Instituto Português da Qualidade

EURAMET

Calibration of Infusion Device Analysers

Final Report

EURAMET research Project no. 1722

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IPQ-DMET - Volume and Flow Laboratory

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Contents

1. Introduction

The purpose of this comparison is to verify the agreement of results and uncertainties in the calibration of an Infusion Device Analyser (IDA). These instruments are used to verify the accuracy of drug delivery devices (DDD) by technical staff or maintenance officers in the hospitals. The participant laboratories should follow the new version of EURAMET cg 27 [1] regarding the calibration procedure. This document presents the guidelines for performing this comparison.

This document presents the guidelines and results of this comparison. The measurements were performed from October to December 2025.

Table 1 – Participants

Institute	Country	Contact	Date of measurements
IPQ	Portugal	Elsa Batista	September 2025 and December 2025
RISE	Sweden	Oliver Büker	September 2025
METAS	Switzerland	Hugo Bissig	October 2025
CMI	Czech Republic	Miroslava Benkova	November 2025

2. The instrument

An IDA with one channel used in this comparison is described in table 2.

Table 2 – Instrument used in the comparison

Manufacturer	Model	Serial number	Minimum flow rate	Maximum flow rate
Fluke	IDA-1S	1863594	0,5 mL/h	1000 mL/h

Figure 1 – One Channel IDA

3. Measurement procedure

The measurement procedure was described in the protocol, and all participants have followed it.

- A measurement of a minimum delivered volume of 10 mL or 20 mL will be necessary depending on the flow rate, but for low flow rates 2 mL will be sufficient.
- The IDA should be switched on and left for at least 6 hours in the laboratory to stabilise the internal temperature which is affected by the heating effect of the electronics in the IDA.
- The starting of the test should be done after stabilization of the system and the priming of the IDA has ended (indication on display and no bubbles inside).
- 5 flow points will be tested with 3 repetition each.
- The measurand is the average flow rate read in the IDA.
- The data can be collected using the IDA software.
- Water and ambient temperature, relative humidity and atmospheric pressure have to be recorded during the calibration.

3. Calibration method

The calibration of an IDA can be done by the gravimetric method or by the displacement method, as described in EURAMET cg 27 [1].

All participants used the displacement method. Each setup is presented in the following figures.

Figure 2 – Measurement setup at IPQ, a Nexus pump 3000 was used as flow generator
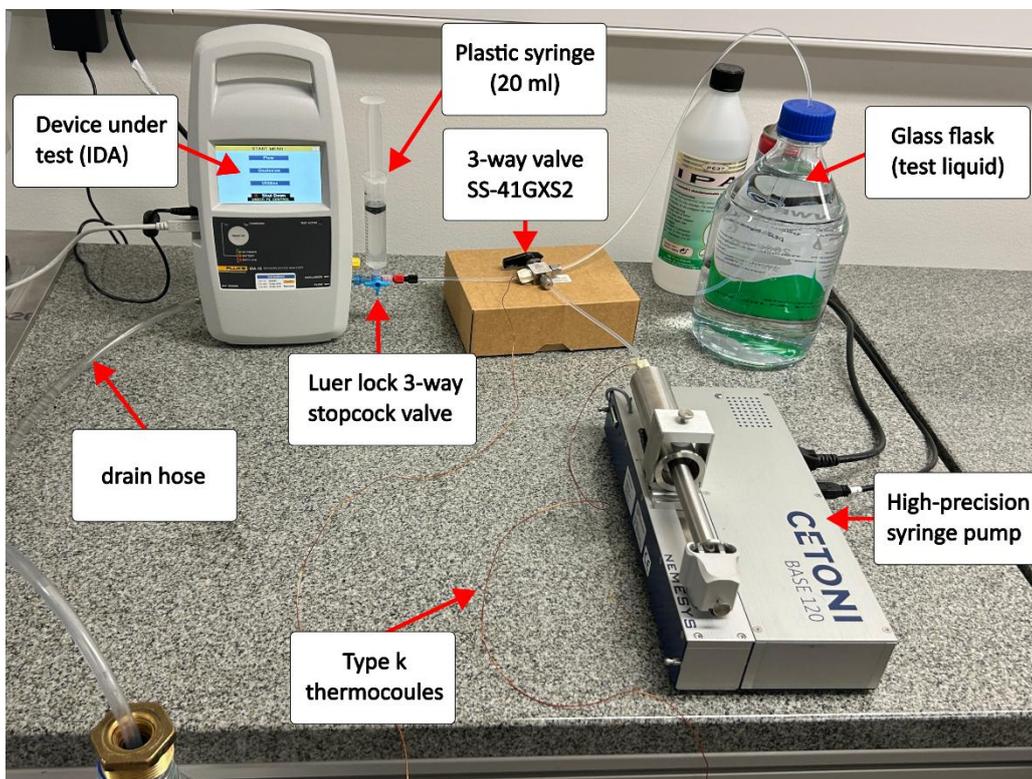

