From device testing to calibration guidelines

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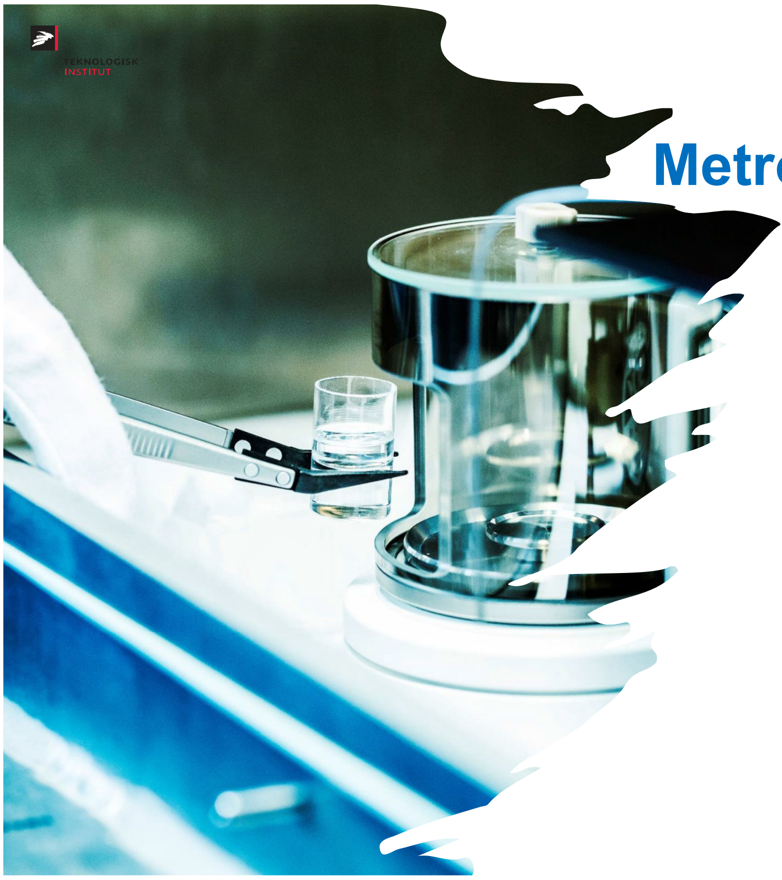
EMPIR
EURAMET
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

domestic water meter

Insulin pump



Metrology for Drug Delivery II - Overview

The overall objective of this project is to enable traceable measurements of the volume, flow rate and pressure of existing drug delivery devices (and other medical devices, like infusion pump analysers and organ on a chip) and in-line sensors that work at a flow rate lower than 100 nL/min. This project will also investigate fast changing flow rates, liquid mixing behaviour and occlusion phenomena in multi-infusion systems in order to improve the dosing accuracy in each infusion line.

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

Needs and motivation

PATIENT SAFETY

- **Infusion therapy** → Main form of therapy in health care.
- **Deviations** in medication dose into the patient bloodstream can have a **dramatic effect** leading to severe health damage or death
- Wide range of applications uses microfluidic solutions (infusion of vasoactive drugs, multi-infusion therapy, pre-term babies therapy, organ-on-a-chip technology, etc.).

The increasing implementations of novel microfluidic solutions in healthcare will require the development of a metrological infrastructure for validating quality and reproducibility.

Crucial for patient safety
and
to advances in:

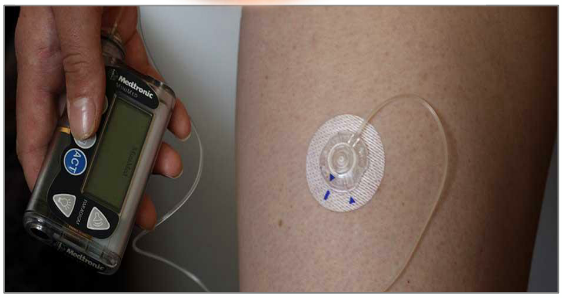
- ✓ microfluidics and organ-on-a-chip faithfull reproduction of multi-organ functions
- ✓ reproducibility and accuracy of multi-infusion therapies
- ✓ reliability of drug delivery devices

Work package 3

OBJECTIVES

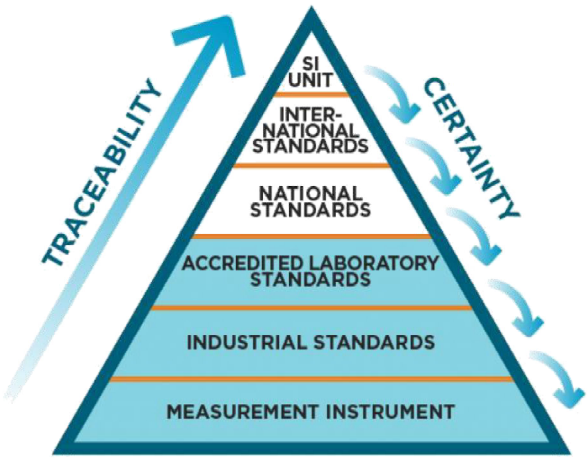
Development of new calibration procedures of existing medical devices and development of a microchip pump.

