Indian Journal of Pure & Applied Physics
Vol. 62, October 2024, pp. 851-863
DOI: 10.56042/ijpap.v62i10.13204

Uncertainty Analysis of Newly Developed Low Liquid Flow Calibration Facility at CSIR-NPL, India

Sanjeet Kumar[a,b*], Shiv Kumar Jaiswal[a,b], Anshul Varshney[a], Chatar Singh[a], Shanay Rab[c] & Sanjay Yadav[a,b]

[a]Fluid Flow Metrology Section, CSIR-National Physical Laboratory, Dr. K.S. Krishnan Marg, New Delhi 110 012, India
[b]Academy of Scientific and Innovative Research, Ghaziabad 201 002, India
[c]School of Architecture, Technology and Engineering, University of Brighton, Brighton, United Kingdom

Received 16 August 2024; accepted 9 September 2024

Over the past decade, micro-liquid flow measurement has become increasingly important, particularly in India, where devices like syringe pumps, infusion pumps, and infusion device analyzers are critical in hospitals and research laboratories. These devices are essential for precise drug dosing in applications such as chemotherapy, pain management, insulin therapy, and other vital treatments, making accurate calibration crucial. To meet this need, the Fluid Flow Metrology Section at the CSIR-National Physical Laboratory (CSIR-NPL) in New Delhi has developed a state-of-the-art calibration facility for micro-liquid flow, capable of measuring flow rates from 10 mL/h to 1500 mL/h. The facility employs a static weighing method, utilizing a dual-range analytical balance with a capacity of 220 g/82 g and a digital timer as reference standards. This setup achieves an expanded uncertainty of 0.30% (at k=2) for both totalized volume and volume flow rate measurements, thereby ensuring the facility's status as a National Metrology Institute (NMI) in micro-liquid flow measurement.

Keywords: Accuracy; Metrology; Flow measurement; Uncertainty; Liquid flow

1 Introduction

Micro-liquid flow measurement plays a crucial role in various industries and applications where precise control and monitoring of liquid flow rates are essential. Such applications include biomedical engineering, healthcare, sensor technology, process control, chemical analysis and synthesis, environmental monitoring, fuel cell technology, micro-reactors and lab-on-a-chip devices, the oil and gas industry, food and beverage industry, semiconductor industry, aerospace and defence, microscale heat transfer, research and development *etc*. There are mainly three methods for micro flow measurements, namely, gravimetric (weighing) method, interferometric method and front tracking method. The flow measurement using the gravimetric method is the most accurate method of flow measurement. In this method, the flow rate is determined by the ratio of the mass change to the time interval, with some minor adjustments. All over the world, the static weighing method is used for flow measurement due to its inherent accuracy. The dynamic weighing method is most suitable for micro flow measurement because there is no bypass line for diverting the flow as it is done in the static weighing method employing a diverter system. However, realization of flow using dynamic method is more complex as it requires advanced instrumentation, modelling, simulation and automation. There is a significant global demand for low-flow liquid mass flow meters[1-6]. This article presents a fundamental calibration system for low liquid flow based on the gravimetric method of measurement. The Device under Test (DUT) in this case could be mass flow meters, microfluidic devices, syringe pumps, infusion pumps, or infusion device analyzers. It's worth noting that syringe pumps or infusion pumps are capable of maintaining a stable flow, making this configuration stand out. A flow that is continuous for several minutes or longer is referred to as a stable flow. Infusion tools are employed in the clinical setting for patient feeding and hydration, but they can also perform therapeutic activities, such as medication administration. Several international studies confirmed that the infusion technique is a technology with underestimated risks due to several influence factors, including the use of very minimal flow in preterm babies, multi-pump administration with the use of multiple administration lines, and individual drug variables. The total supplied volume (mass) is usually

*Corresponding author:
(E-mail: sanjeet11792@gmail.com)

the most critical criterion for optimal drug delivery. However, for a major proportion of medicines, the precise flow rate is quite critical for optimal patient treatment. A flow rate uncertainty of 5% is enough for the most important medicines[7-8]. Worldwide, calibration facilities for micro liquid flow were developed to calibrate the syringe pumps, infusion devices, etc. The more focused efforts for such developments were placed in Europe where under EURAMET, the European Metrology Programme for Innovation and Research (EMPIR), MeDD (Metrology for Drug Delivery) project, several calibration facilities were developed and upgraded in EURAMET National Metrology Institutes (NMIs) & Designated Institutes (DIs)[4,5,9-19]. Keeping in view of the above, CSIR-NPL, India (NPLI) also developed a micro (low) liquid flow calibration facility to support biomedical and other sectors in the country[20]. The international capability of the various NMIs and DIs on low-liquid flow is listed in Table 1.

As the nation's NMI, the Fluid Flow Metrology Section of CSIR-NPL has the responsibility to develop, maintain, upgrade and disseminate national flow standards in India. After these targeted research and development (R&D) activities, a new system was successfully designed, fabricated and integrated, and its performance evaluation and uncertainty analysis were done.

In Section 2, we present the design and development of the low liquid flow calibration system. This includes the detailed methodology used for the calibration process, a comprehensive description of the system's design, and an analysis of the potential sources of error and uncertainty in micro-liquid flow measurement. Section 3 discusses the results obtained from the calibration system, providing an in-depth analysis and comparison with existing standards, and exploring the implications of these findings. Finally, in Section 4, we conclude the paper by summarizing the key outcomes of the study, discussing the impact of the developed system on the field, and outlining potential directions for future research and development.

2 Design and Development of the Low Liquid Flow Calibration System

2.1 Methodology of low liquid flow calibration system

A gravimetric method-based system for calibrating low liquid flow rates comprises of several components: a flow generation module, a device under test (DUT)/ device under calibration (DUC), a precision balance equipped with a collection container, and a timer. Fig. 1 shows the schematic representation of this low-liquid flow calibration system. Here, the syringe pump has been used as a flow generation module/ source. The overhead tank may be also used as a flow generation source. The DUT has been connected between the flow source and weighing balance/ analytical balance using flexible

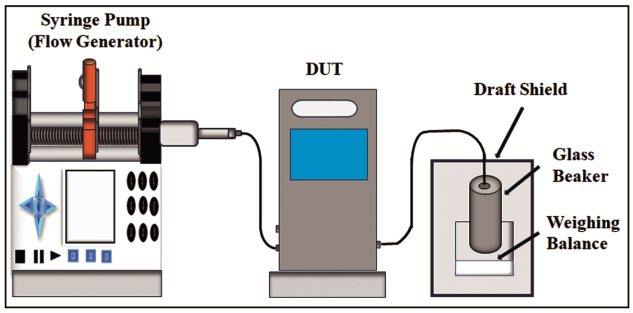

Fig 1 — Schematic diagram of a Low-Liquid Flow Calibration System

Table 1 — International Status of various NMIs/ DIs on Low Liquid Flow Measurement

