Calibration of Infusion Pumps Analyser

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ABSTRACT. Nowadays, infusion pumps such as syringe pumps and peristaltic pumps are commonly used for drug delivery, in situations where the delivery dose has stringent limits and high risk impact. In order to ensure the metrological traceability of these flow and volume measuring equipment it is necessary to use suitable calibration methods and standards. One of the methods typically used in hospitals is relying on an Infusion Device Analyser (IDA). This is a secondary method, and consists on comparing directly the flow generated by the infusion pump with the IDA. The IDA can be calibrated by gravimetric or by the use of a precision syringe pump. In this paper the results of the two calibration methods are compared. Moreover, a new calibration method using a Coriolis meter is evaluated. The uncertainty budgets of the three methods are described in detail.

1. Introduction

Medical infusion instruments are widely used, as they are fundamental for primary health care, namely for providing drugs, nutrition and hydration to patients. Hence, it is crucial that the volume and flow generated by the devices are the most accurate and precise as possible, especially in situations related to neonatology (newborn babies) or cancer treatment. To ensure this, it is necessary to have appropriate calibration methods, including appropriate measurement uncertainty evaluation.

The Metrology for Drug Delivery (MeDD) project [1] funded by the European Metrology Research programme (EMRP), developed during 2012-2015, had a major goal of studying such calibration methods [2].

The outcomes of this project were discussed in several international conferences and presented in scientific papers, reports and best practice guides that can be found in www.drugmetrology.com. Nonetheless, this data was never formalized in the way of amendments to the relevant standards, specifically ISO 7886-2 [3] and IEC 60601-2-24 [4].

Aiming to disseminate the knowledge obtained from MeDD JRP, a new project (Support for Impact Project (SIP) 15SIP03 – Infusion Uptake) funded by the European Metrology of Innovation and Research Programme (EMPIR) has started in May 2016. It has two main goals, to develop an E-learning module made available on the E-learning platform of the European Society for Intensive Care Medicine (ESICM) and to incorporate the best metrology practices relating calibration of infusion devices in international standards, namely ISO 7886-2 [3] and IEC 60601-2-24 [4].

In order to develop the E-learning modules and to identify the necessary contents to incorporate in the standards it was necessary to identify the different calibration methods and to validate them. This work was done in [5]. One of the methods described was a comparison method that used an Infusion Device Analyser (IDA). In order to ensure traceability it is necessary to calibrate the IDA. There are several calibration methods that can be used. The methods used in this work will be explained in the next section. Finally, experience has shown [6] that in micro flow and volume, measurement uncertainty becomes critical and this will also be discussed in this paper.
2. Calibration methods
In this work three different calibration methods were used to calibrate an Infusion Device Analyzer – IDA – 1S (Figure 1), namely the gravimetric method, the precision pump method and the Coriolis meter method.

![Figure 1 – Infusion Device Analyzer 1S](image)

2.1. Gravimetric method
The gravimetric method is considered as a primary method and is commonly used by the National Metrology Institutes [2,7,8] to calibrate syringe pumps and infusion pumps analyzers. This relies on weighing the mass of water delivered by the pump during a period of time. The flow rate is then determined by the quotient of the mass of reference liquid, usually water, and the time interval, including some corrections and further details on this method can be found in [5].

2.2. Precision syringe pump
This method relies on the use of a precision syringe pump (Figure 2), calibrated by gravimetry and consists on comparing directly the flow generated by the precision syringe pump with the IDA. In this work a Nexus 3000 syringe was used.

![Figure 2 – Nexus 3000](image)

Before starting the calibration all the apparatus under test (precision syringe pump and the IDA) and the reference liquid should reach a steady state condition as close as possible to the reference temperature of 20 °C (during 24 hours).

During the calibration, the temperature of the water and the air temperature, relative humidity and atmospheric pressure should be continually measured and/or recorded.

The Nexus pump is filled with degassed ultrapure water [9]. The line should then be filled by running the syringe pump at a high rate until a steady flow of drops comes out at the end of the tube. Finally, the tube is connected with the IDA.

Next, the target flow is programmed in the Nexus pump. Data acquisition of IDA begins after 10 minutes of steady flow and over at least 15 minutes. The data can be directly recorded by software or read at the display as the average flow rate. The described time measurements were obtained by experimental work in the Volume and Flow Laboratory (LVC) of the Portuguese Institute for Quality.
The recording time depends on the flow rate, bearing in mind that the lower the flow the larger should be the recording data time.

