MeDD

Metrology for Drug Delivery

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Overview

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Overview results – today's program MeDD Part I & II

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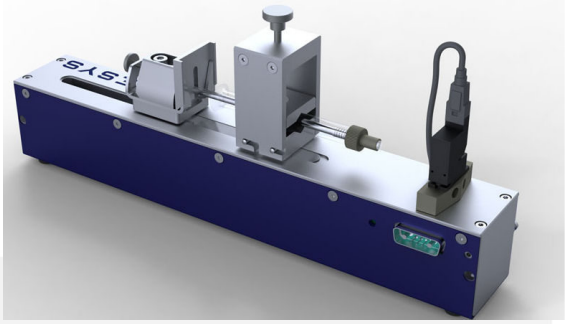
Motivation

In various studies infusion technology is considered a technology with underestimated risks due the following challenges:

- Setting and controlling ultra-low flow rates (< 1 ml/h)
- Setting and controlling the outflow concentration for multi-pump infusion
- Drug delivery device characteristics of system not well known (start-up delay, compliance, flow stability, impact operating conditions)

Motivation

Low to ultra-low flow rates



- Applications
  - Drug delivery by means of implanted infusion pumps (e.g. Tricumed IP 2000V down to 0.01 mL/h)
  - Drug delivery for patients with fluid restrictions (down to 0.1 mL/h)
  - Critical drug delivery, e.g. anesthetics and vasoactive drugs (down to 0.1 mL/h)
- Difficult to measure and control flow rate
  - Technology not applicable (e.g. 50 mL syringe for 0.1 mL/h)
  - Technology in development (e.g. implanted infusion pumps)
  - Metrological infrastructure not in place
    - No traceable calibrations possible for flow rates < 0.5 mL/h
    - Calibration facilities below 100 mL/h not validated
    - Current commercial devices not validated

Motivation

Multi-pump infusion

- Applications
  - Greater patient comfort
  - Better hygienic
  - Lower risk of vein damage
- Difficult to control individual flow rates (effective concentration drugs)
  - Long start up time to reach steady flow
  - No direct control on flow rates (flow rates follow from pump set points)
  - Measurement of individual infusion lines is difficult

Motivation

Device characteristics

- Effective flow rate, stability and start up time depend on the complete system (pump plus accessories)
- Dependency on fluid and process parameters? (temperature, viscosity, flow rate, …)
- No standard protocols application of infusion devices (there are existing written standards w.r.t. manufacturing and maintenance of infusion devices, e.g. IEC 60601-2-24)

Motivation

Clinical relevance

- A flow rate of ~ >0.5 mL/h can distort the fluid balance of a neonate with severe consequences
- Implanted drug delivery devices (insulin pumps, pain treatment) are stand alone devices
- Critical drug delivery, 5% uncertainty allowed for:
  - Flow rate variations, e.g. in vasoactive drugs (control heart rate and blood pressure) correspond to variations in blood pressure and heart rate
  - Over or undershoots can be potentially dangerous, e.g. vasocactive drugs, anesthetics, blood thinning and insulin

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Goals

- Metrological tools that can facilitate improvements in drug delivery
  - Validated primary standards for liquid flow rates from 0.1 µL/h to 1000 mL/h
  - Traceable calibration services for flow rates from 0.1 µL/h up to 1000 ml/min (uncertainty < 1 ~ 2 %)
  - Metrological assessment (commercial) flow meters (applicability in (research) of infusion)
- Assessment drug delivery devices
  - Various show cases with the developed infrastructure
  - Review calibration and testing methods
- Input written standards and protocols

Traceability

Guarantee sound and low uncertainty

- Calibrating occurs by comparing a device with a standard with accepted uncertainty
- The SI units are the start of the calibration process and are realized with primary standards (calibration facilities)
- Traceability implies an unbroken chain (of calibrations) to the SI unites
- National Metrology Institutes maintain and develop the primary standards
- Why do we need traceable measurements
  - Rigid uncertainty analyses
  - Guarantee for low uncertainty

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Consortium

- National Metrology institutes: VSL (NL), CETIAT (FR), CMI (CZ), DTI (DK), IPQ (PT), METAS (CH), UME (TR)
- University Medical Centre Utrecht (NL)
- University of Lübeck (DE)
- Consortium of Metrology institutes capable of setting up the required infrastructure for traceable flow rate calibrations needed by the Health care industry (and other industries)
- EMRP Grant (2012, Health call)
  - Metrology-focused European programme
  - Accelerate innovation and competitiveness in Europe whilst continuing to provide essential support to underpin the quality of our lives

EMRP European Metrology Research Programme Programme of EURAMET

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Presenting the results of MeDD

Today's program Part I and II

- Clinical relevance (Annemoon Timmerman - UMC)
- Calibration facilities based on the gravimetric principle (Hugo Bissig - METAS)
- Calibration facility based on volumetric expansion (Peter Lucas - VSL)
- Calibration facility based on front tracking in a capillary (Martin Ahrens – FH Lübeck)
- Preliminary results assessment drug delivery devices (Elsa Batista - IPQ)
- Dosing errors in multi-infusion (Roland Snijder – UMC)

Outlook

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- Metrological infrastructure developed for liquid flow rates ranging from ~ 0.1µL/h to 100 mL/h
  - Traceability for infusion technology (and other sectors)
  - Facilitate development of and research in infusion devices (and other sectors)
- Calibration of various infusion devices and flow meters
  - Input 'Best Practice Guide' infusion technology
  - Input written standards dealing with infusion
  - Assist hospitals with uncertainty calculations


VSL
Thank you for your attention!
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