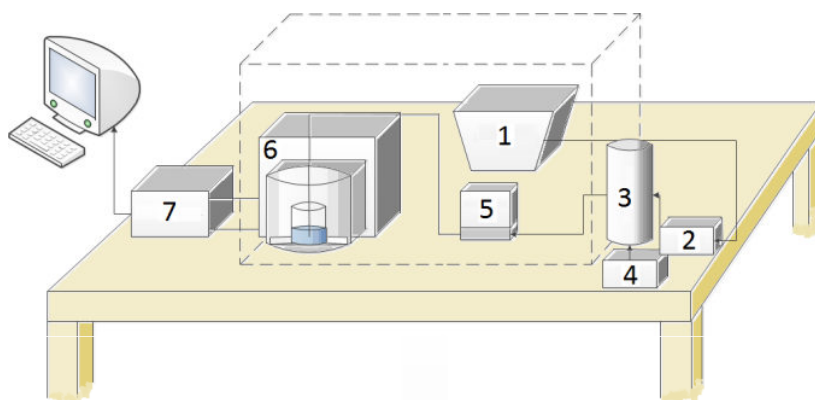
Peter Lucas, PLucas@vsl.nl

Harm Tido Petter, HPetter@vsl.nl

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Micro Flow Facility – Gravimetric setup



- (1) reservoir
- (2) degasser
- (3) pressure driven pump
- (4) compressor
- (5) flow meter
- (6) balance
- (7) balance electronics

Flow rates: 16 ml/min – 100 nl/min

Uncertainties: 0.05 % - 0.6 %

Pressure range: 0 bar – 5 bar

Temperature: ambient

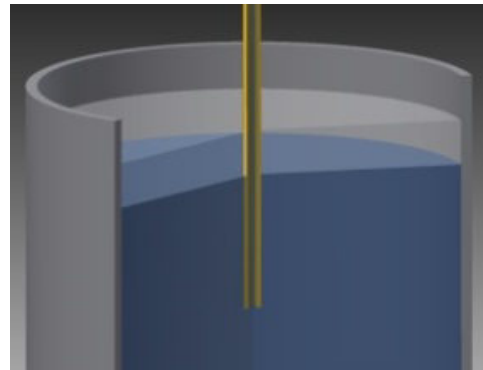
Contact:

*Anders Koustrup Niemann,
aknn@teknologisk.dk*

Lübeck, 24.09.2014

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Micro Flow Facility – Gravimetric setup



Flow rates: 16 ml/min – 100 nl/min

Uncertainties: 0.05 % - 0.6 %

Pressure range: 0 bar – 5 bar

Temperature: ambient

Contact:

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aknn@teknologisk.dk*

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Micro Flow Facility – Gravimetric setup

Influence factors

- Degassing water
- Priming the tubing and the flow meter under test
- Flow rate stability
- Buoyancy correction of the delivered water
- Buoyancy correction of the beaker
- Evaporation (saturated air or oil layer)
- Buoyancy correction due to the immersed tube into the water
- Jet force out of the immersion tube
- Linearity of the balance
- Drift of the balance

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Micro Flow Facility – Gravimetric setup

Characteristics



	METAS	DTI	CETIAT	IPQ	VSL
Flow rate range	1 ml/min – 100 nl/min	16 ml/min – 100 nl/min	133 ml/min – 16 µl/min	10 ml/min – 50 nl/min	16 ml/min – 4.2 µl/min
Uncertainty (k = 2)	0.1 - 0.6 %	0.05 - 0.6 %	0.04 – 1 %	0.15 - 6 %	0.06 - 1.4 %
Water temperature	Ambient	Ambient	10 - 50 °C	Ambient	Ambient
Pressure range upstream DUT	0 – 2.5 bar	0 – 5 bar	0 – 10 bar	0 – 2 bar	0 – 5 bar
Flow generator					
Water collection					

