METROLOGY for DRUG DELIVERY



Traceable pipe viscometers for in-line measurement of dynamic viscosities

18HLT08 MeDD II – WP2 Partners

14th Workshop Low Liquid Flows in Medical Technology Lübeck, Germany, September 15th, 2021



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

Agenda

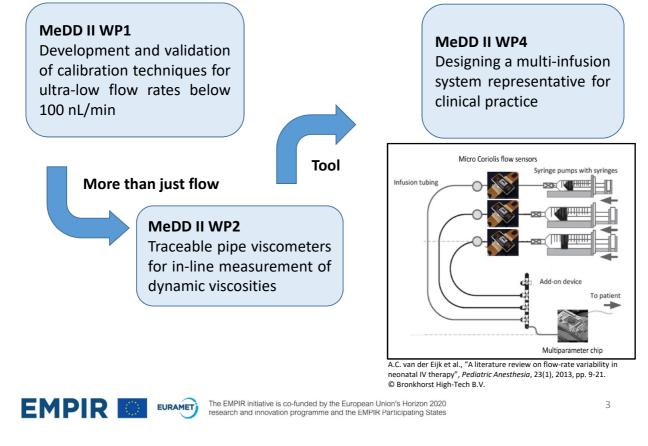
- ✓ 18HLT08 MeDD II WP2 Motivation
- ✓ 18HLT08 MeDD II WP2 Deliverables
- ✓ Traceable pipe viscometer
 - Facility NEL
 - Facility RISE
 - Facility METAS
- ✓ Devices for in-line measurement of viscosity
- ✓ Validation pipe viscometer & devices
- ✓ Application: determination of mixtures of drugs
- ✓ Summary





18HLT08 MeDD II WP2 Motivation





18HLT08 MeDD II WP2 Deliverables



Task: Upgrading flow facilities for the in-line measurement of viscosity

Validation report on the primary standards developed for the in-line measurement of the dynamic viscosity of Newtonian liquids with a target uncertainty of 2 %.

Task: Characterisation of devices for in-line measurements

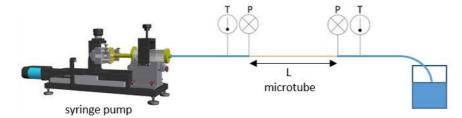
Report on the use of a calibrated microfluidic multi-parameter chip for the in-line measurement of pressure, viscosity and temperature



Traceable pipe viscometer



Scheme of the facilities (NEL, RISE, METAS)



Laminar flow regime

Determination of the inner radius of the micro-tube:

 $r_{exp} = \sqrt[4]{8 \eta L Q/(\pi \Delta P)}$, using water with known viscosity

Determination of the dynamic viscosity of the liquid:

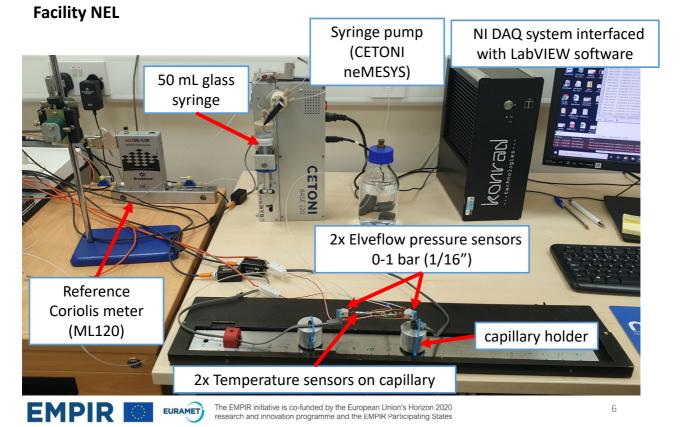
 $\eta = \pi r_{exp}^4 \, \Delta P / (8 \, L \, Q)$

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Traceable pipe viscometer



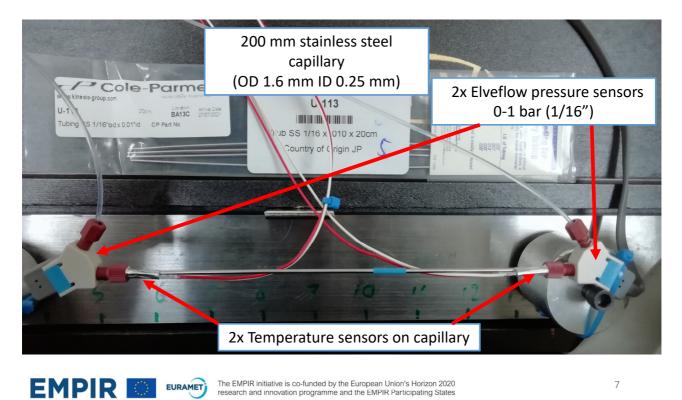
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Traceable pipe viscometer