Sr. No.	Name of NMI/DI	Flow Range	Uncertainty at k=2
1.	NIST (USA)	60 µL/h to 6 mL/h	4.5% to 0.04% [5]
2.	METAS (Switzerland)	6 µL/h to 600 mL/h	0.60% to 0.10% [12]
3.	LNE-CETIAT (France)	1 mL/h to 10000 mL/h	0.60% to 0.10% [12]
4.	IPQ (Portugal)	3 µL/h to 600 mL/h	6% to 0.15% [12]
5.	DTI (Denmark)	1 µL/h to 600 mL/h	5% to 0.05% [12]
6.	VSL (Netherlands)	0.25 mL/h to 5000 mL/h	1% to 0.05% [12]
7.	CMS (Taiwan)	6 µL/h to 600 mL/h	2% to 0.20% [13]
8.	CMI (Czech)	10 mL/h to 6000 mL/h	0.60% to 0.20% [14]
9.	NIMT (Thailand)	10 mL/h to 1000 mL/h	0.35% to 0.24% [14]
10.	NMC (Singapore)	2 mL/h to 100 mL/h	0.70% to 0.10% [14]
11.	NMIJ (Japan)	20 mL/h to 1000 mL/h	0.078% [14]
12.	KRISS (Korea)	2 mL/h to 1000 mL/h	0.70% to 0.30% [14]
13.	NIM (China)	6 µL/h to 9000 mL/h	1.5% to 0.10% [15]
14.	CSIR-NPL (India)	10 mL/h to 1500 mL/h	0.30% [20]

plastic tubing. The glass beaker is placed on the weighing balance which collects the flowing liquid through the transparent flexible PVC tubing and the needle. To minimize the impact of the vibration due to external effects (*e.g.* air current), the weighing balance is covered with the draft shield. The measurement of flow is conducted using the "standing start and standing finish" method. This system assesses the quantity of mass or volume passing through the DUT and collected by a standard reference. This measurement approach is referred to as the "totalized mass/volume method". When comparing the flow rate between the DUT and the standard reference, it is known as the "flow rate method." To determine the standard flow rate, a timer is employed to measure the collection time, and the mass flow rate or volume flow rate is calculated based on the ratio of the collected mass or volume to the collection time[4-6,21]. During operation of the system, first, the flow rate is selected on the syringe pump. Thereafter, the volume to be dispensed is selected on it. Now, the initial mass of the beaker placed on balance is noted. The syringe pump is started. The timer is triggered at the same time of syringe pump starts. The timer is stopped when the syringe pump stops after dispensing the set volume. Now final mass reading on the balance is noted. Also, the volume and average flow rate indicated on the DUT are noted. The temperature of the water collected in the beaker is measured using a digital thermometer after noting of final mass on the balance. During the measurement, laboratory temperature, relative humidity and ambient pressure are measured using a digital temperature & humidity indicator and barometer. These acquired data are used to determine the error and uncertainty of the DUT.

2.2 Design details of the developed system

CSIR-NPL developed a primary standard based on the weighing method. The syringe pump is used as a flow source/ generator in the flow rate range of 10 mL/h to 1500 mL/h. Two syringe pumps are used to provide a flow rate to the DUT. The first syringe pump (Make: WPI, Model: SP100IZ, syringe volume: 10 mL) is used to provide flow in the range of 0.1 mL/h to 125 mL/h whereas the second syringe pump (Make: Amogh Healthcare, Model: SP-1200, syringe volume: 50 mL) is used to provide flow rate in the range 0.1 mL/h to 1500 mL/h. The 220 g/ 82 g (dual range) weighing balance (make: Radwag, model: AS82/220.R2 PLUS) is used for weighing water collected in the beaker. The static weighing method is used. The mass flowmeter or infusion device analyzer (IDA) is used as a DUT. The flow source may be also used as a DUT. In the set-up for low liquid flow calibration system as shown in Fig. 2, the syringe pump has been used as a DUT. The collection time is measured by a digital timer through manual triggering. The beaker of 80 mL capacity was taken for collecting the liquid (*i.e.* distilled water). The cork is placed on the top of the beaker. The flexible PVC tubes are used to connect various devices. The tube connecting to the cork of the beaker has gauge no. 18 needle. This needle has an outer diameter (OD) of 1.27 mm and an inner diameter (ID) of 0.838 mm. We have checked the flow through this needle upto a flow rate of 6000 mL/h, although measurement has been done upto 1500 mL/h. The hole is made on the cork for smooth entry of the needle inside the beaker. This reduces the evaporation effect. The high-precision digital thermometer is used for measuring the temperature of liquid in the beaker.

2.3 Sources of error and uncertainty in low liquid flow measurement

In static-weighing method, the mass flow rate, q_m, the ratio of mass and time, is determined as follows;

$$q_m = \frac{m}{t} \qquad ...(1)$$

Here, 'm' represents the mass of water collected over a specific time interval 't,' the volumetric flow rate 'q_v' is obtained through Eq. 2 by dividing the mass flow rate by the density of water, denoted as 'ρ';

$$q_v = \frac{q_m}{\rho} = \frac{m}{t.\rho} \qquad ...(2)$$

Consequently, when measuring the mass flow rate, the primary sources of errors and uncertainties are the

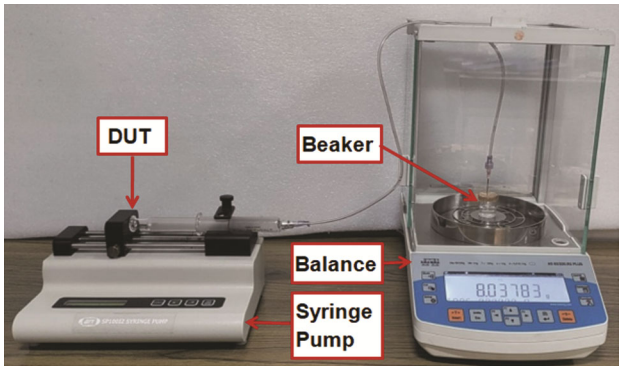

Fig 2 — Set-up for Low Liquid Flow Calibration System

mass and time components. In contrast, when measuring the volume flow rate, these sources expand to include mass, time, and density[6].