Figure 3 – Measurement setup at RISE, a Cetoni pump was used as a flow generator
(The inlet of the IDA, the Swagelok 3-way valve and the outlet of the syringe are at the same height.)
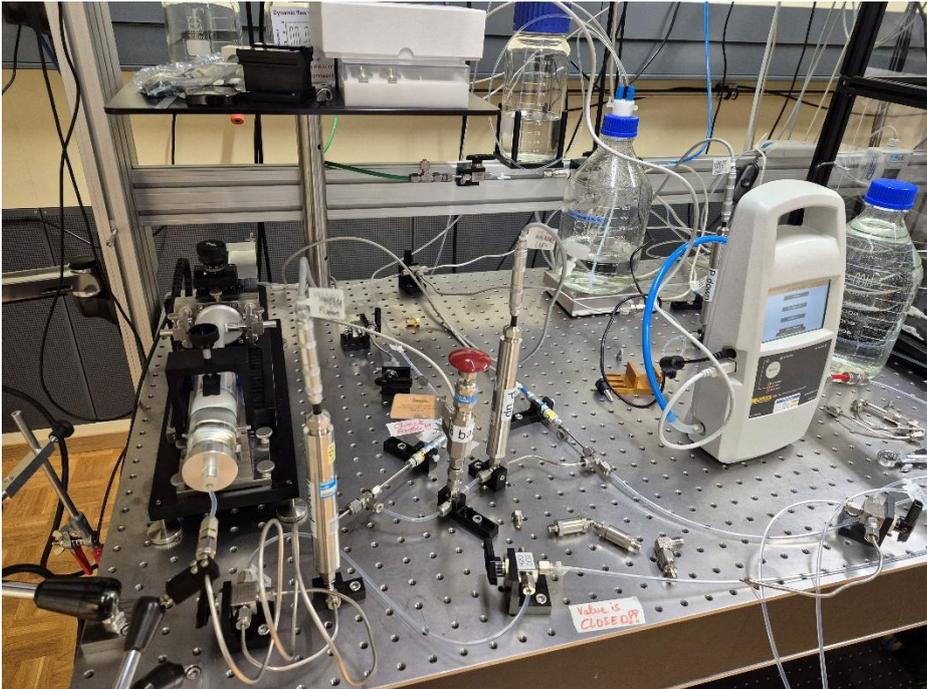
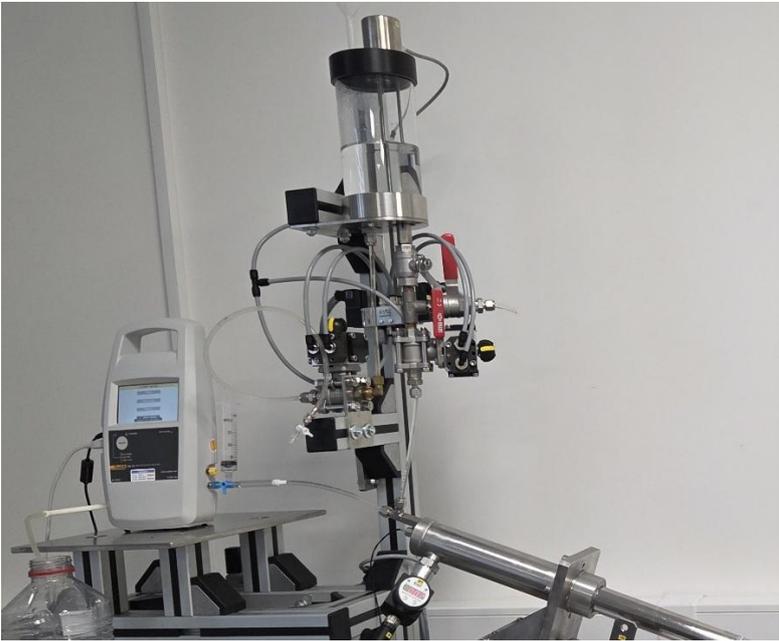Figure 4 - Measurement setup at METAS, a piston prover was used as flow generator.

