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Assessment of Flow Meters and Drug Delivery Devices

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Introduction

- With the development of science and nanotechnology, the measurement of fluid flow quantities is getting smaller, in the order of microliter per minute or even nanoliter per minute.
- In order to provide traceability to industry and laboratories, it was identified the need of developing primary standards for microflow measurement and to perform the assessment of drug delivery devices and flow meters already in the market.
- In the scope of the European Metrology Research Programme (EMRP) developed by the European Association of National Metrology Institutes (EURAMET) the project Metrology for Drug Delivery - MeDD was created in 2011.

MeDD

This project has the purposes:

- Developing a primary standard for flow measurements between 150 microliter per minute and 1 nanoliter per minute.
- Characterization of flow meters and flow generators already in the market.
- Assuring the traceability of the syringe pumps measurements used in drug delivery.

Collaborators of the project: CMI, CETIAT, DTI, METAS, IPQ, VSL, UME

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EMRP
European Metrology Research Programme
Programme of EURAMET

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EURAMET
European Association of National Metrology Institutes

Drug Delivery Devices

Drug delivery devices are used in clinical environmental for nutrition and hydration of patients and can also have therapeutically functions, namely drug delivery.

Infusion pumps

Used for delivery of small amount of liquid at low flow rate

Peristaltic pumps

Used for drug delivery at flow rates higher than 10 mL/h

Drug Delivery Devices

Relevant questions in therapeutics:

- Volume and flow rate
- Interference by using multiple pumps
- Administration lines
- Individual variables like density and viscosity of the used drug
- Interference between different drugs
- Human error

Drug Delivery Devices assessment tests

To test how the compliance and start up delay depend on several physical parameters, drug delivery devices and accessories. The flow rate error and flow rate stability are also studied. The following aspects are considered:

- accessories: infusion line, filter and check valve;
- pump types: syringe and peristaltic;
- syringe types: Omnifix and OPS;
- syringe volumes: 10 mL and 50 mL;
- operating conditions: viscosity, back pressure and temperature

$$\varepsilon = 100\% \frac{q_{pump} - q_{actual}}{q_{actual}}$$

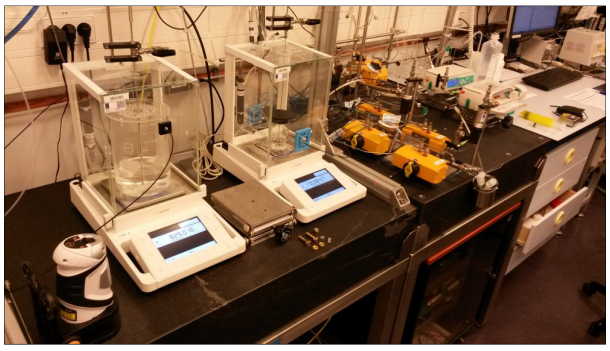
Other brands will be tested later.

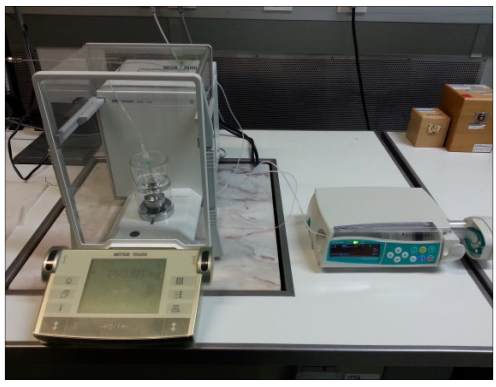
Insuline pump will be assessed.

Setups for the assessment tests

VSL and IPQ have performed measurements using the gravimetric method.

The set up and calibration methods used by IPQ are in accordance with standard IEC 60601-2-24, but includes evaporation and buoyancy correction.





Scenarios

- Pump with glass/rigid or with a standard syringe (OPS or Omnifix).
- Pump connected to a typical infusion line (1.5m) or with elongated infusion line (achieved by 1 time 1.5 m and 2 times 2 m infusion lines)
- Pump connect to a rigid line
- With a filter installed
- With a check valve installed
- Neonatology line is used

Syringe pump tested at 0,5 ml/h, 2 ml/h and 10 ml/h

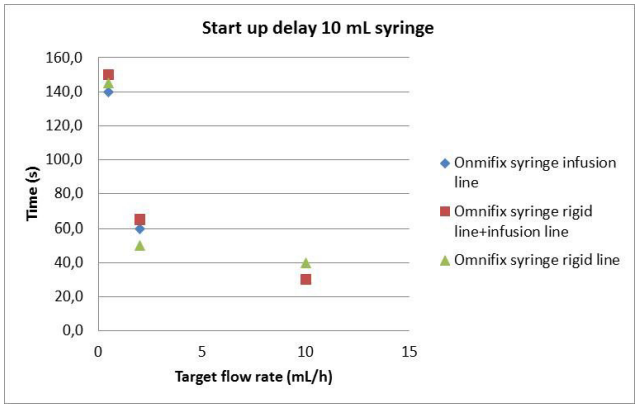
Peristaltic pump tested at 2 ml/h, 10 ml/h and 50 ml/h