The parameter related to DUT (such as a mass flowmeter, syringe pump, infusion pump, or infusion device analyzer), to be calibrated, is evaluated based on its error ('Δq'). This error is determined by comparing the volume flow rate indicated by the device under test ('DUT') to the value calculated by the standard ('standard'),[22] and this relationship is expressed as a following mathematical model;

$$\Delta q = \underbrace{\left[q_{\text{vDUT}} + \delta q_{\text{REP}} + \delta q_{\text{RES}} + \delta q_{\text{ZD}} + \delta q_{\text{STAB}}\right]}_{\text{Device Under Test (DUT)}} - \underbrace{\left[q_{\text{vSTD}} + \delta q_{\text{vSTD}}\right]}_{\text{Standard}} \quad ...(3)$$

Where;

Δq = error of the measurement,

q_{vDUT} = volume flow rate from the DUT,

δq_{REP} = error due to repeatability in measurement of DUT,

δq_{RES} = error contribution due to resolution of DUT,

δq_{STAB} = error contribution due to stability of DUT,

δq_{ZD} = error contribution due to zero drift of DUT,

q_{vSTD} = volume flow rate from the standard,

δq_{vSTD} = error contribution from the standard

The units of various terms in Eq. 3 are in absolute units. Since the gravimetric method has been used for flow measurement, the standard flow is derived in fundamental SI units of mass, length and time as per equation (1) or (2) depending upon whether it is mass flow or volume flow. For uncertainty estimation, the relative (%) form of uncertainty estimation is easier due to uncertainty parameters being in the product (*i.e.* multiple or quotient) form as shown in Eqs 1 & 2. Hence, a sensitivity coefficient of 1 has been used for these flow equations. Also for uncertainty estimation, it has been assumed that various sources of uncertainty are uncorrelated[23-25].

For low liquid flow measurement, the various other sources of uncertainties apart from the collected mass, collection time and water density are evaporation, flow rate stability of flow source, repeatability in the error measurement of DUT, zero offset/ drift of DUT and resolution of DUT. The stability of the flow source is reflected in error measurement and estimation of its repeatability. The water temperature; ambient temperature, relative humidity and barometric pressure are also measured to determine air buoyancy correction factor. However, for the safer side, the standard air buoyancy correction factor of 1.00106 may be taken[26-27]. If all the uncertainty sources are combined, the resultant relative combined uncertainty equation for error determination in the volumetric flow rate is given by the following equation:

$$u_{\text{r}\Delta\text{q}} = \sqrt{u^2_{\text{rm}} + u^2_{\text{rt}} + u^2_{\text{r}\rho} + u^2_{\text{rREP}} + u^2_{\text{rSTAB}} + u^2_{\text{rEVAP}} + u^2_{\text{rZD}} + u^2_{\text{rRES}}} \quad ...(4)$$

Where,

$u_{\text{r}\Delta\text{q}}$ = relative combined uncertainty in error determination of volumetric flow rate

u_{rm} =relative standard uncertainty in collected mass measurement,

u_{rt} =relative standard uncertainty in collection time measurement,

$u_{\text{r}\rho}$ =relative standard uncertainty in water density measurement,

u_{rREP} =repeatability in the error measurement of the DUT,

u_{rSTAB} =relative standard uncertainty due to the stability of the water source,

u_{rEVAP} =relative standard uncertainty due to the evaporation of collected mass,

u_{rZD} =relative standard uncertainty due to the zero drift/offset of the DUT

u_{rRES} =relative standard uncertainty due to the resolution error of the DUT

The relative expanded uncertainty for the volumetric flow rate is determined by the following formula:

$$U_{\text{r}\Delta\text{q}} = k \times u_{\text{r}\Delta\text{q}} \quad ...(5)$$

where, k is a coverage factor which is determined from the effective degree of freedom for the selected confidence level as per Welch-Satterthwaite Formula[23].

3 Results and discussion

In the present section, various sources of uncertainties, their quantification and their contribution to overall microflow measurement have been reported. All the standards used in the measurement *i.e.* weighing

balance, digital timer, digital thermometer, and reference weights are traceable to their respective national standards.

3.1 Collection mass

The mass of the flowing liquid is collected in the beaker and placed on the analytical balance/ weighing balance. The various sources of uncertainty in the collected mass measurement are weighing balance calibration, weighing balance drift, weighing balance resolution, leaks and splashes, and evaporation. The effect of evaporation will be separately described. The analytical balance used is dual range 220g/ 82 g, make: Radwag, model: AS82/220.R2 PLUS. It has a resolution (least count) of 0.0001 g in the 220 g range and 0.00001 g in the 82 g range. Before use, it was calibrated using reference weight in the range of 1 g to 220 g by the Mass Metrology Section at NPLI. The actual error and uncertainty at each mass value are much less than the maximum permissible error (MPE). However, for the safe side, the uncertainty has been reported based on MPE. The uncertainties of this analytical balance at 200 g, 100 g, 50 g, 20 g and 10 g standard weights are 0.00075%, 0.001%, 0.001%, 0.0025% and 0.005% (at k=2) respectively. The absence of observed leaks and splashes in the system leads to the assumption that their impact is minimal. The current study has specifically examined the storage and evaporation effects, and their influence will be accounted for in the uncertainty budget, as demonstrated independently.

3.2 Collection time

The collection time is measured by a digital timer using manual triggering. The resolution of this timer is 0.01 s. It was calibrated through the Time & Frequency Metrology Division. It has the maximum expanded uncertainty of 0.14 s (at k=2) which corresponds to expanded uncertainty of 0.117%, 0.023%, 0.012%, 0.008% and 0.004% at collection times of 120 s, 600 s, 1200 s, 1800 s and 3600 s respectively. The totalized method of flow measurement is done by the standing start and finish method. The minimum collection time for the totalized method of measurement is 60 seconds. However, a collection time of a minimum of 120 s (2 minutes) is taken for totalized mass/ volume measurement at a maximum flow rate (*i.e.* 1500 mL/h) which is limited by syringe volume (50 mL). This method is further used for flow rate measurement. At a low flow rate (*i.e.* 10 mL/h), the minimum collection time of 1 h (3600 s) is taken and 10 mL liquid is collected in the weighing balance. This large time reduces the manual error in making the flow circuit on-off. Therefore, the large collection time is taken in flow rate measurement. However, the highest error in making the flow circuit on-off occurs at the highest flow rate (1500 mL/h) due to the limitation of miximum collected volume of 50 mL which takes 120 s to fill the liquid in the beaker. Thus, the effect of evaporation is very less at 1500 mL/h due to the short collection time and is significant/ dominant at a flow rate <50 mL/h due to the long collection time.