Figure 5 - Measurement setup at CMI, a piston prover was used as flow generator.

The flow generator characteristic is described in table 3.

Table 3 – Flow generator characteristics

Flow generator	Characteristics
IPQ	Nexus 3000 precision syringe pump from Chemyx with a range from 2 pL/min to 500 mL/min
RISE	Ultra-high precision syringe pump (CETONI neMESYS Base 120 controller and neMESYS Low Pressure module 290N with a range of 0,006 nL/min to 150 mL/min
METAS	The METAS Microflow and Milliflow facilities consist of homemade piston provers to generate the flow, with a speed range from 0,1 mm/s to 0,1 μm/s and from 4 mm/s to 4 μm/s.
CMI	Homemade piston prover PP002 with a range of 1 ml/h to 6 000 mL/h

5. Ambient conditions

The ambient conditions requirements were described in the technical protocol and all participants have followed it, namely:
- humidity higher than 45 %,
- ambient temperature between 17 ºC up to 23 ºC,
- the water temperature must be near the air temperature and shall not vary more than 0,5 ºC during the measurements.

6. Evaluation of the measurement results

6.1 Reference value

To determine the reference value at each flow rate the formula of the weighted mean is used, by means of the inverses of the squares of the associated standard uncertainty are the weighting factors [2]:

$$y = \frac{x_1/u^2(x_1)+...+x_n/u^2(x_n)}{1/u^2(x_1)+....+1/u^2(x_n)} \tag{2}$$

To determine the standard uncertainty u(y) associated with y is used the following expression:

$$u(y) = \sqrt{\frac{1}{1/u^2(x_1)+...+1/u^2(x_n)}} \tag{3}$$

6.2 Consistency determination

To identify an overall consistency of the results a chi-square test can be applied to all n calibration results.

$$\chi^2_{obs} = \frac{(x_1 - y)^2}{u^2(x_1)} + ... + \frac{(x_n - y)^2}{u^2(x_n)} \tag{4}$$

where the degrees of freedom are: $v = n - 1$

The consistency check is regarded as failed if: $\Pr\{\chi^2(v) > \chi^2_{obs}\} < 0,05$. The function *CHIINV(0,05; n-1)* in MS Excel was used. The consistency check was failing if *CHIINV(0,05; n-1) < χ^2_{obs}*.

If the consistency check did not fail then *y* was accepted as the RV x_{ref} and $U(x_{ref})$ was accepted as the expanded uncertainty of the RV.

If the consistency check failed then the laboratory with the highest value of $\dfrac{(x_i - y)^2}{u^2(x_i)}$ is excluded from the next round of evaluation and a new RV, reference standard uncertainty and chi-squared value is calculated again without the excluded laboratory.

The normalized error (En value) was also calculated. This value is defined as [3]:

$$E_{n\,lab-i} = \left| \frac{\varepsilon_{lab-i} - \varepsilon_{RV}}{\sqrt{U^2(\varepsilon_{lab-i}) - U^2(\varepsilon_{RV})}} \right| \tag{5}$$

where ε_{lab-i} is the error of lab-i for a certain point, ε_{RV} is the comparison reference value (RV) for the error and $U(\varepsilon_{lab-i})$ and $U(\varepsilon_{RV})$ and the expanded uncertainties (*k*=2) of those values.

With the absolute value of E_n one can conclude that:
- The results of the laboratory for a certain point are consistent (passed) if $E_n < 1$
- The results of the laboratory for a certain point are inconsistent (failed) if $E_n > 1$

IPQ performed two calibrations, one at the beginning and another at the end of the to access the stability of the artefacts.
The first result of IPQ was considered for the determination of reference value, along with its value of uncertainty.