- **Identify the metrology infrastructure** for drug delivery devices and multi infusion systems and select devices for test.
- Develop and validate **calibration procedures** for "Flow measurements" for drug delivery devices and on-chip flow micropump demonstrator.
- Fabricate and characterize a novel on-chip flow micropump as a **transfer standard**

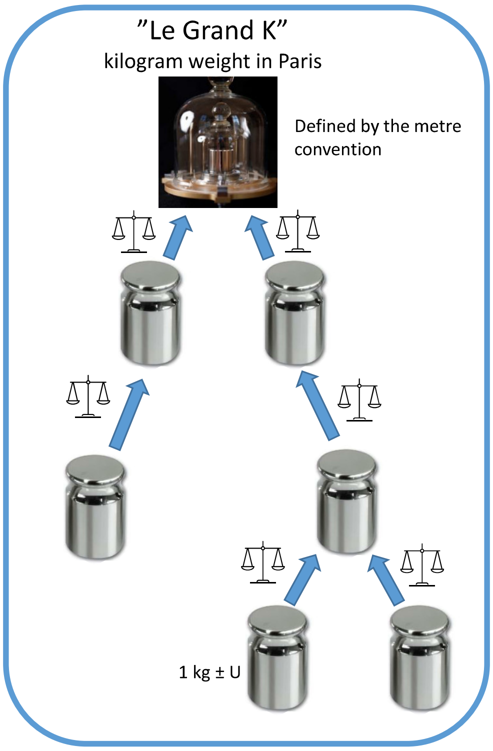


Metrology example 1

- Metrology is the scientific study of measurement. It establishes a tracebility chain to a commonly agreed reference for all basic units



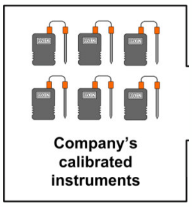
Metrological infrastructure on Mass



Metrology example 2

Traceability chain

U = 0.5 K

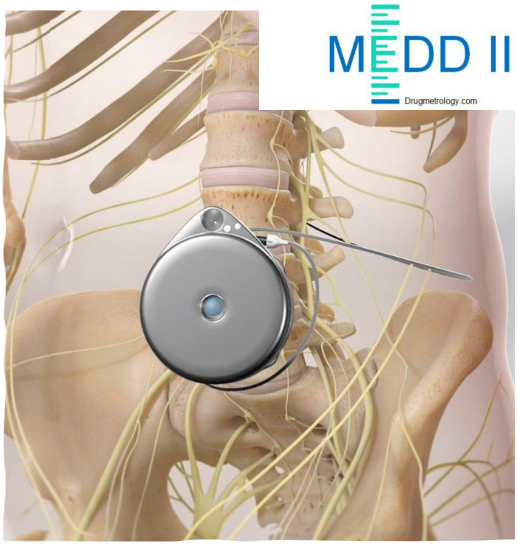


Increasing uncertainty

Medical Devices

Flow rate is a crucial parameter

- Implantable pain pump (≈ 20 µL/hr)
- Insulin pump (≈ 10 µL/hr)
- Syringe pump (> 0.1 mL/hr)
- Infusion device analyser (IDA)

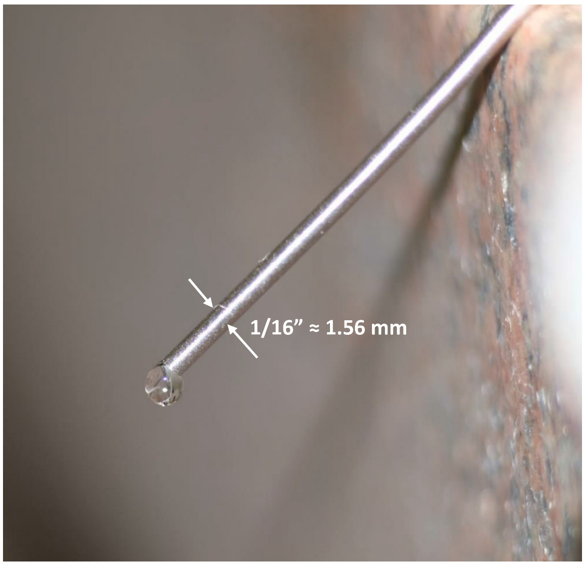


Microflow sizes
- Gravimetric method

- **Flow rates from 16,6 µL/min and down to 15 nL/min => 1000 µL/h down to 0.9 µL/h**

