Australian Government
Department of Industry, Innovation and Science
National Measurement Institute

Proficiency Test Report
AQA 19-01
Methamphetamine

July 2019

ACKNOWLEDGMENTS

This study was conducted by the National Measurement Institute (NMI). Support funding was provided by the Australian Government Department of Industry, Innovation and Science.

I would like to thank the management and staff of the participating laboratories for supporting the study. It is only through widespread participation that we can provide an effective service to laboratories.

The assistance of the following NMI staff members in the planning, conduct and reporting of the study is acknowledged.

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TABLE OF CONTENTS

SUMMARY

AQA 19-01 was conducted in March 2019. Three test samples of methamphetamine hydrochloride were sent to twenty-four laboratories. Two laboratories requested two sets of the test samples. Twenty-six sets of results were submitted by the due date.

Test samples were prepared at the NMI laboratory in Sydney using methamphetamine hydrochloride approximately 80% base (m/m) supplied by the Australian Federal Police (AFP).

The assigned values for Samples S1 and S2 were the reference values determined by quantitative nuclear magnetic resonance spectrometry (QNMR) with maleic acid (NMI certified reference material QNMR010) as internal standard.

Traceability: The reference values are traceable to the SI through Australian Standards for mass via balance calibration certificates and the purity of the NMI maleic acid certified reference material QNMR010.2018.01.

The assigned value for Sample S3 was the robust average of participants' results.

Traceability: The consensus of participants' results is not traceable to any external reference, so although expressed in SI units, metrological traceability has not been established.

The outcomes of the study were assessed against the aims as follows:

- *assess the proficiency of laboratories measuring methamphetamine in samples typical of a routine seizure;*

Laboratory performance was assessed by z-score and E_n-score.

Laboratories **3**, **4**, **6**, **7**, **8**, **9**, **11** (only two results submitted), **13**, **14**, **15**, **17**, **18**, **21**, **22**, **23**, **24**, **25** and **26** returned satisfactory z and E_n-scores for all results.

Laboratory **10** returned unsatisfactory z-scores and E_n-scores for all samples.

Of the 77 results for which z-scores were calculated, 70 (91%) returned $|z| \leq 2$ indicating a satisfactory performance.

Of the 77 results for which $|E_n|$-scores were calculated, 68 (88%) returned $|E_n| \leq 1$ indicating agreement of the participants' results with the assigned value within their respective expanded uncertainties.

- *develop a practical application of traceability and measurement uncertainty and provide participants with information that will assist uncertainty estimates; and*

71 results (92%) were reported with an associated expanded uncertainty. Laboratories **16** and **22** did not report an uncertainty. These laboratories were not accredited.

Laboratory **12** reported an identical uncertainty for samples which were of significantly different concentrations.

The magnitude of reported uncertainties was within the range 1% to 27% relative.

- *test the ability of participants to identify a cutting agent commonly found in controlled drug preparation*

Caffeine was used to prepare Samples S1 and S2. Twenty-five laboratories reported on the diluent and correctly identified it.

Dimethylsulfone (DMS or MMS) was used to prepare Sample S3. Eighteen laboratories reported the diluent and correctly identified it.

INTRODUCTION

1.1 NMI Proficiency Testing Program

The National Measurement Institute (NMI) is responsible for Australia's national measurement infrastructure, providing a range of services including a chemical proficiency testing program.

Proficiency testing (PT) is: 'evaluation of participant performance against pre-established criteria by means of interlaboratory comparison.'[1] NMI PT studies target chemical testing in areas of high public significance such as trade, environment, law enforcement and food safety. NMI offers studies in:

- pesticide residues in fruit and vegetables, soil and water;
- petroleum hydrocarbons in soil and water;
- PFAS in water, soil and biota;
- metals in soil, water, food and pharmaceuticals;
- controlled drug assay and clandestine laboratory;
- allergens in food; and
- folic acid in flour.

1.2 Study Aims

The aims of the study were to:

- assess the proficiency of laboratories measuring methamphetamine in samples typical of a routine seizure;
- develop a practical application of traceability and measurement uncertainty and provide participants with information that will assist uncertainty estimates; and
- test the ability of participants to identify a cutting agent commonly found in controlled drug preparation.

The choice of the test method was left to the participating laboratories.