3.3 Water density

In the experiment, the distilled water is used. The temperature of the water collected in the beaker is measured by a high-precision digital thermometer make: Fluke, model: 1523 which has a resolution of 0.001 °C and an accuracy of ±0.02 °C. The density of water is derived from the standard density table of pure water against water temperature. The density value is used to convert mass or mass flow rate into volume or volume flow rate. Admittedly, in our system, there is no provision of inline temperature measurement for the flowing water. It is measured in the beaker after completing the measurement of the collected mass. The thermometer sensor is immersed completely. As temperature is maintained in the laboratory, therefore, syringe volume temperature is almost same as laboratory temperature due to thermal stabilization. However, when we collect this water in the beaker and thereafter measure its temperature, there is a difference of 0.2 °C to 1.0 °C depending on collection time as the temperature rises due to friction in the tube and heat energy added by the syringe pump during flow. At the highest flow of 1500 mL/h, collection time is 120 s and this temperature difference is approx. 0.2 °C in the water temperature measurement. However, at low flow (<50 mL/h), collection time is 3600 s and this temperature difference is approx. 1.0 °C in the water temperature measurement. This temperature effect is considered as an uncertainty component. From the distilled (pure) water temperature versus density table, it is observed that the effect of a change of 0.2 °C to 1.0 °C in the water temperature leads to a density change of approx. 0.005% to 0.028% in the temperature range of 23 °C to 27 °C. Thus, the maximum effect of temperature uncertainty (including calibration uncertainty) in density values is not more than 0.03%

at k =2. For the safe side, we are taking the density uncertainty of 0.03% at k =2 for all the flow rates.

3.4 Evaporation effect

The evaporation effect is one of the dominant factors of error and uncertainty in micro/ low flow measurement. To study the evaporation effect, the volume of distilled water was kept without cork and with cork (for entry of needle) on the weighing scale. The initial mass was noted. Then another (final) measurement was taken after approx. 60-65 minutes. The change in the mass value from its initial to the final measurement is the evaporation effect/ evaporation error. It is defined as follows:

$$\% \text{ Evaporation error} = (\text{final mass} - \text{initial mass}) \times 100/ \text{ initial mass} \quad \ldots(6)$$

Thus, the evaporation effect is always negative due to loss of mass. The temperature and relative humidity greatly affect the evaporation. If the temperature is high and humidity is low, the evaporation will be higher. If, for the same temperature, humidity is high, then evaporation error will be less. For the study of the evaporation effect, the environmental temperature in the laboratory is maintained through hot and cold air-conditioners but no control of the humidity. This study was done in the temperature range of 23 °C to 27 °C *i.e.* calibration temperature (25±2) °C. For this study, we took 2 nos. of 80 mL identical glass beakers, one for use without cover and the other with cover to have the same temperature and humidity conditions during the measurement. The reason for selection of 80 mL beaker is that maximum syringe volume of 50 mL can be filled up apart from some volume is filled during priming of the flow line. Normally, the syringe volume is 60 mL and about 10 mL is used in priming of the flow line to remove the bubbles. The inner diameter and depth of the beaker are 39.5 mm and 52 mm respectively. In this beaker, 50 mL water was filled. The hole of approx. 2 mm was made on cork cover which is used to cover the 80 mL beaker. This hole is sufficient for smooth entry of needle having gauge no. 18. We studied the glass beakers in two different conditions *i.e.* (i) glass beaker without cover and (ii) glass beaker with cover. First, we set the laboratory temperature to 23 °C. The temperature and relative humidity were measured three times during one cycle of the experiment i.e. start, mid and finish of the experiment. The average values of these 3 readings give one reading for evaporation, temperature and relative humidity. This was repeated two more times at 23 °C. This completes the evaporation effect at 23 °C. The similar experiments were repeated at 25°C and 27 °C. Fig. 3 shows the effect of evaporation for pure water taken at different temperature and humidity conditions where measurement was done for 60-65 minutes. The temperature, relative humidity and evaporation shown in Fig. 3 are the average value of 3 readings. This time of 60-65 minutes was chosen keeping in view of the flow measurement for approx. 60 minutes (1 hour) at lower flow (≤ 50 mL/h). We found that the evaporation effect without the cover on the beaker was in the range of -0.15% to -0.31 % whereas this effect was found in the range of -0.0035% to -0.0060% when the beaker was covered with cork cover. Thus, evaporation error is reduced more than 50 times when beaker is covered by a cork. Evaporation depends on the effective exposed area of the beaker. Due to the cover on the beaker, the effective exposed area to the environment is greatly reduced leading to a reduction in the evaporation error. From Fig. 3(a), we find that evaporation error is high at 23 °C and low at 27 °C. The explanation for this decrease in evaporation error at 27 °C is that

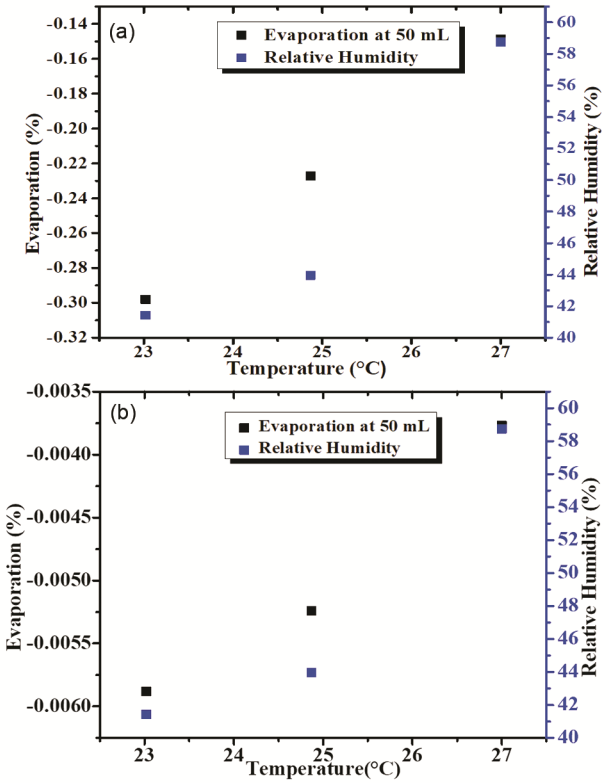

Fig 3 — Effect of evaporation at 50 mL volume using pure water (a) Evaporation effect without cover on the 80 mL beaker (b) Evaporation effect with cover on the beaker

relative humidity is very high (*i.e*. approx. 59%) as compared to approx. 42% at 23 °C. The evaporation effect is considered an uncertainty component in the uncertainty budget. In actual measurement at high flow, the collection time is much lower and consequently evaporation will be also very low but as a worst-case scenario (& for the safer side), the maximum value of the evaporation error is taken. The evaporation error can be corrected if its value during study is found fairly constant[4,12,26-28].