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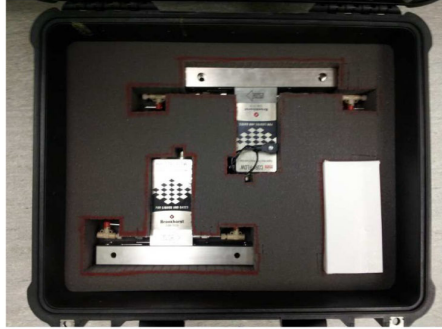
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Validation of primary standards by means of inter comparison

- Research inter-comparison for small liquid flow rates from 10 ml/min down to 10 µl/min (task 1.1)
 - completed
- Research inter-comparison for very small liquid flow rates from 100 µl/min down to 10 nl/min (task 1.4)
 - Starting in January 2014

Research inter-comparison for small liquid flow rates from 10 ml/min down to 10 μ l/min

■ *Transfer standards (2 Coriolis meters: M12P and M13)*



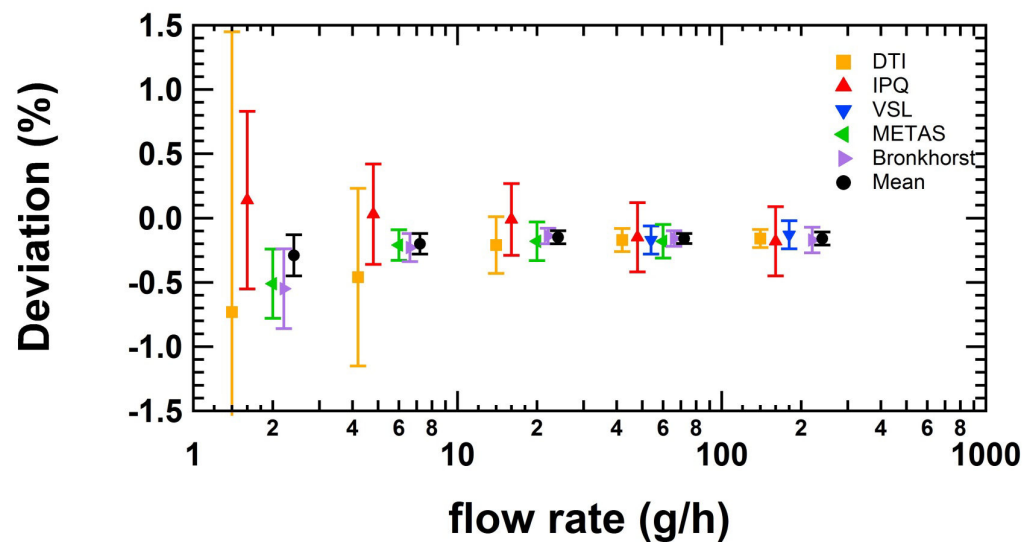
Research inter-comparison for small liquid flow rates from 10 ml/min down to 10 μ l/min

■ *Protocol*

- Flow through the meter 30 min:
 - ☞ Aiming to degas the water in the meter
- Performing a zero:
 - ☞ Aiming to prevent environmental effects
 - Liquid pressure and temperature influence,
 - Piping influence,
 - Ambient condition influence,
 - Long term drift of the meters.
- Realize tests:
 - ☞ Upstream pressure: 0,5 to 2,5 bar
 - ☞ Water temperature: 20 °C +/- 1 °C
 - ☞ M13 : 600 and 200 g/h
 - ☞ M12P : 200; 60; 20; 6 and 2 g/h

