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Calibration and use of syringe pumps

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Abstract. There are several types of infusion instruments used for drug delivery, e.g. syringe pumps and infusion pumps, with different capacities according to their use and applied therapeutic. In order to ensure the traceability of these flow and volume measuring equipment is necessary to use suitable calibration methods and standards. Current calibration services of microflow do not go below 16 µL/min (4 % uncertainty), whereas the lowest comparison between primary standards has been of 100 mL/min, hence, below the latter flow rate, the primary standards have not been validated. Also there are several influence factors in the use of drug delivery devices that are not yet studied in detail. Therefore, a need for the development of a research project in the scope of the EMRP - European Metrology Research Programme, was identified. In order to validate the microflow gravimetric calibration method, developed at the Volume Laboratory of the Portuguese Institute for Quality in the scope of the participation in the EMRP project – Metrology for drug delivery (MeDD), several infusion instruments supplied by the Hospital Garcia de Orta/ Neonatology Service were tested at different volumes and rates. From the obtained results, it can be implemented several improvements for the use and calibration procedures.

1 Introduction

Infusion instruments are used in clinical environment for nutrition and hydration of patients and can also have therapeutically functions, namely drug delivery. In several international studies [1] it was verified that the infusion technique is a technology with underestimated risks due to several influence factors, namely the use of very small flow (300 nL/min) in preterm babies, multipump administration with the use of several administration lines and the individual variables of the different drugs.

Typically, for a proper drug delivery the total delivered volume (mass) is the most important parameter. However, there are a significant percentage of drugs for which the actual flow rate is very important for a proper patient treatment.

For most critical drugs, a 5 % uncertainty in flow rate is sufficient. There is doubt, however, whether this uncertainty criterion is satisfied for (ultra-) low flow rates and for multi-pump infusion. Also, the overall drug delivery characteristics are not properly known. The clinically relevant drug delivery characteristics are start-up time, flow rate stability and response time to occlusion-alarm. An incomplete knowledge of these characteristics can also result in unexpected flow rates and/or flow rate fluctuations.

Several other problems associated with these instruments were observed, namely, under or over administration of the therapeutic, incorrect data integration/structural failure, operation interruption without alarm, incorrect warning of block and failure in the alarm of identified condition.

1.1 EMRP-MeDD

The European Association of National Metrology Institutes, EURAMET, started, in 2007, the European Metrology Research Programme – EMRP, supported by the 7th Framework Program of the European Commission. This Program opens a call every year for Joint Research Projects (JRPs), in strategic themes defined by EMRP. These JRPs are developed by the member countries and can be supported by Universities and other entities that work in scientific areas were measurements are critical and fundamental.

In 2011, one of the chosen JRP subjects was “Health”. This choice had the main purpose of developing science and technology in the field of health, specifically, to assure the traceability of clinical data, allowing the comparability of diagnostic and treatment information.

The JRP “MeDD - Metrology for Drug Delivery” was accepted for the development of a primary standard for flow measurements between 150 µL/min and 1 nL/min. This JRP will also characterize the flow meters and flow

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generators already in the market and will assure the traceability of the syringe pumps measurements used in drug delivery. This work will allow in the future the increase of efficiency and trust in the flow delivered by the drug delivery systems, which are fundamental instruments for patient therapy.

In order to validate the microflow gravimetric calibration method developed at the Volume Laboratory (LVO) of the Portuguese Institute for Quality (IPQ), and in the frame of LVO participation in the EMRP MeDD project, several infusion instruments supplied by the Hospital Garcia de Orta/ Neonatology Service were tested at different volumes and flow rates.

2 Methods and Instrumentation

There are several methods for calibration/verification of infusion devices: the comparison method "in situ" using a flowmeter and the gravimetric method used in the laboratory [2]. The later was the one used in this work.

2.1 Gravimetric method

The gravimetric method consists on weighing an amount of water delivered or contained from/in a volume instrument. A conversion is then performed from mass to volume at a reference temperature of t_0 (normally 20 ºC). The recommended equation is described in ISO 4787 standard:

$$V_0 = (I_L - I_E) \times \frac{1}{\rho_w - \rho_A} \times \left(1 - \frac{\rho_A}{\rho_B}\right) \times [1 - \gamma(t - t_0)] \qquad (1)$$

2.1.1 Flow measurement

The flow measurement can be done by a static or a dynamic method. The static method is generally used for the calibration of volumetric meters and consists of the measurement of a volume at a preset flow rate. The dynamic method used in the calibration of flowmeters consists in the determination of the mass or volume per unit of time. In this text we describe the dynamic gravimetric method of flow measurement.

2.1.2 Calibration procedure for infusion instruments

The calibration procedure of infusion instruments is based on the IEC 60601-2-24 [3]. The syringe is filled with ultra-pure water without air entrapment. A sufficient amount of water is passed to the tube in order to remove all air bubbles. The flow to be calibrated is then programed in the pump and the water is collected in a balance (figure 1). The volumetric flow is directly calculated by a computer program written in "LabVIEW".