3.5 Repeatability and Flow rate stability

When the flow rate is unstable (having large variations in its values), the average flow rate or totalized flow volume is measured. The flow rate stability is covered in the error determination. For repeatability (& Type A uncertainty) estimation at each flow rate, the measurements were repeated 4 times. If flow changes more, the error values determined will be more scattered and repeatability & Type A uncertainty will be higher. The flow rate stability is much affected by collection time. When we use standing start and standing finish method, initially, it takes about 10 s to reach the flow from zero flow to full flow when we make flow circuit 'ON'. Then it remains at the constant flow condition for the pre-determined time. It takes about 10 s to reach from full flow to zero flow when flow circuit is made 'OFF'. Thus, in total collection time, unstable flow duration is approx. 20 s. At the highest flow (*i.e.* 1500 mL/h), the collection time is 120 s which is limited by syringe volume. Therefore, efforts are always made to have longer collection times to reduce the effect of unstable flow duration. In our calibration, we take a maximum collection time of 1 h (3600 s) to reduce this unstable flow duration without compromising the uncertainty of mass and time. If we increase the collection time more, it will take long time for calibration of the micro flowmeter. So a balance is to be drawn between calibration time and uncertainty requirement.

3.6 Zero Drift/ Offset of the DUT

The zero drift/ offset of the DUT plays an important role. Some flowmeters (for example, mass flowmeter) may exhibit zero drift problems. At full flow range, the zero offset may have a minimum effect on the accuracy of the flowmeter but when used at lower flow range, this zero offset/ drift might have a significant effect on the accuracy of the flowmeter. Therefore, before using the flowmeter for calibration or other purpose, its zero offset may be verified. If the zero offset is not adjustable (*i.e.* nullified), then this value should be either corrected or should be included into the uncertainty budget.

3.7 Resolution of the DUT

The resolution of the DUT plays an important role in the uncertainty determination. When we use the DUT (IDA) at a low flow rate (say less than 20%), its resolution becomes the dominant factor of uncertainty. Therefore, one should use different DUTs for different flow ranges.

3.8 Measurement Result

After quantification of various sources of uncertainty, the DUT was calibrated at various flow rates starting from 10 mL/h to 1500 mL/h using the standing start and standing finish method. For totalized volume measurement, we have calibrated several syringe pumps and infusion device analyzers. We found that the syringe pump, model: Fusion 6000, make: Chemyx has very good repeatability and accuracy (±0.35%), hence, chosen as the best DUT for Calibration and Measurement Capability (CMC) demonstration[29]. Admittedly, we do not have an arrangement for pressure measurement during flowing conditions. However, from the user manual, the pressure generated by the syringe pump is available. In the case of the Chemyx make, Fusion 6000 model syringe pump, the maximum pressure generated by the syringe pump is 10 bars. Table 2 shows the results of calibration of the syringe pump in the totalized volume mode at various flow rates whereas Table 3 shows its detailed uncertainty budget. Since the syringe pump does not show the flow rate (at a particular set flow rate, it shows the dispensed/infused volume), therefore, it cannot be used as a DUT for flow rate measurement when its resolution is to be considered as an uncertainty component. We can indirectly measure the flow rate from the infused volume and collection time without considering its resolution. Most of the infusion device analyzers have a resolution of 0.01 mL/h, therefore, the same resolution of 0.01 mL/h has been considered for syringe pumps in the estimation of flow rate uncertainty. Table 4 shows the results of calibration of the syringe pump in the volume flow rate mode at various flow rates whereas Table 5 shows its detailed uncertainty budget.

Observations compiled in Table 3 reveal that the expanded uncertainty for the totalized mode, with a

Table 2 — Results of calibration of the syringe pump, model: Fusion 6000, make: Chemyx in totalized volume mode at various flow rates

S.No.	Nominal Flow Rate q (mL/h)	Average DUT collected volume V_{DUT} (mL)	Average Standard collected volume V_{STD} (mL)	Reading Error (V_{DUT}- V_{STD}) ×100/ V_{STD} (%)	Expanded Uncertainty U (%)
1.	10.0	10.0000	9.9722	0.26	0.12
2.	50.0	50.0000	49.8928	0.22	0.22
3.	100.0	50.0000	49.9347	0.13	0.07
4.	600.0	50.0000	49.9261	0.15	0.12
5.	1000.0	50.0000	49.9432	0.11	0.04
6.	1500.0	50.0000	49.9525	0.10	0.06

Table 3 — Uncertainty budget of syringe pump model: Fusion 6000, make: Chemyx calibration in totalized volume mode at various flow rates

Sources of uncertainty	Flow rate / Collected water mass [Relative standard uncertainty (%)]					
	10 mL/h	50 mL/h	100 mL/h	600 mL/h	1000 mL/h	1500 mL/h
	10 g	50 g	50 g	50 g	50 g	50 g
1. Weighing scale calibration	0.0025	0.0005	0.0005	0.0005	0.0005	0.0005
2. Air buoyancy correction	0.0015	0.0015	0.0015	0.0015	0.0015	0.0015
3. Water density determination	0.015	0.015	0.015	0.015	0.015	0.015
4. Evaporation effect	0.00346	0.00346	0.00346	0.00346	0.00346	0.00346
5. Zero drift/ offset of the DUT	0.000	0.000	0.000	0.000	0.000	0.000
6. Resolution of the DUT	0.002880	0.000577	0.000577	0.000577	0.000577	0.000577
7. Type A uncertainty of the DUT	0.0307	0.0653	0.0213	0.0371	0.0089	0.0189
Relative combined uncertainty (u_c)	0.0409	0.0671	0.0263	0.0402	0.0178	0.0244
Relative expanded uncertainty (U) for approx. 95% confidence level	0.12	0.22	0.07	0.12	0.04	0.06
Coverage factor k	2.87	3.31	2.52	2.87	2.06	2.37

Table 4 — Results of calibration of syringe pump, model: Fusion 6000, make: Chemyx in volume flow rate mode at various flow rate.

S.No.	Nominal Flow Rate q (mL/h)	Average DUT flow rate q_{VDUT} (mL/h)	Average Standard flow rate q_{VSTD} (mL/h)	Reading Error (q_{VDUT}- q_{VSTD}) ×100/ q_{VSTD} (%)	Expanded Uncertainty U (%)
1.	10.0	10.000	9.9772	0.23	0.12
2.	50.0	50.000	49.8928	0.22	0.22
3.	100.0	100.000	99.8695	0.13	0.07
4.	600.0	600.000	599.1135	0.15	0.11
5.	1000.0	1000.000	998.8645	0.11	0.09
6.	1500.0	1500.000	1498.5763	0.10	0.13

coverage factor, k varying from 2.06 to 3.31, is well within the range of 0.04% to 0.22% for flow rates spanning from 10 mL/h to 1500 mL/h. Notably, this uncertainty does not exhibit a linear trend. As we lack formal interlaboratory comparisons (ILCs) to substantiate the system's Calibration and Measurement Capability (CMC) claim, we refrain from reporting uncertainties more precisely than 0.30% for flow rates from 10 mL/h to 1500 mL/h in the totalized volume mode. Table 5 provides insight into the uncertainty budgets for the calibration of the syringe pump at flow rates of (10, 50, 100, 600, 1000, 1500) mL/h when measuring the collection time using a digital timer. From the data in Table 5, it becomes evident that the expanded uncertainty, considering a coverage factor k varying from 2.00 to 3.31, falls within the range of 0.07% to 0.22% across the flow range from 10 mL/h to 1500 mL/h. Similar to the approach used for totalized volume measurements, we refrain from reporting uncertainties more precise than 0.30% for flow rates spanning from 10 mL/h to 1500 mL/h in the flow rate mode. The same level of uncertainty as applied to totalized volume and volume flow rate is also applicable to totalized mass and mass flow rate measurements. In Tables 3 & 5, we find that Type A uncertainty (repeatability in measurement) is

