

MeDDII - Aims, Partners, Methods

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Coordinator



14th Workshop Low Liquid Flows in Medical Technology

EMPIR 



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

EMPIR – MeDDII – 18HLT08



Call: 2018 Health

JRP name: Metrology for drug delivery

JRP reference: 18HLT08 MeDDII

Total budget: ~ 1,7 M€

Total labour: ~200 MM

Duration: 36 months (6 month extension)

Start date: June 2019

Coordinating Organisation: IPQ

Partners - 9 NMIs/DIs, 5 universities, 2 manufacturers. 11 countries

Colaborators – 40

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**



Needs and motivation



- **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.).

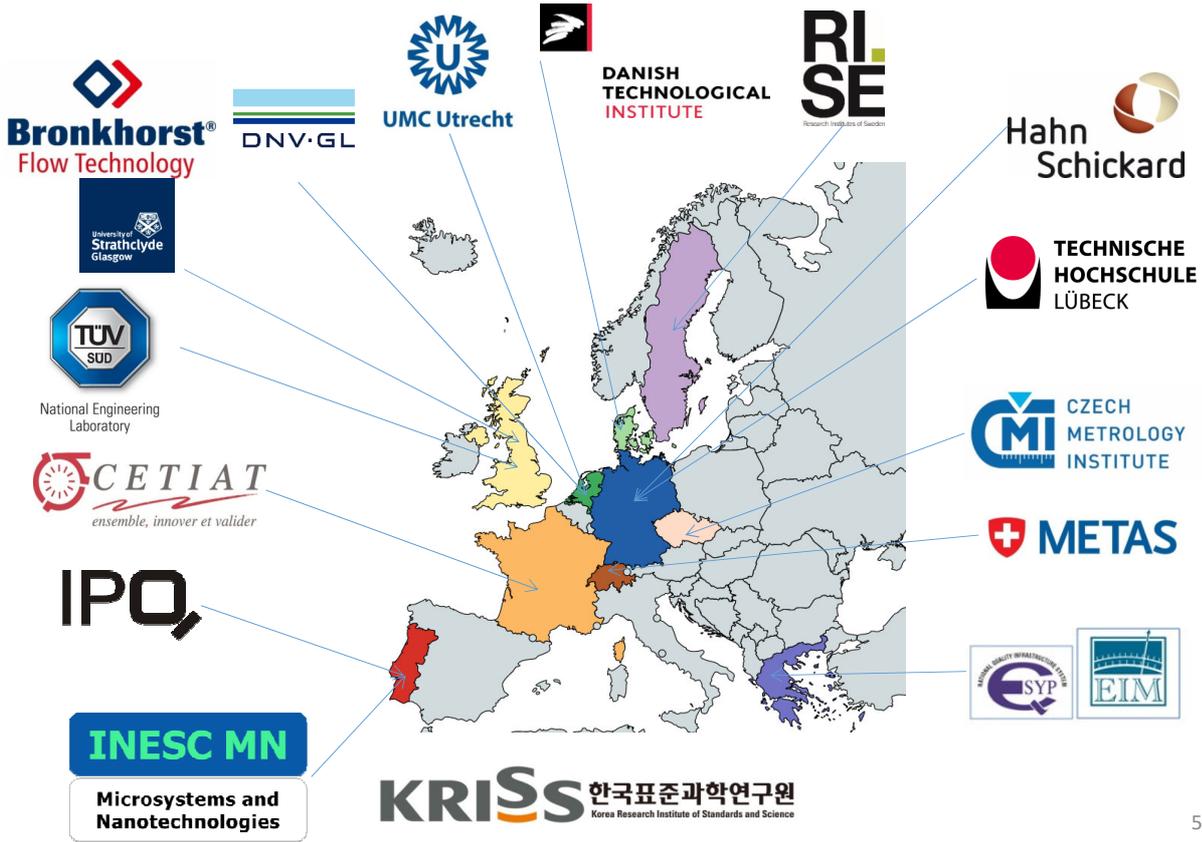
Validated metrological infrastructure for traceable measurement and calibration

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

Crucial for patient safety and to advances in:

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

Consortium

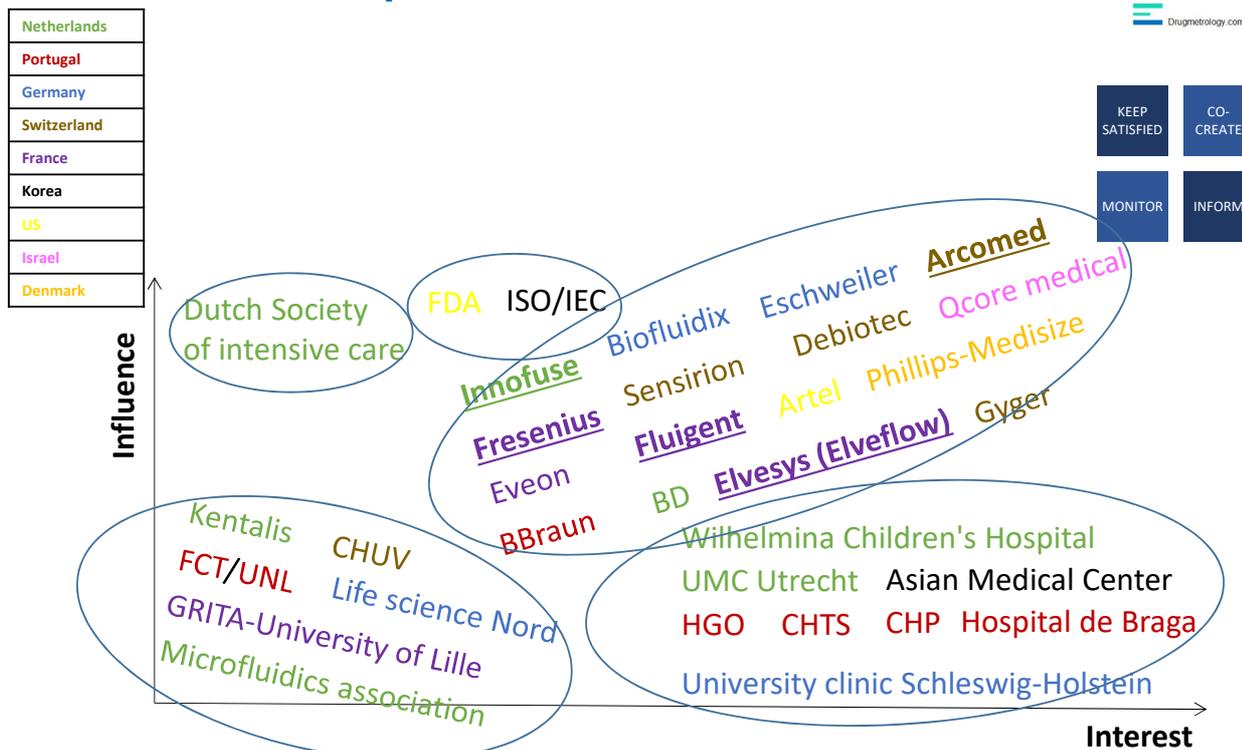


Consortium



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Stakeholder map 18HLT08 MeDDII



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Regulation: EU, national medical Surveillance Authorities:

"our project facilitates the control of drug delivery devices described in the medical directive 93/42/EEC"

Hospitals and end users:

"our measurement will allow traceability and accuracy of drug delivery devices used in hospitals leading to better measurements and better health treatments"

Standardisation:

"our test and calibration procedures can help the revision of standards and the development of new ones in the field of drug delivery devices"

Instrument manufacturers:

"our reference facilities support sales of your instrumentation, by proving its accuracy and reliability"
"our prototype instrumentation can be the basis for your future instrumentation and sales"

Academia:

"our new developed technology can help students and universities"

- WP1 - Development of metrology infrastructure for ultra-low flow rates
- WP2 - In-line measurement of physical and thermodynamic properties
- WP3 - Development of a microchip pump and new calibration procedures of existing medical devices
- WP4 - Design and characterization of a multi-infusion system
- WP5 – Delivering Impact
- WP6 - Coordination

WP1 OBJECTIVE 1

Development of metrology infrastructure for ultra-low flow rates

- Upgrade existing flow facilities and/or develop new techniques for measurement of **flow rates down to 5 nL.min⁻¹** for steady and fast transient flows.
- Establish robust and realistic **uncertainty budgets**. Target uncertainties at 1 % ($k = 2$) for steady flows and 2 % ($k = 2$) for fast transient flows.
- **Validate primary standards**, needed for the characterization of drug delivery devices and multi infusion systems.