Flow rate **16,6 µL/min**,
time to get the droplet: **18 sec**

Flow rate **15 nL/min**,
time to get the droplet: **5.6 hours**



Gravimetric calibration method

Steady flow:

$$Q_{vol} = \frac{V_{delivered}}{\Delta time}$$

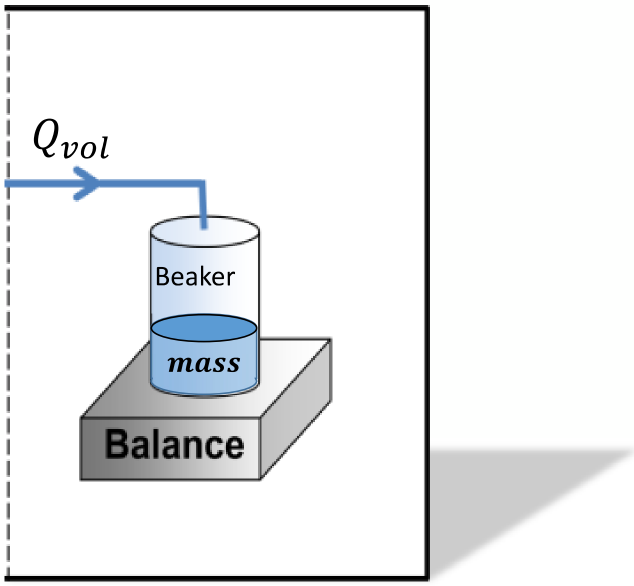
Most medical devices specifies flow rates as volume flow

$$V_{delivered} = V_{finish} - V_{start}$$

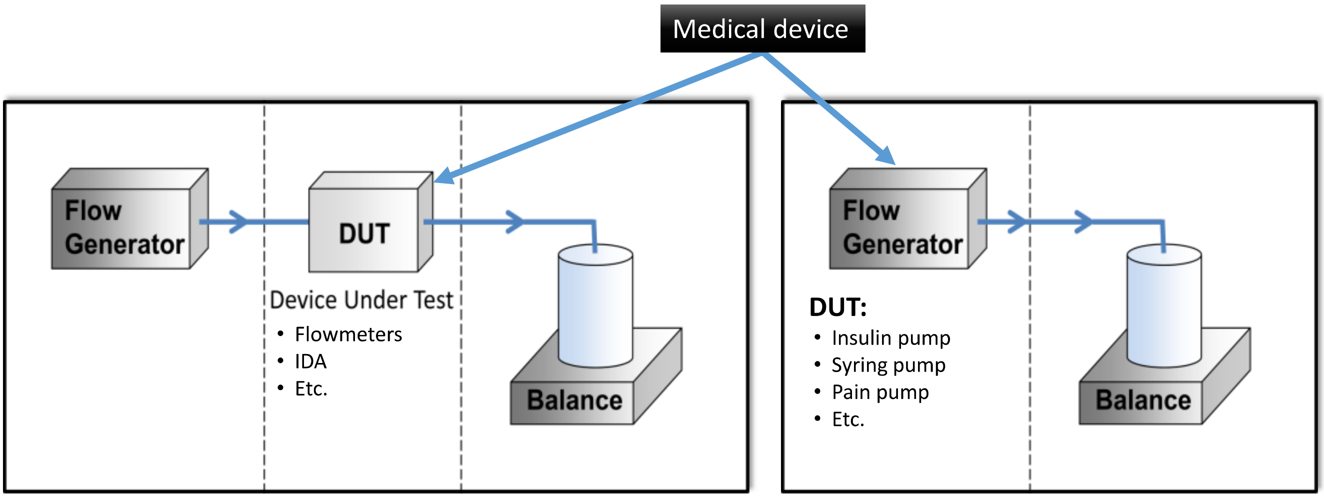
$$\Delta time = t_{finish} - t_{start}$$

$$V = \frac{mass}{density}$$

Density is a function of temperature and is different from liquid to liquid

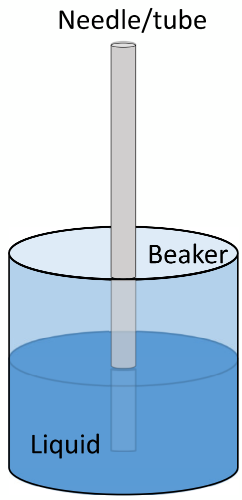


Calibration method



Parameters influencing the measurements

- Evaporation
- Water/liquid degassing
- Flow rate stability
- Timing/measurement of time
- Temperature stability
- Buoyancy correction of the delivered liquid
- Buoyancy correction due to the immersed tube into the liquid
- Jet force out of the immersion tube
- Stick/slip of needle and liquid
- Drift and Linearity of the balance
- Etc. Etc.



Tendencies

- why calibration guidelines are needed

- More and more microfluid solutions in a huge number of diverse applications
- More use of concentrated medications
  - Eg in pain treatment with pain pumps
- More electronical devices on the hospitals
  - More measurements and critical equipment
- More treatment at home with ”home care”

Why don’t we, then, see more accidental incidences?

- Awareness on the limitations of the devices e.g., accuracy
- The patient is surveilled on more parameters e.g., during surgery
  - Pulse, blood pressure, visually, blood gases, etc.
- Well educated and trained personnel
- Treatment response is very different from patient to patient

Thank you for your attention

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