Table 5 — Uncertainty budget of syringe pump model: Fusion 6000, make: Chemyx calibration in flow rate mode at various flow rates

Sources of uncertainty	Flow rate / Collected water mass [Relative standard uncertainty (%)]					
	10 mL/h	50 mL/h	100 mL/h	600 mL/h	1000 mL/h	1500 mL/h
	10 g	50 g	50 g	50 g	50 g	50 g
1. Weighing scale calibration	0.0025	0.0005	0.0005	0.0005	0.0005	0.0005
2. Air buoyancy correction	0.0015	0.0015	0.0015	0.0015	0.0015	0.0015
3. Timer calibration	0.002	0.002	0.002	0.0233	0.0389	0.0583
4. Water density determination	0.015	0.015	0.015	0.015	0.015	0.015
5. Evaporation effect	0.00346	0.00346	0.00346	0.00346	0.00346	0.00346
6. Zero drift/ offset of the DUT	0.000	0.000	0.000	0.000	0.000	0.000
7. Resolution of the DUT	0.02887	0.00577	0.00289	0.00005	0.00003	0.00019
8. Type A uncertainty of the DUT	0.0377	0.0653	0.0219	0.0371	0.0197	0.0265
Relative combined uncertainty (u_c)	0.0500	0.0671	0.0268	0.0465	0.0462	0.0659
Relative expanded uncertainty (U) for approx. 95% confidence level	0.12	0.22	0.07	0.11	0.09	0.13
Coverage factor k	2.32	3.31	2.43	2.43	2.05	2.00

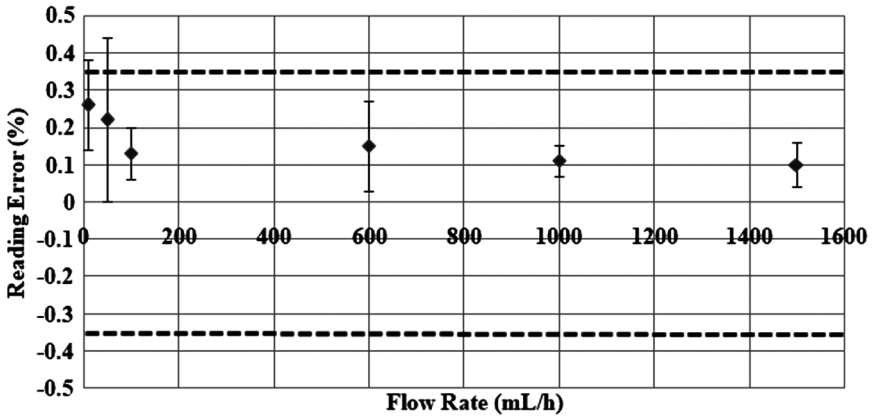

Fig 4 — Errors of the syringe pump, model: Fusion 6000, make: Chemyx at various flow rates for totalized volume mode

a dominant factor at several flow points. Accordingly, the expanded uncertainty has been compensated by using the student's t-distribution and effective degree of freedom as per GUM Annex Table G.2 for which procedure has been mentioned in Eqs 5 & 6[23].

For performance verification of the developed system, there are two ways. Firstly, we calibrated the syringe pump at various flow rates and determined its errors. If our system's performance is satisfactory, all the measured errors should be within the manufacturer's specification i.e. within accuracy of ±0.35% in the present case. Figs 4 & 5 depict a graphical representation of the syringe pump's errors at various flow rates for totalized volume and volume flow rate respectively. The uncertainty has been shown as error bars. The dashed lines on the plot show the accuracy of the syringe pump. The analysis of Figs 4 & 5 leads to the conclusion that all measured errors fall within the accuracy (*i.e.* ±0.35%) of the syringe pump. Normally, manufacturers do not take into account the uncertainty of the measurement while deciding the accuracy of the syringe pump. In this case, when uncertainty of measurement is taken into account, the error ± uncertainty values lie within the manufacturer's specification (*i.e.* ±0.35%) except at 10 mL/h and 50 mL/h which is slightly higher. This verifies the performance of our developed micro-liquid flow calibration system.

In a second way, the performance of the system is verified through participation in interlaboratory comparison (ILC) or international intercomparison using the appropriate artefacts[30-32]. Since in micro liquid flow, there is no formal international intercomparison conducted so far, as registered in the BIPM Keycomparison Database (KCDB). However, there have been a few international intercomparisons within EURAMET and also between other NMIs/ DIs unofficially to prove the performance of the micro

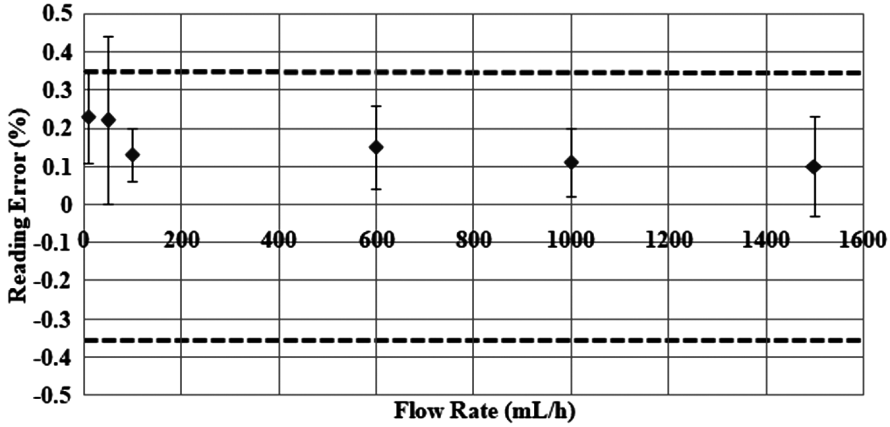

Fig 5 — Errors of the syringe pump, model: Fusion 6000, make: Chemyx at various flow rates for volume flow rate mode

Table 6 — Informal comparison results of infusion device analyzer (IDA-5).