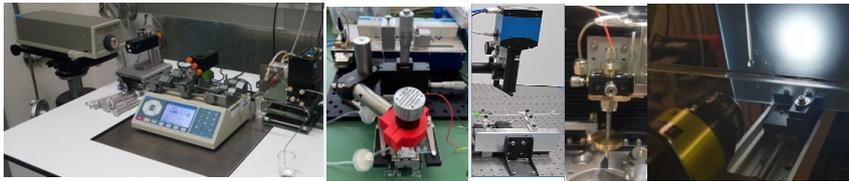


National Engineering Laboratory

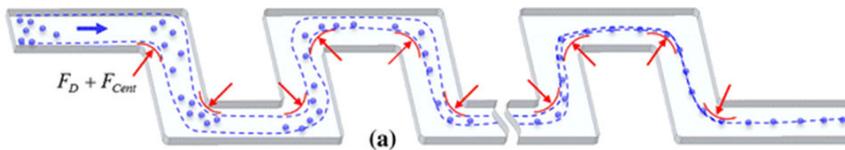
Development of metrology infrastructure for ultra-low flow rates

- ☐ Comprehensive report produced on the new calibration methods for steady and dynamic flow rates

- ☐ report freely available on the MeDD II website for download - D1 www.drugmetrology.com/the-first-deliverable-of-project-medd-ii-is-now-available/



- ☐ Intercomparison exercise to validate the new techniques & uncertainties will start almost completed



Work Packages

WP2 OBJECTIVE 2

In-line measurement of physical and thermodynamic properties

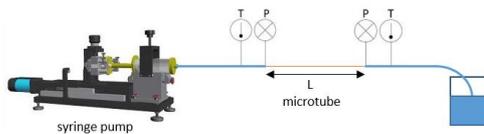


- Upgrade the existing flow facilities of the participant NMIs in order to enable **traceable inline measurement** of the dynamic viscosity of Newtonian liquids, as a function of the flow rate and pressure difference, with a target uncertainty value of 2 % ($k=2$).
- Characterize flow devices for in-line measurements of **physical and thermodynamic properties**. These properties are needed to determine the proportion of components of a mixture of liquids.

In-line measurement of physical and thermodynamic properties

- **Development of primary standards for in-line measurements of dynamic viscosities.**
 - The facilities are currently developed and will be validated with reference liquids (traceable density and dynamic viscosity). Validation measurements with saline solutions and glucose solutions (various concentrations) and mixtures of them.

- **Pipe viscometer**



- pipe viscometers are in place
- start measurements for characterization of pipe viscometer
- report template is available
- validation procedure with different liquids starts in September 2021

Work Packages

WP3 OBJECTIVE 3

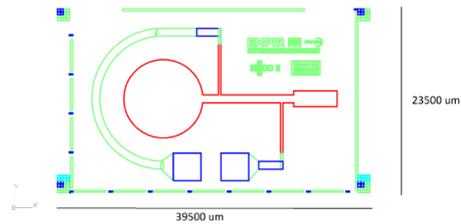
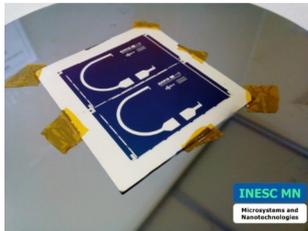
Development of a microchip pump and new calibration procedures of existing medical devices



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

Development of a microchip pump and calibration procedures

- Development and characterisation of a prototype microchip flow pump
 A design for a micro fluidic pump has been developed and a numerical prototype of the pump has been tested to prove the design. A physical prototype is concluded.



- Development of calibration procedures for drug delivery devices and the microchip flow pump

Tests are completed. The data is under analysis.



Work Packages

WP4 OBJECTIVE 4

Design and characterization of a multi-infusion system



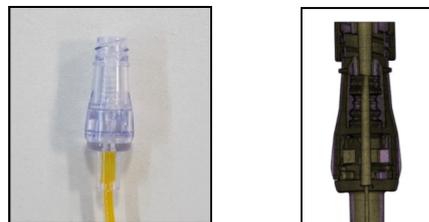
- Develop **multi-infusion setups** to investigate mixing and drug concentration at the patient's point of medication entry.
- Extend and validate a **predictive model** for multi-infusions.
- Develop a **Best Practice Guide** providing methodologies to build/assemble/use multi-infusion set-ups to guarantee the most effective dosing of drugs and fluids to the patient.