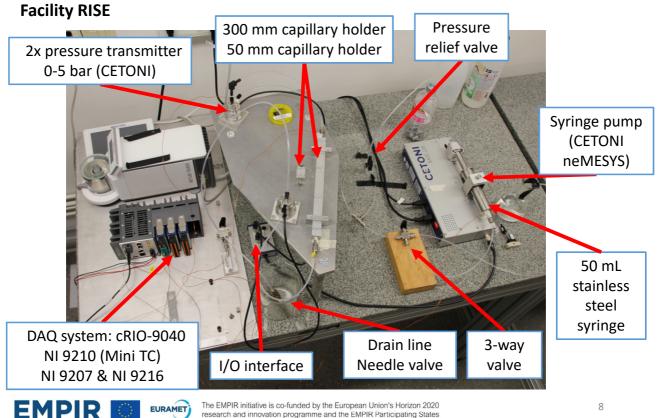


Facility NEL



Traceable pipe viscometer

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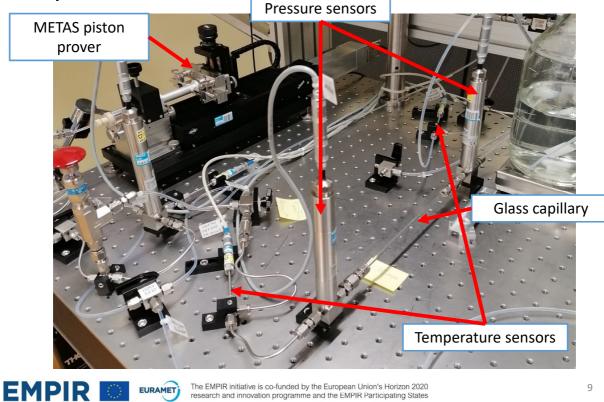
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MEDD II

Traceable pipe viscometer



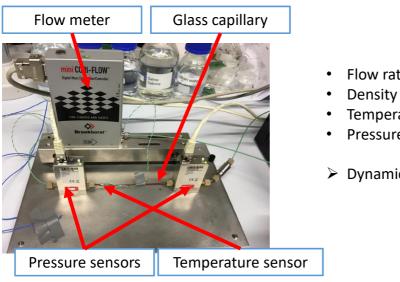
Facility METAS



Devices for in-line measurement of viscosity



Bronkhorst High-Tech B.V. Conventional Multiparameter Measurement System Technology Demonstrator (not commercially available)



- Flow rate
- Temperature
- Pressure
- > Dynamic viscosity

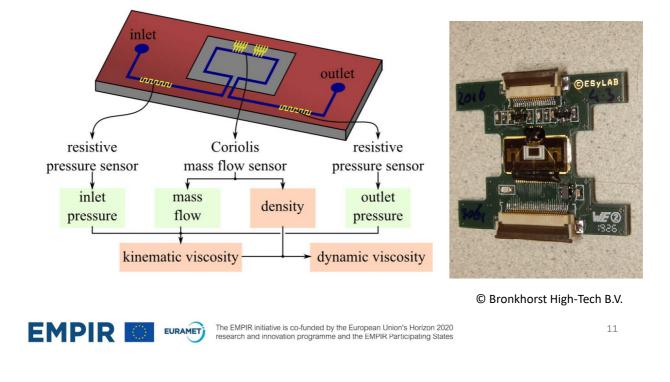
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Devices for in-line measurement of viscosity



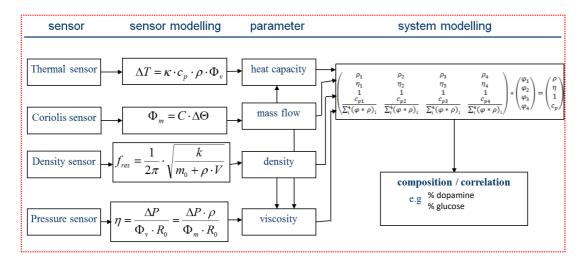
Bronkhorst High-Tech B.V. MEMS Multiparameter Measurement System Technology Demonstrator (not commercially available)



Devices for in-line measurement of viscosity



Bronkhorst High-Tech B.V. MEMS Multiparameter Measurement System Technology Demonstrator (not commercially available)



Mixtures of known drugs can be determined (WP4 Multi-Infusion Systems)

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Devices for in-line measurement of viscosity

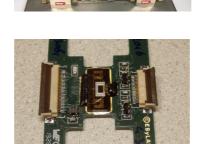


TrueDyne Sensors AG VLO-M1



Bronkhorst High-Tech B.V. Conventional Multiparameter Measurement System Technology Demonstrator (not commercially available)