Sr. No.	Nominal Flow Rate (mL/h)	NPLI assigned value		Fluke Biomedical assigned value		E_n value = (A-B)/ $\sqrt{(U_A^2 + U_B^2)}$
		Average Error A (%)	Expanded Uncertainty U_A (%)	Average Error B (%)	Expanded Uncertainty U_B (%)	
		Totalized volume mode: 25 mL@200 mL/h and 45 mL@800 mL/h				
1.	200	-0.54	0.30	-0.12	0.34	-0.93
2.	800	-0.82	0.30	-0.56	0.50	-0.45
		Volume flow rate mode: 20 mL@100 mL/h and 20 mL@830 mL/h				
3.	100	0.20	0.30	0.38	0.34	-0.40
4.	830	-0.13	0.30	0.03	0.50	-0.27

liquid flow calibration facilities[4,12,13,18]. Whenever such an opportunity for participation in international intercomparison is available to us, we will participate in those comparisons to verify our system's performance and support our CMC claim. Here, the system's performance was unofficially verified through calibrated infusion device analyzer, model: IDA-5, make: Fluke Biomedical, USA. This infusion device analyzer (IDA), to be used as a DUT, was recently received as a part of a new automated primary micro liquid flow calibration facility at CSIR-NPL in the flow range 10 mL/h to 1000 mL/h which uses a constant head tank along with infusion pump as a flow source. The 520 g analytical balance along with the digital timer will be used as reference standards in this automated primary facility. This new system is expected to improve the uncertainty of flow rate in the flow range of 100 mL/h to 1000 mL/h. At present, the system is under installation. For the performance verification of the newly developed system, the infusion device analyzer (IDA-5) was calibrated at the same flow rate and volume, as it was calibrated by the manufacturer (*i.e.* Fluke) at their USA facility and E_n values were calculated. The laboratory temperature and relative humidity during measurement were (24±1) °C and (43±9) %RH. The channel 1 of the IDA-5 has been used for the measurement. Table 6 shows the results of the verification/informal comparison. From the results, it is concluded that the $|E_n|$ values are less than or equal to 1 which proves the satisfactory performance of the micro liquid flow calibration facility. It is to be noted that Fluke Biomedical uses a calibrated syringe pump as a reference standard for routine calibration of IDAs, therefore, the uncertainty of IDA calibration is higher.

Several infusion device analyzers of various models like IDA-1S, IDA-4 and IDA-5, make: Fluke Biomedical, USA have been calibrated using this developed micro liquid flow calibration facility. The accuracy of these infusion device analyzers are in the range of ±1% to ±2% for the totalized volume and volume flow rate measurements. Fig. 6 shows the errors of one infusion device analyzer, model IDA-1S at various flow rates. In the figure, the uncertainty has been shown as error bar and accuracy has been represented by the dashed line. From the figure, it is concluded that error ± uncertainty values are within

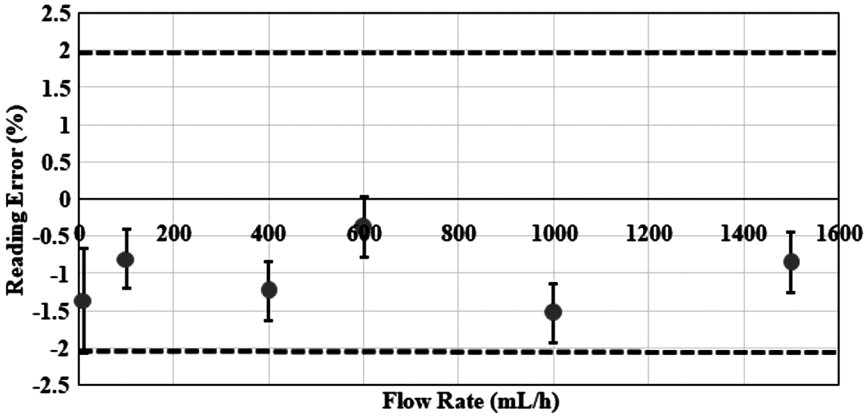

Fig 6 — Errors of the infusion device analyzer IDA-1S at different flow rates

manufacturer's specifications (accuracy) of the infusion device analyzer.

4 Conclusion and Way Forward

From the above studies, the following conclusions are drawn;

i) A new Primary Low Liquid Flow Calibration Facility based on the weighing method has been designed and developed indigenously to support biomedical laboratories, hospitals and accredited laboratories. This has enabled NPLI to maintain NMI status in micro-liquid flow measurement.

ii) The facility uses the standing start and standing finish method for calibration of mass flowmeters, microfluidic devices, syringe pumps, infusion pumps, infusion device analyzers, etc. in the flow range of 10 mL/h to 1500 mL/h. The study to extend this flow range down to 1 mL/h is being carried out where a mineral oil is mixed with distilled water in the glass beaker for minimizing the evaporation. Due to its lower density as compared to water, it forms a thin film over water surface and reduces evaporation.

iii) The relative expanded uncertainty of measurement for both totalized and flow rate parameters is found to be 0.30 % (at k=2) for the above flow range. The evaporation effect and repeatability have the dominant effect on the uncertainty of measurement.

iv) The performance of the system has been verified through a calibrated infusion device analyzer (model: IDA-5) from M/s. Fluke Biomedical, USA. In the future, we will participate in international intercomparisons to support our claimed CMC for a whole flow range and thereafter go for the International peer review for approval of CMCs in the low liquid flow area.

v) The improvements to the low liquid flow calibration facility can be done in the following way:

a) By implementing an automated data acquisition system where the timer is triggered automatically minimizing the error due to manual triggering of the digital timer.

b) To reduce the evaporation effect, the mineral oil can be mixed with distilled water or an evaporation trap may be employed.

c) By designing the overhead-based system with an infusion pump for continuous flow, the large mass/ volume can be collected in a larger capacity analytical balance to increase the collection time, thereby, reducing the timing error/ uncertainty. We are developing this system with higher capacity (i.e. 520 g) analytical balance, automatic data acquisition and automatic timer triggering. At present, this system is under the installation & commissioning stage. The uncertainty of the system is expected to improve (<0.30%) in the flow range (100 to 1000) mL/h.

d) By adopting the dynamic weighing method, the same weighing scale can be utilized for higher flow calibrations with enhanced uncertainty. This approach has already been implemented by several National Metrology Institutes (NMIs) and Designated Institutes (DIs). In the future, NPLI aims to implement this system to extend its flow range capabilities and further improve measurement uncertainty.

e) NPLI maintains five gravimetric-based primary water flow standards covering a flow range from 10 mL/h to 650 m³/h (spanning approximately eight orders of magnitude), utilizing five weighing balances: 82g/220g dual range, 12 kg, 300 kg, 3000 kg, and 6000 kg. All of these are

electromagnetic force compensation type balances designed for high-accuracy mass measurement. However, there is a gap in the flow range between 1000 mL/h (1 L/h) and 10,000 mL/h (10 L/h). The syringe pump currently used in our system has coarser accuracy. The best existing device (BED), a syringe pump model Fusion 6000 by Chemyx, used for CMC demonstration, is customer-owned. Based on our experience of calibrating this DUT, which has a broad flow range of 1 mL/h to 24,480 mL/h using a 300 mL stainless steel syringe, we find that this syringe pump can extend the micro-flow range and bridge the gap between 1000 mL/h and 10,000 mL/h, while also improving uncertainty if used in place of our existing syringe pump. The 520 g capacity analytical balance from the overhead-based new primary micro liquid flow calibration facility will be employed to calibrate the flow generated by this 300 mL syringe. We intend to acquire this syringe pump to improve flow range uncertainty and extend the flow range.