Design and characterization of a multi-infusion system

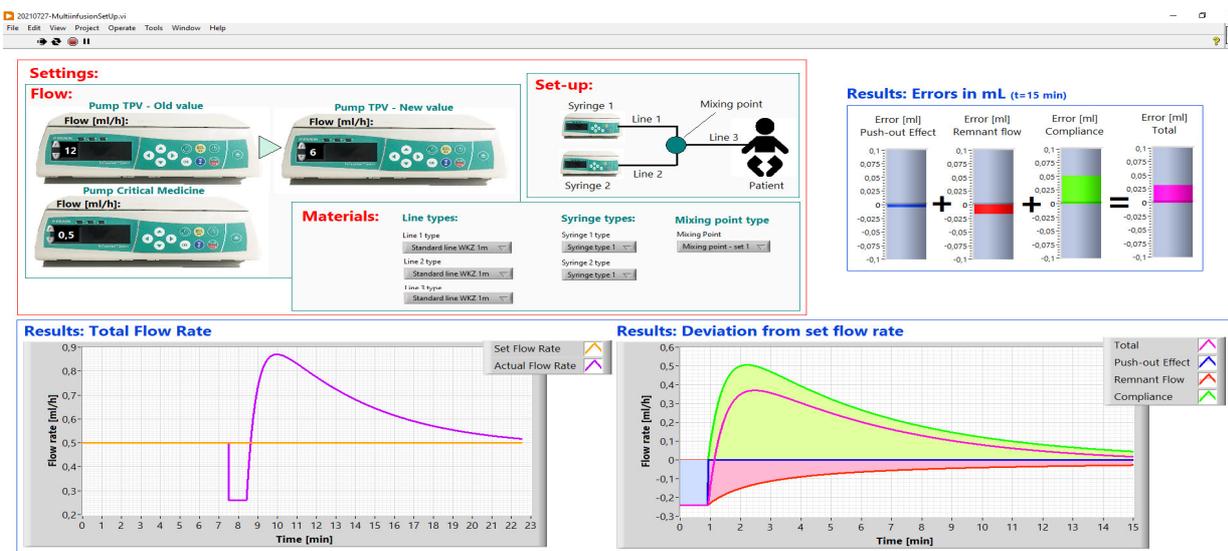
- ❑ **Multi-infusion setups were built in Lübeck and in Utrecht.** The component list was adapted. The setup record was adapted accordingly. Sensor integration is now on schedule. The work on prototypes started, as well as the flow cell development



- ❑ **Extend and validate a predictive model for multi-infusions:** Air bubbles and viscosity have been included in the model by UMC Utrecht. CFD calculations were performed. The incorporation of check valves in the model has also started.



Impact application from Task 4.3 artist impression



NEW GUIDANCE DOCUMENTS

- Draft **new calibration procedures and guides** of drug delivery devices and multi infusion systems



INPUT FOR THE REVISION OF REFERENCE DOCUMENTS

- Promote **Knowledge transfer and exchange** with International Standards Committees.



Standardization contacts established so far

ISO TC	Standard	Status	Representative
ISO TC 84	ISO 7886-2	Completed	Elsa Batista Anders Niemann
ISO TC 210	ISO TR 24971:2019	Completed	Maria do Céu Ferreira
TC62/SC62D/MT 23	ISO/IEC 60601-2- 24	Under revision	Elsa Batista and Hugo Bissig
AAMI	TIR 101 and TIR 111	Under revision	Elsa Batista
ISO TC48/WG4	FDIS ISO 8655-1,6 and 9	Under revision	Elsa Batista and Zoe Metaxiotou
ISO TC48/WG5	DIS ISO 23783-1, 2 and 3	Under revision	Elsa Batista and Sabrina Kartmann
ISO TC48/WG3	ISO/FDIS 22916 CD ISO 10991:2009 ISO/AWI TS6417	Under revision	Elsa Batista, Hugo Bissig and Vania Silverio
ISO/TC 150/SC 6	DIS ISO14708-4	Under revision	Oliver Bükér

WP 5 - Impact



TRAINING

- Present the project results in workshops for end users and metrologists



DISSIMINATION

- To disseminate the project information and outcomes in conferences and publications



Information dissemination



- 27 Presentations in conferences
- 8 publications in international magazines
- 4 newsletters published on the webpage (every 6 month)
- Online workshop on measurement methods organized by CETIAT was held virtually in November 2020 with more than 70 participants

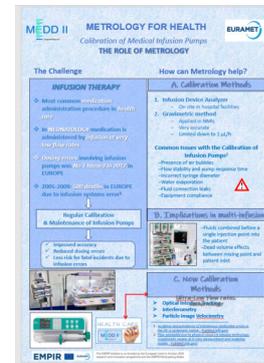


www.drugmetrology.com

<https://zenodo.org/communities/medd2>

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- ❑ Two case studies published on the webpage
 - A case study on COVID-19 crisis & Emergency Practices with Infusion Pumps in ICU. The role of Metrology. Our project and this document was recognized as relevant by the European Commission (EC) and is now also available in the EC [website](#)
 - [Measurement error: two opposite definitions](#)
- ❑ [Best Practice guide and flyer on Calibration of Medical Infusion Pumps published on the webpage.](#)
- ❑ Video on traceability of syringe pumps on the webpage <https://youtu.be/Fws7J1Lu2XQ>



THANK YOU

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