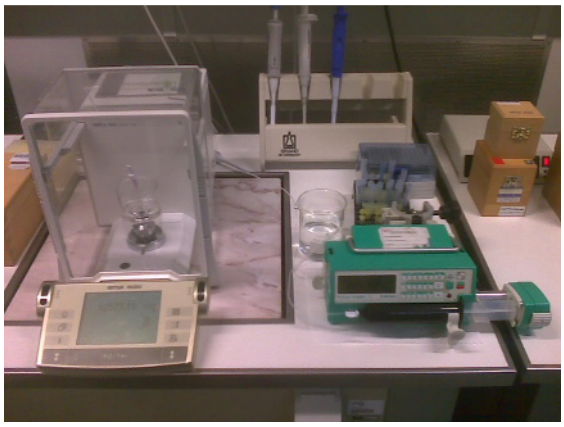

Figure 1. Experimental assembly for the calibration of infusion instruments

The obtained volumetric flow is determined using equation 2.

$$Q = \frac{1}{t_f - t_i}\left[\frac{\left(1 - \frac{\rho_A}{\rho_B}\right) I_f [1 - \gamma(T - 20)]}{\rho_w - \rho_B} - \frac{\left(1 - \frac{\rho_A}{\rho_B}\right) I_i [1 - \gamma(T - 20)]}{\rho_w - \rho_A} + \delta V_{evap}\right] \qquad (2)$$

2.2 Type of infusion instrument used

There are several types of infusion instruments used for drug delivery, with different capacities according to their use and applied therapeutic, e.g. syringe pumps and infusion pumps. In this work the syringe pump perfusor compact S from BBraun was used. The instrument characteristics are presented in table 1.

Table 1. Perfusor Compact S caracteristics

Perfusor Compact S	
Flow range	10,1 mL/min – 999,9 mL/min
Resolution	0,01 mL/h
Precision	2,5 %

3 Analysis of results

3.1 Calibration of syringe pumps

Several calibrations were performed at a flow rate of 1 mL/h using the Perfusor Compact S, with 50 mL, 20 mL and 5 mL syringes. Three repetitions for each syringe was performed in order to assess the repeatability of the instrument, the results are presented in the following tables and figures:

Table 2. Test results with 50 mL and 5 mL syringes

Nominal flow	Syringe	Obtained flow (mL/h)	Error (%)	Uncertainty (%)
1 mL/h	50 mL	0,9839	1,61	0,12
		0,9888	1,12	0,21
		0,9835	1,64	0,17
	5 mL	0,9987	0,13	0,34
		0,9988	0,12	0,41
		0,9989	0,11	0,41

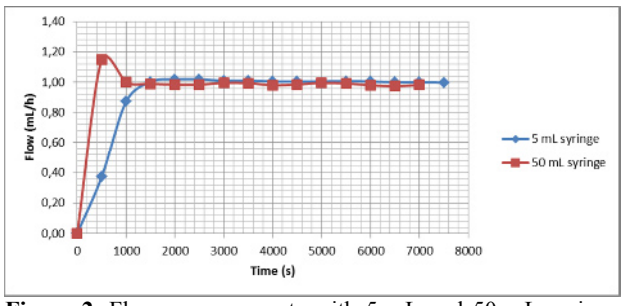

Figure 2. Flow measurements with 5 mL and 50 mL syringe. The syringe of 50 mL showed an abnormal stabilization situation due to its characteristics.

Table 3. Test results with 20 mL syringe

Nominal flow	Syringe	Obtained flow (mL/h)	Error (%)	Uncertainty (%)
1 mL/h	20 mL	1,1050	10,5000	0,43
		1,0896	8,9600	0,46
		1,1050	10,5000	0,42

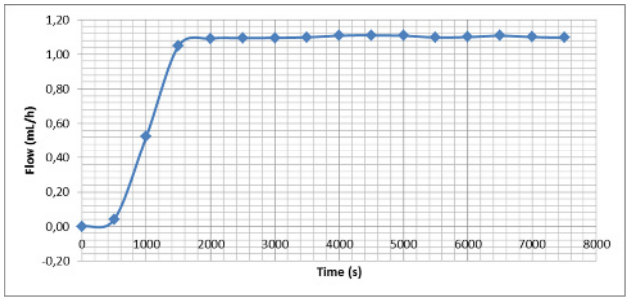

Figure 3. Flow measurements with 20 mL syringe

For the 50 mL and 5 mL syringe the errors are always smaller than 2,5 % (value described by the manufacturer as the maximum permissible error) [4].

However for the 20 mL syringe the obtained results had an error about 10 % which is much larger than the maximum permissible error as described by the manufacturer.

This situation was investigated and it was observed that the system had an incorrect code for the 20 mL disposable syringe. The correct code was then inserted and the results are now within the MPE of the manufacturer (see Table 4):

Table 4. Test results for the 20 mL syringe with the correct code

Nominal flow	Syringe	Obtained flow (mL/h)	Error (%)	Uncertainty (%)
1 mL/h	20 mL	0,9990	0,1000	0,38
		0,9890	1,1000	0,36
		0,9964	0,3600	0,40

One can also verify that for a flow of 1 mL/h the suitable syringe with the smaller error is the one of 5 mL.

The calibration results have a good repeatability with uncertainties between 0,1 % e 0,4 %. The flow stabilizes after 20 minutes of testing.

4 Conclusion

The regular maintenance and calibration of instruments infusion allows the identification and correction of errors, minimizing potential risk situations for the patient. The Volume Laboratory of IPQ recently implemented the gravimetric determination of flow with an uncertainty on the order of 0,5 %.

During the development and validation of the standard for flow measurements several tests were performed with different infusion instruments used by the Hospital Garcia de Orta. These tests allowed comparing the results of the accuracy of instruments, obtained experimentally with those indicated by the manufacturers and also identified an incorrect programing situation effect.

We can conclude that it is essential to follow the manufacturer instructions and specifications, specially the ones related to the consumables in use with the infusion systems, in order to prevent significant errors.

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