Declaration of Competing Interest

The authors affirm that they do not possess any identifiable financial conflicts or personal affiliations that might be perceived as influencing the findings presented in this paper.

Acknowledgement

The authors express their gratitude to the Director, CSIR-National Physical Laboratory, New Delhi, for his unwavering encouragement and guidance. One of the authors, Sanjeet Kumar, extends his thanks to the Council of Scientific and Industrial Research (CSIR) in New Delhi, India, for the financial support in terms of fellowship.

References

1 Knight K H, Brand F M, Mchaourab A S & Veneziano G, *Croat Med J*, 48 (2007) 22.
2 Hayek S M, Deer T R, Pope J E, Panchal S J & Patel V P, *Pain Physician*, 14 (2011) 219.
3 Capes D F, *et al*., *Am J Health-Syst Pharm*, 52 (1995) 1646.
4 Schmidt J W & Wright J D, "Micro-Flow Calibration Facility at NIST", 9th International Symposium on Fluid Flow Measurement (ISFFM), Arlington, Virginia, (2015).
5 Wright J D & Schmidt J W, *Proceeding of the 18th International Flow Measurement Conference (FLOMEKO 2019),* Lisbon (Portugal), 2019.
6 Jaiswal S K, Yadav S, Bandyopadhyay A K & Agarwal R, *MAPAN – J Metrol Soc India*, 27 (2012) 63.
7 Snijder R A, *et al.*, *Biomed Eng/Biomedizinische Technik*, 60 (2015) 277.
8 Lee P T, Thompson F & Thimbleby H, *Brit J Nursing*, 21 (2012) S12.
9 Elsa B, et al., Calibration and use of syringe pumps. *16th Int Cong Metrol,* EDP Sciences, (2013) 02007.
10 Ogheard F, Batista E, Bissig H, Petter H T, Lucas P & Niemann A K,Metrological assessment of microflow meters and drug delivery devices in the scope of the "MeDD" EMRP project, *17 Int Cong Metrol,* (2015) 09004.
11 Bissig H, Tschannen M & Huu M de, Micro flow standard for steady, pulsating flow, In *2nd Int Conf Microfluid Handl Syst Freiburg, Germany*, (2014).
12 Hugo B, *et al*., *Biomed Eng/Biomedizinische Technik*, 60 (2015) 301.
13 Su C M, The Micro Water Flow Calibration Facility at CMS and Brief Overview of those at Other NMIs, *APMP 2015 Technical Committee for Fluid Flow (TCFF) Workshop* held at NIM, Beijing, China (2015).
14 Chiang C L, Micro flow measurement and application, *APMP 2023 Technical Committee for Fluid Flow (TCFF) Workshop* held at Shenzhen, China, (2023).
15 Meng T, Establishment of micro liquid flow facility at NIM, *Technical Committee for Fluid Flow (TCFF) Workshop* held at Shenzhen, China, (2023).
16 Batista E, Godinho I, Martins R F, Mendes R & Robarts J, *Flow Meas Instr*, 75 (2020) 101789.
17 Elsa B, et al., *Flow Meas Instr*, 71 (2020) 101691.
18 Mills C, Elsa B, Hugo B, Florestan O, Abir W B, Oliver B, Krister S, John M, Sabrina K, Kerstin T, Guilherme M, Anders N, Stephan K, Gijs R & Joost L, *Biomed Eng-Biomed Tech*, 68 (2023) 13.
19 Melvad C & Frederiksen J, *Proc Flomeko*, Paris, (2013).
20 Kumar S, Jaiswal S K, Varshney A, Singh C, Rab S & Yadav S, "Uncertainty analysis of newly developed Low Liquid Flow Calibration Facility at CSIR-NPL", presented in *the 11th Int Conf Adv Metrol (AdMet-2022)*, held at CSIR-National Physical Laboratory, New Delhi, (2022).
21 NEL Documents, Good Practice Guide, The Calibration of Flow Meters, www.tuvnel.com, available at link: https://pasargadabzar.com/wp-content/uploads/2022/06/The_Calibration_of_Flow_Meters.pdf [accessed on 23-5-2024].
22 BIPM JCGM 200:2008, International vocabulary of metrology — Basic and general concepts and associated terms (VIM), 3rd Edition, 2012, available at link: http://www.bipm.org/utils/common/documents/jcgm/JCGM_200_2012.pdf. [accessed on 23-5-2024].
23 JCGM 100:2008 *Evaluation of measurement data – Guide to the expression of uncertainty in measurement,* available at link*: https://www.bipm.org/documents/20126/2071204/JCGM_100_2008_E.pdf/cb0ef43f-baa5-11cf-3f85-4dcd86f77bd6* [accessed on 23-5-2024].
24 ISO 5168:2005, *Measurement of liquid flow in closed conduits – Procedure for the evaluation of uncertainties*, 2nd Edn, (2005) 1.
25 Jaiswal S K, Ojha V N & Singh A, *J Sci Indus Res*, 64 (2005) 666.
26 ISO 4185, *Measurement of Liquid Flow in Closed Conduits – Weighing Methods*, 1st Edn, (1980) 1.
27 Jaiswal S K, Singh C, Kumar S, Varshney A, Rab S & Yadav S, *Flow Meas Instr*, 86 (2022) 1.
28 Batista E, Almeida N, Filipe E & Godinhol I, *Uncertainty calculation in gravimetric microflow measurements*, St Petersburg: AMCTM, (2014).

29 WGFF Guidelines for CMC uncertainty and Calibration Uncertainty, October 21, 2013. Available in BIPM website at link: https://www.bipm.org/documents/20126/44756349/ccm-wgff-guidelines.pdf/eda74c50-1192-a20e-fc16-a3760e11329e [accessed on 23-5-2024].

30 NABL 162, Guidelines for proficiency testing program for testing and calibration laboratories, (2008).

31 NABL 164, Guidelines for inter-laboratory comparison for calibration laboratories where formal PT programs are not available, (2012).

32 Cox M G, *Metrologia*, 39 (2002) 589.