The research leading to the results discussed in this report has received funding from the European Metrology Research Programme (EMRP). The EMRP is jointly funded by the EMRP participating countries within Euramet and the European Union.

MeDD
Metrology for Drug Delivery
Peter Lucas (VSL) Project coordinator

8th Workshop on low flows in medical technology
September 2014, Lübeck, Germany

Overview
Motivation
Goals
Consortium
Overview results – today’s program MeDD Part I & II
Motivation

In various studies infusion technology is considered a technology with underestimated risks due to 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)

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 \( >0.5 \text{ mL/h} \) can distort the fluid balance of a neonate with severe consequences
- Implanted drug delivery devices (insulin pumps, pain treatment) are standalone 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. vasoactive drugs, anesthetics, blood thinning and insulin

MeDD

Goals

- Metrological tools that can facilitate improvements in drug delivery
  - Validated primary standards for liquid flow rates from 0.1 \( \mu \text{L/h} \) to 1000 \text{mL/h}
  - Traceable calibration services for flow rates from 0.1 \( \mu \text{L/h} \) up to 1000 \text{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 units
- National Metrology Institutes maintain and develop the primary standards
- Why do we need traceable measurements
  - Rigid uncertainty analyses
  - Guarantee for low uncertainty

MeDD

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
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

- 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
Thank you for your attention!

www.drugmetrology.com