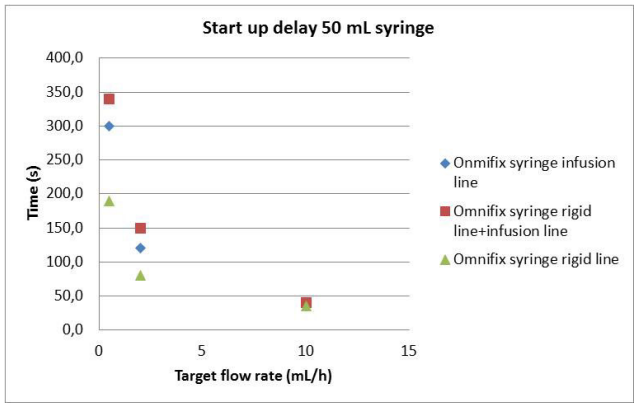
Drug Delivery Devices assessment tests

- Start up delay
- Compliance based on occlusion measurements
- Delay time in doubling the flow rate
- Impact of drug delivery accessories
- Impact of viscosity (2 and 4 times the viscosity of water)
- Back pressure dependency*
- Impact of temperature*
- Impact of model and procedure (reproducibility)*
- Flow rate stability and responds time to a step change in flow rate*

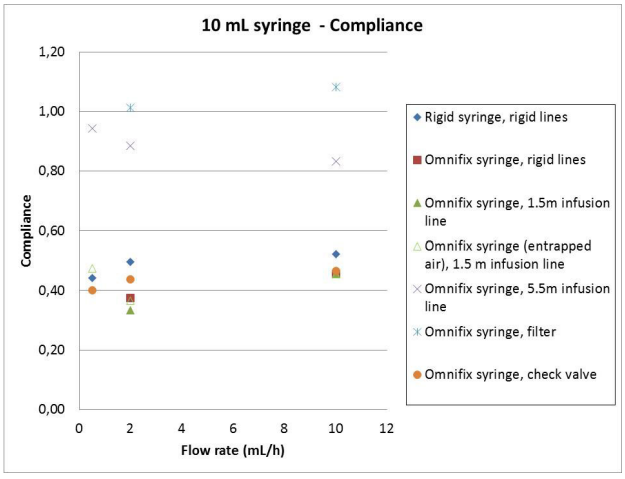
*** No results yet**

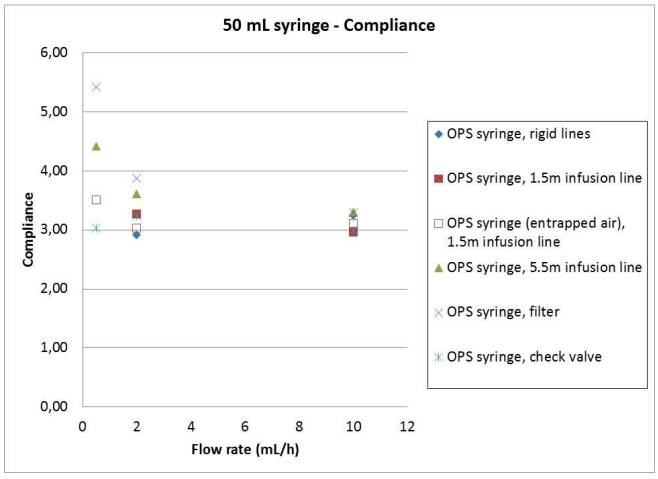
Start up delay – syringe pumps





Compliance based on occlusion measurements – syringe pumps

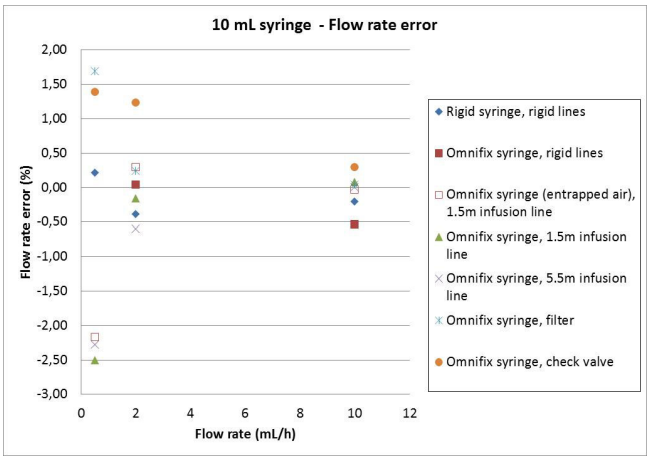


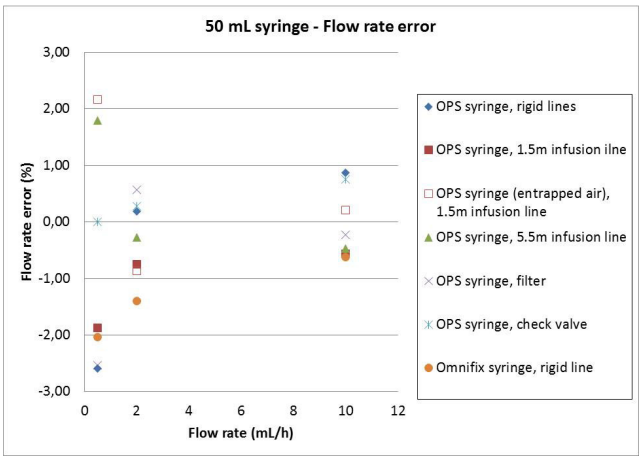


$$C = \frac{\Delta V}{\Delta p}$$

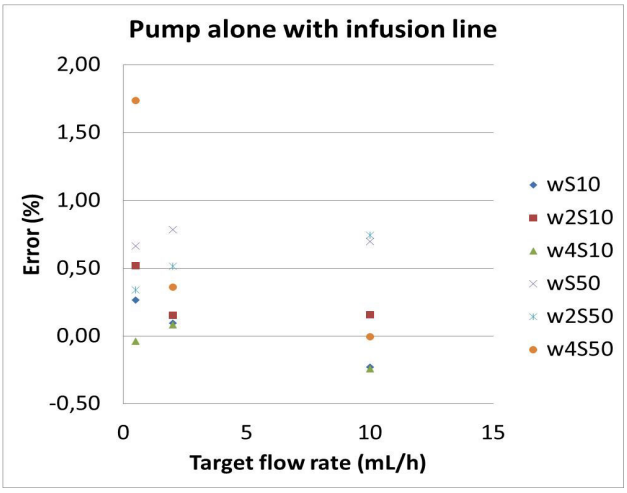
ΔV is the volume increase due to an applied pressure increase Δp

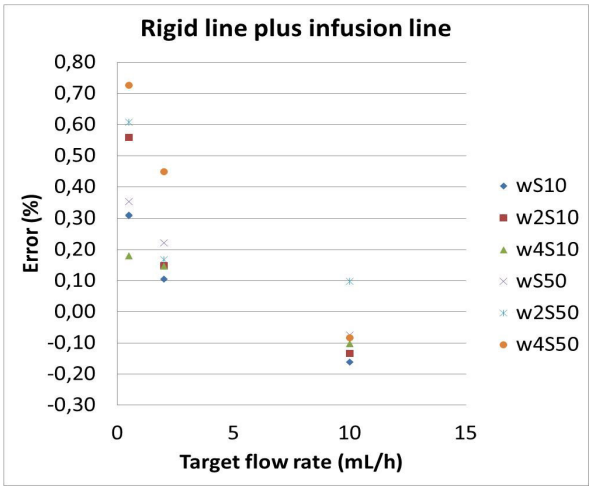
Impact of drug delivery accessories – syringe pumps





Impact of viscosity – syringe pumps





Uncertainty determination in microflow

In gravimetric determination of microflow the major sources of uncertainty are:

- Mass
- Evaporation
- Buoyancy correction
- Standard deviation of the measurements

Uncertainty values from 2 % to 0,4 %

Major conclusions for the pumps tests

- The errors using the 50 mL syringe are always larger than the 10 mL syringe.
- There is no significant difference in errors when using solutions with different viscosity .
- A larger variability can be found at lower flow rate for both syringes.
- The measured SUD is lower for the system including the 10 mL syringe as compared to system including the 50 mL syringe.

Major conclusions for the pumps tests

- The much lower compliance for the 10 mL syringe system confirms that the syringe has the biggest impact on the overall compliance.
- For both systems, including a filter increases the compliance and start up time the most pronounced. Most probably this is caused by entrapped air inside the filter.
- For all cases, the pumps performs within its claimed accuracy specifications of 2% .

Flow meters

Microflow meters are used in :

- Bio/Medical laboratories
- Food & Pharmaceutical industries (flavours, additives)
- Analytical laboratories and systems (HPLC)
- Flow chemistry using microreactors

Flow meters assessment

The 3 types of flow meters used for the assessment were the following:

Pressure drop Alicat flow sensor

Thermal Sensirion flow sensor

Coriolis flow meter

Flow meters assessment tests

- Temperature dependency
- Viscosity dependency
- Back pressure dependency
- Pulsation dependency
- Regular calibration
- Flow profile

Measurements have started but no results yet available

Thank you for your attention!!!!

Questions?

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