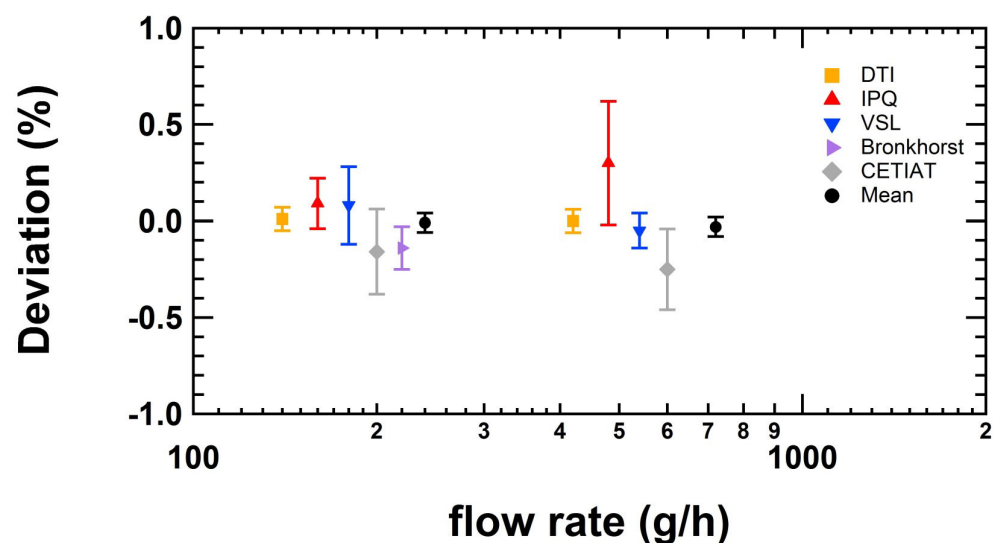
Research inter-comparison for small liquid flow rates from 10 ml/min down to 10 μ l/min

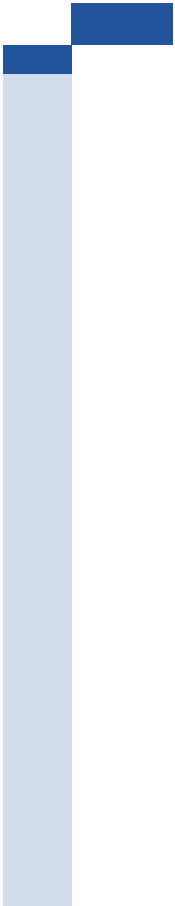
Results Coriolis flow meter M12P



Research inter-comparison for small liquid flow rates from 10 ml/min down to 10 μ l/min

Results Coriolis flow meter M13





Micro Flow Facility – metrological infrastructure for low flow rate testing

Testing and calibration of

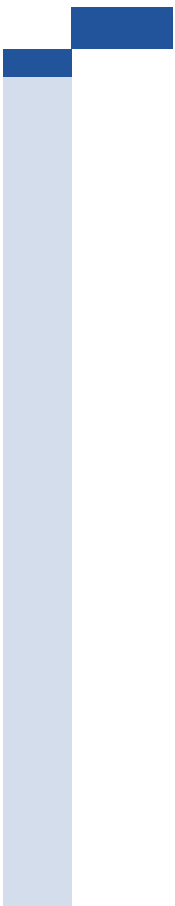
- Flow meters
- Flow generators
 - Syringe pump
 - Peristaltic pump
 - Insulin pump

Within this infrastructure it is possible to perform calibrations for different viscosities, temperatures and back pressure.

**“Assessment of Flow Meters and Drug Delivery Devices”
(Elsa Batista, IPQ)**

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Micro Flow Facility – metrological infrastructure for low flow rate testing

Other measurement principles

**“Flow Source Based on Expansion Principle as Primary Standard for Flow rates above 10 nL/min”
(Peter Lucas, VSL)**

**“An Optical Measurement Method for Flow Rates above 10 nL/min”
(Martin Ahrens, FH Lübeck)**

Lübeck, 24.09.2014

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Micro Flow Facility – Gravimetric setup

Contacts



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Elsa Batista, ebatista@ipq.pt



*Peter Lucas, PLucas@vsl.nl
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Questions ?



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