2.3. **Coriolis meter**

This method uses a Coriolis meter with an incorporated pump, calibrated by gravimetry and consists in comparing directly the flow generated by the Coriolis meter with the IDA. In this work a Bronkhorst M13 Coriolis meter (Figure 3) was used.

![M13 Coriolis meter with pump](image)

**Figure 3 – M13 Coriolis meter with pump**

Before starting the calibration all the apparatus under test (Coriolis meter and the IDA) and the reference liquid should reach a steady state condition as close as possible to the reference temperature of 20 ºC (during 24 hours).

During the calibration, the temperature of the water and the air temperature, relative humidity and atmospheric pressure should be continually measured and/or recorded.

The Coriolis meter is filled with degassed ultrapure water [9]. The line should then be filled by running the Coriolis meter at a high rate until a steady flow of drops comes out at the end of the tube. Finally, the tube is connected with the IDA.

Next, the target flow is programmed in Coriolis meter. Data acquisition of IDA begins after 10 minutes of steady flow and over at least 15 minutes. The data can then be recorded directly by software or read at the display as the average flow rate.

3. **Method comparison results**

The IDA 1 S instrument was calibrated at different flow rates using the different methods described above. The results can be found in the following figures.
Figure 4 – Calibration of IDA 1s using the gravimetric method and the Coriolis meter

Figure 5 – Calibration of IDA 1s using the gravimetric method and the syringe pump

It can be verified from figure 4 and 5 that the methods are all consistent with each other but the Coriolis meter has a very large uncertainty when compared with the other two methods. This is due to the instable behaviour of the device when connect to IDA1S. This variability can be identified in figure 6.
Coriolis flow meter are very sensible to pressure changes and each time the IDA 1s records a value there is a pressure drop that can be observed in the Coriolis flow meter chart. This leads to a very large standard deviation that reflects on the uncertainty and also on the error, being the flow much smaller than for the other two methods.

4. Uncertainty determination
The uncertainty budget of the calibration methods was estimated based on the Guide to the Expression of Uncertainty in Measurement (GUM) and supplements [10,11] and additional work [12,13].

The uncertainty budget for the gravimetric method is well explained in [6]. For the comparison method using the Nexus 3000 pump or the Coriolis meter the uncertainty budget is explained below.

The uncertainty of the comparison method includes the calibration uncertainty (namely, possible drift and error) of the standard, Nexus pump or Coriolis meter ($u(Q_{std})_{cal}$), its resolution ($u(Q_{std})_{res}$) and repeatability of measurements ($u(Q_{std})_{rep}$). The instrument to be calibrated (IDA) will contribute to the uncertainty with its resolution ($u(Q_{IDA})_{res}$). The uncertainty of the temperature of the water is obtained considering the calibration uncertainty of the thermometer used ($u(T)_{cal}$), and the expansion of the IDA material ($u(\gamma)$). Finally, the uncertainty due to water loss ($u(\delta_{loss})$) is also taken into account in the uncertainty budget. Detailed information regarding the uncertainty sources is described in Table 1.

Table 1 - Uncertainty components in the calibration of IDA by comparison method

| Source / Symbol | Standard uncertainty component | Evaluation process | Evaluation type | Distribution |
|----------------|--------------------------------|--------------------|----------------|--------------|
| Standards flow / $Q_{std}$ | $u(Q_{std})_{cal}$ | Calibration | A | Normal |
| | $u(Q_{std})_{res}$ | Resolution | B | Rectangular |
| | $u(Q_{std})_{rep}$ | Flow measurement standard-deviation | A | Normal |
| IDA flow / $Q_{IDA}$ | $u(Q_{IDA})_{res}$ | Resolution | B | Rectangular |
| Water temperature / $T$ | $u(T)_{cal}$ | Calibration | A | Normal |
| | $u(T)_{res}$ | Resolution | B | Rectangular |
5. Conclusions

Infusion device analysers are widely used in hospitals to calibrate or check the infusion pumps. This procedure ensures traceability of the measurements, being needed to calibrate the IDA using appropriate methods. In this work several methods were described along with the uncertainty budget. In general, both the syringe method and gravimetric method can be used to calibrate the IDA with acceptable uncertainty values. The Coriolis method has some problems with the pressure drop of the device and so it’s not recommended to be used. This information should now be disseminated in the appropriated standards, since there is no document that describes in detail the calibration methodology for these devices.

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