7. Measurement results

The IDA was calibrated at the following points:

- 1 mL/h (minimum 2 mL volume)
- 10 mL/h (minimum 10 mL volume)
- 50 mL/h, 100 mL/h, 500 mL/h (minimum 20 mL volume)

7.1. Determination of the stability of the IDA

In order to determine the comparison reference value (RV) and access the stability of the IDA two measurements were performed by IPQ - one at the beginning and other at the end of the comparison. The results are presented in table 4.

Table 4 – Stability of the transfer standard

1 mL/h	IPQ1		IPQ2		
	Error (%)	**Uncertainty (%)**	**Error (%)**	**Uncertainty (%)**	ΔQ **(%)**
	0,13	1,2	0,12	1,18	0,01
10 mL/h	**Error (%)**	**Uncertainty (%)**	**Error (%)**	**Uncertainty (%)**	ΔQ **(%)**
	-0,18	0,33	-0,08	0,32	0,10
50 mL/h	**Error (%)**	**Uncertainty (%)**	**Error (%)**	**Uncertainty (%)**	ΔQ **(%)**
	-0,32	0,18	-0,30	0,16	0,02
100 mL/h	**Error (%)**	**Uncertainty (%)**	**Error (%)**	**Uncertainty (%)**	ΔQ **(%)**
	-0,31	0,19	-0,30	0,18	0,01
500 mL/h	**Error (%)**	**Uncertainty (%)**	**Error (%)**	**Uncertainty (%)**	ΔQ **(%)**
	-0,47	0,25	-0,46	0,24	0,01

The result variation of IPQ is smaller than the declared uncertainty and therefore it is assumed that the IDA was stable during the comparison.

Only the first result of IPQ was used to determine the comparison reference value (RV).

7.2. Error results - Flow measurements

The measurement results along with absolute En value is presented in the following tables and figures for all points and all participants.

7.2.1 - 1 mL/h

Table 5 – Measurement results – 1 mL/h

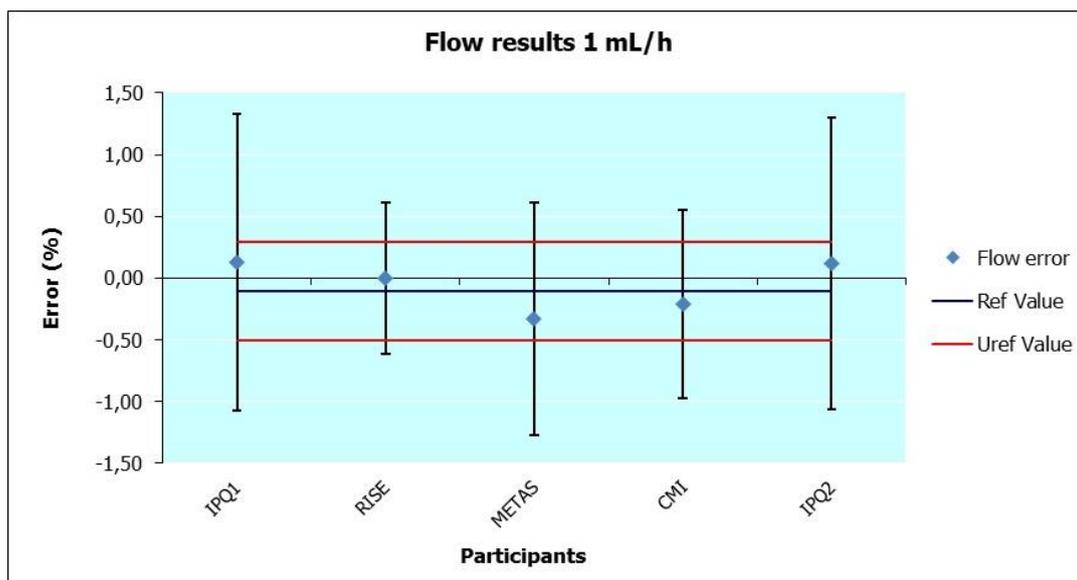| Participant	Error (%)	Expanded Uncertainty (k=2) (%)	En value
IPQ1	0,13	1,20	0,21
RISE	0,00	0,61	0,22
METAS	-0,33	0,94	0,27
CMI	-0,21	0,76	0,17
IPQ2	0,12	1,18	
Ref	-0,10	0,40	

Figure 6 –Results with reference value – 1 mL/h

As can be seen from the table and figure above, all the results are consistent with the reference value, passed the chi-square test and have En values smaller than 1.