Bronkhorst High-Tech B.V. MEMS Multiparameter Measurement System Technology Demonstrator (not commercially available)



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- Dynamic viscosity
- > Density
- > Temperature
- > Dynamic viscosity
- Density
- > Temperature
- ➢ Flow rate
- > Pressure
- > Dynamic viscosity
- > Density
- > Temperature
- ➢ Flow rate
- Pressure
- > Heat capacity

13

EDD II

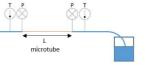
Validation pipe viscometer

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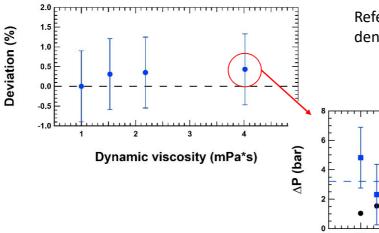


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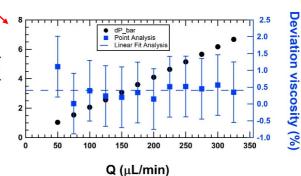
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Laminar flow regime



Reference liquids with traceable density and dynamic viscosity values



Validation pipe viscometer & Devices

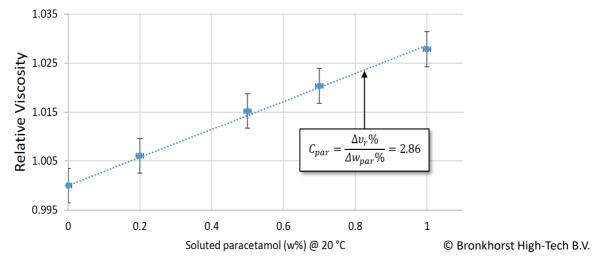
- Newtonian Liquids (T = $20 \degree C 27 \degree C$)
 - A Saline solution (0.9%)
 - B Glucose solution (10%)
 - C Glucose solution (20%)
 - D Sodium chloride solution (0.22%) and glucose (2.75%)
 - E Sodium chloride solution (0.22%) and glucose (5.55%)
 - F Sodium chloride solution (0.45%) and glucose (5.54%)
 - G Glycerol solution (52.04%)
 - H Glycerol solution (58.8%)
- Characterisation of the dynamic viscosity
 - by means of well established measurement techniques (including CMCs)
 - o by means of the newly developed pipe viscometers
 - by means of Rheometer

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- Characterisation of the density and thermal properties
 - The EMPIR initiative is co-funded by the European Union's Horizon 2020 EURAMET research and innovation programme and the EMPIR Participating States
- Application: determination of mixtures of drugs MEDD II

Dynamic viscosity measured with conventional measurement system; Paracetamol in DI water, from 0 to 1%.

(Preliminary results by technology demonstrator)



Paracetamol can be well distinghuished from water via viscosity the viscosity changes ca. 3% over the measurement range of 0 - 1% paracetamol



- (~ 0.87 mPa*s @ 23°C) (~ 1.14 mPa*s @ 23°C) (~ 1.54 mPa*s @ 23°C) (~ 0.87 mPa*s @ 23°C) (~ 0.94 mPa*s @ 23°C)
- (~ 1.02 mPa*s @ 23°C)
- (~ 4.80 mPa*s @ 23°C)
- (~ 7.40 mPa*s @ 23°C)



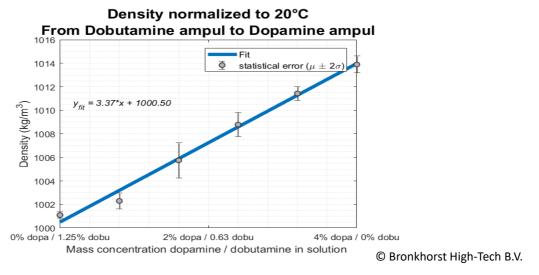




Application: determination of mixtures of drugs MEDD II



Density measured with conventional measurement system; From Dobutamine ampul to Dopamine ampul (Preliminary results by technology demonstrator)



Dobutamine can be well distinghuished from dopamine via density the density changes ca. 1.5% over the measurement range from dobutamine to dopamine

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research and innovation programme and the EMPIR Participating States



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Summary

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17

- Traceable pipe viscometer (NEL, RISE, METAS) are built for low flow rates
- Devices for in-line measurement of viscosity are commercially available or are currently developed for low flow rates
- Validation of pipe viscometer & devices is ongoing
- Important application is the determination of mixtures of drugs occurring in Multi-Infusion Systems
- Not limited to any fields of applications