7.2.2. 10 mL/h

Table 6 – Measurement results – 10 mL/h

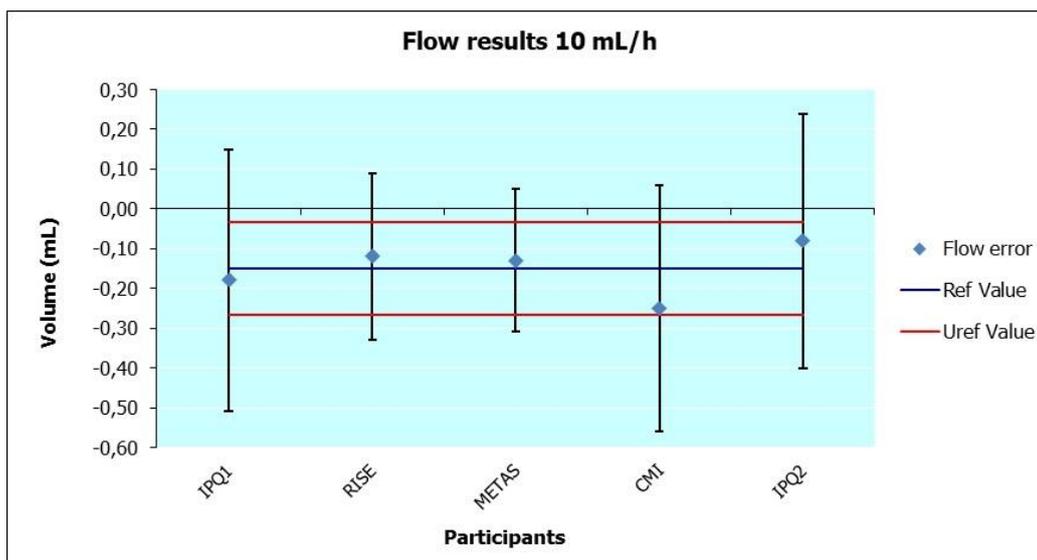| Participant	Error (%)	Expanded Uncertainty ($k=2$) (%)	En value
IPQ1	-0,18	0,33	0,10
RISE	-0,12	0,21	0,17
METAS	-0,13	0,18	0,15
CMI	-0,25	0,31	0,35
IPQ2	-0,08	0,32	
Ref	-0,15	0,12	

Figure 7 –Results with reference value – 10 mL/h

As can be seen from the table and figure above, all the results are consistent with the reference value, passed the chi-square test and have En values smaller than 1.

7.2.3. 50 mL/h

Table 7 – Measurement results – 50 mL/h

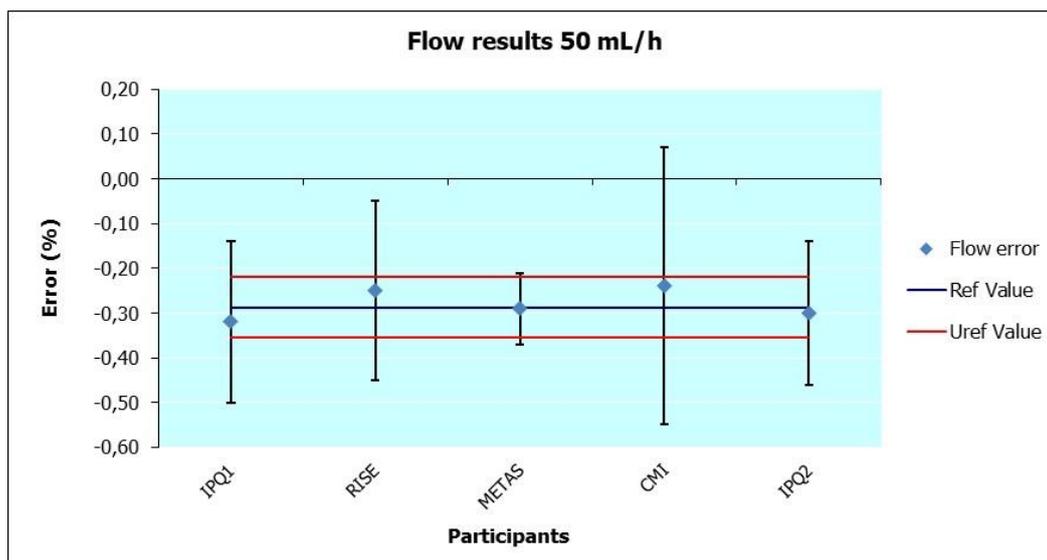| Participant	Error (%)	Expanded Uncertainty (*k*=2) (%)	En value
IPQ1	-0,32	0,18	0,20
RISE	-0,25	0,20	0,20
METAS	-0,29	0,08	0,06
CMI	-0,24	0,31	0,16
IPQ2	-0,30	0,16	
Ref	-0,29	0,067	

Figure 8 –Results with reference value – 50 mL/h

As can be seen from the table and figure above, all the results are consistent with the reference value, passed the chi-square test and have En values smaller than 1.

7.2.4. 100 mL/h

Table 8 – Measurement results – 100 mL/h

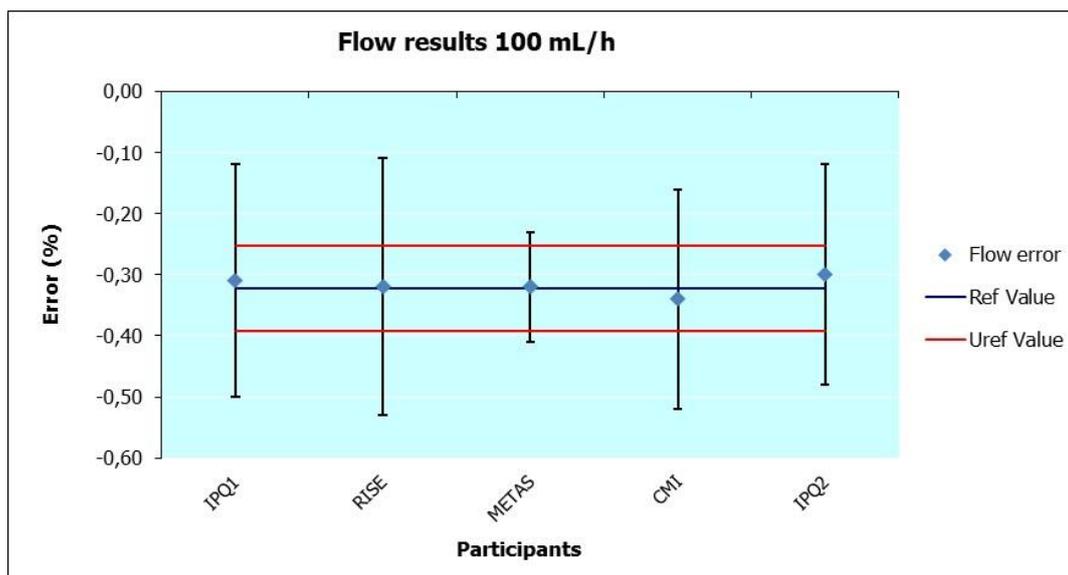| Participant	Error (%)	Expanded Uncertainty (k=2) (%)	En value
IPQ1	-0,31	0,19	0,07
RISE	-0,32	0,21	0,01
METAS	-0,32	0,09	0,03
CMI	-0,34	0,18	0,11
IPQ2	-0,30	0,18	
Ref	-0,32	0,070	

Figure 9 –Results with reference value – 100 mL/h

As can be seen from the table and figure above, all the results are consistent with the reference value, passed the chi-square test and have En values smaller than 1.

7.2.5. 500 mL/h

Table 9 – Measurement results – 500 mL/h

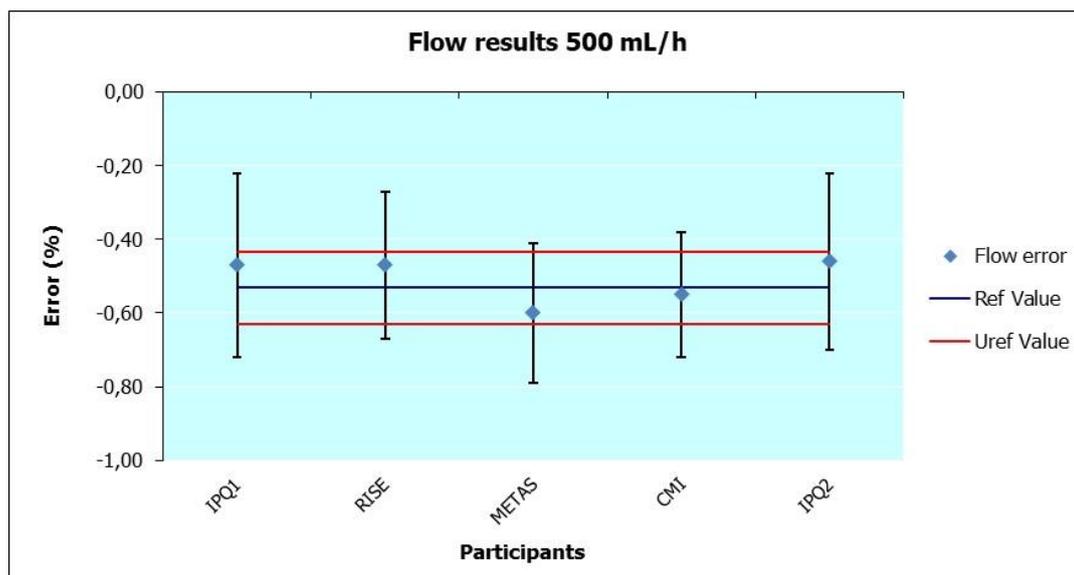| Participant	Error (%)	Expanded Uncertainty (k=2) (%)	En value
IPQ1	-0,47	0,25	0,27
RISE	-0,47	0,20	0,35
METAS	-0,60	0,19	0,42
CMI	-0,55	0,17	0,13
IPQ2	-0,46	0,24	
Ref	-0,53	0,098	

Figure 10 –Results with reference value – 500 mL/h

As can be seen from the table and figure above, all the results are consistent with the reference value and have En values smaller than 1.

8. Uncertainty calculation

The laboratories calculated the uncertainty according to GUM [4] and the proposed uncertainty components, standard uncertainty, resolution and repeatability of the results.

In general, the uncertainty claims are very similar. The components used by all laboratories were the reference standard calibration, the repeatability of the measurements and the IDA resolution.

9. Conclusions

In this comparison between IPQ, RISE, METAS and CMI, an Infusion Device Analyser was calibrated. The stability of the instrument was confirmed by the initial and final calibration of IPQ.

The measurements results, from all participants, in all points are consistent with the comparison reference values and have En values lower than 1.

The described uncertainty components were previously agree and harmonized by the participants and the presented values are very similar for all participants.

This was the first comparison in the field of the calibration of an IDA and has the purpose of validating the new version of EURAMET cg27. The obtained results allows the validation of the calibration procedure described in this guide for this type of instrument used to verify the accuracy of drug delivery devices by the users or maintenance officers in the hospitals.

10. CMC table

In order to assess the support of CMCs entries provided by this comparison Table 10 is provided.

For NMIs without CMC on this range, the label n/a is shown

Table 10 - Consistency check for CMC entries for flow (IDA, displacement method)

NMI	Method	U_{CMCs} /%	$U_{Comparison}$/%	Comments
IPQ	Displacement	n/a	1,20 – 0,16	No published CMC for displacement method
RISE	Displacement	0,20	0,61 – 0,20	Comparison flow rate: 1 mL/h – 500 mL/h
METAS	Displacement	0,30 – 0,07	0,94 – 0,08	Comparison flow rate: 1 mL/h – 500 mL/h
CMI	Displacement	0,16 - 0,10	0,80 – 0,17	CMC range published from 500 mL/h to 6000 mL/h The laboratory would like to extent the flow range down to 1 mL/h

11. References

1. **EURAMET cg 27 -** Guidelines for the Calibration of Drug Delivery Devices and Infusion Device Analysers | TC-F | Version 1.0, 02/2024

2. **JCGM 100:2008** - *Guide to the expression of uncertainty in measurement* (GUM). (1993, amended 1995) (published by ISO in the name of BIPM, IEC, IFCC, IUPAC, IUPAP and OIML)

3. M.G. Cox, The evaluation of key comparison data, Metrologia, 2002, Vol. 39, 589-595.

4. **ISO 13528:2005** - Statistical methods used in proficiency testing by interlaboratory comparison