1.3 Study Conduct

NMI is accredited by the National Association of Testing Authorities, Australia (NATA) to ISO 17043[1] as a provider of proficiency testing schemes. This controlled drug proficiency test is within the scope of NMI's accreditation.

The conduct of NMI proficiency tests is described in the NMI Chemical Proficiency Testing Study Protocol.[2] The statistical methods used are described in the NMI Chemical Proficiency Testing Statistical Manual.[3] These documents have been prepared with reference to ISO 17043 and The International Harmonized Protocol for the Proficiency Testing of Analytical Chemistry Laboratories.[4]

2 STUDY INFORMATION

2.1 Study Timetable

The timetable of the study was:

Invitation issued:	8 January 2019
Samples dispatched:	25 March 2019
Results due:	17 June 2019
Interim report issued:	17 June 2019

The results due date was changed from 3 May 2019 to 17 June 2019 due to delays in dispatch to overseas laboratories.

2.2 Participation

A total of ninety-nine international, national, state government and private laboratories were invited to participate.

Twenty-four laboratories agreed to participate and submitted results. Two laboratories requested two sets of samples to be analysed independently by two different analysts.

2.3 Test Material Specification

Three test samples were prepared in February 2019. The starting material for samples S1, S2 and S3 was methamphetamine hydrochloride approximately 80% base (m/m), supplied by the Australian Federal Police. Caffeine and dimethylsulfone, purchased from Sigma Aldrich, were used as cutting agents. Sample S1 and S2 were blind duplicates, cut with caffeine, and Sample S3 was cut with dimethylsulfone.

The methamphetamine was ground and sieved through a 180 μm sieve. The cutting agents were processed similarly to the methamphetamine powder.

Test samples were then prepared by mixing a known mass of sieved drug material with a known mass of sieved cutting agent in a tumbler overnight.

Portions of 150 mg of each of the test samples were weighed into labelled glass vials.

Sample S1 was prepared to contain 56.9% methamphetamine base (m/m).

Sample S2 (duplicate) was identical with Sample S1.

Sample S3 was prepared to contain 24.9% methamphetamine base (m/m).

2.4 Laboratory Code

Each participant was randomly assigned a confidential laboratory code.

2.5 Test Sample Homogeneity

The preparation of homogeneous test samples is an important part of a proficiency testing study. Given the small (<150 mg) test portions normally used for controlled substances analysis the particle size must be sufficiently small and uniformly distributed to ensure minimal influence on analytical precision.

The homogeneity testing of Samples S1 and S2 is described in Appendix 2. Samples were demonstrated to be sufficiently homogeneous for the purpose of this PT study.

Sample S3 was prepared using the same procedure and the results returned by participants gave no reason to question the homogeneity of the test samples.

2.6 Sample Dispatch and Receipt

A set of three test samples, each containing approximately 150 mg of test material, were dispatched on 25 March 2019.

The following items were packaged with the samples:

- a covering letter with instructions for participants; and
- a form for participants to confirm the receipt of the test samples.

An Excel spreadsheet for the electronic reporting of results was e-mailed to participants.

2.7 Instructions to Participants

Participants were asked to analyse the samples using their routine quantitative method and return the following information:

- one result for each sample as % m/m methamphetamine base;
- an estimate of the expanded uncertainty associated with the result as % m/m methamphetamine base at the 95% confidence level;
- brief detail on how the uncertainty was calculated e.g. uncertainty budget method;
- the identity of the cutting agents in all three samples, if part of routine analysis;
- origin and stated purity of the analytical reference standard used;
- brief summary of the quantitative method used;
- the completed results sheet by 3 May 2019. This date was later modified to 17 June 2019 due to delays in delivery of samples overseas; and
- any other comments.

2.8 Interim Report

An interim report was emailed to all participants on 17 June 2019.

3 PARTICIPANT LABORATORY INFORMATION

3.1 Test Method Summaries

Reported participant method summary is presented as received for information in Table 1.

Table 1 Participant Summary of Test Methods

Lab. Code	Extraction solvent	Internal standard	Calib. points	Technique	Detector	Column
1	ACN/MeOH/H2O	Analog of methamphetamine	7	UPLC	MSMS	C-18 coloumn
2	Methanol	N/A	6	HPLC	UV 258nm	Phenomenex Luna C18, 0.5% DEA pH 8.5:CH3OH 40:60
3	Methanol:KOH buffer (50:50)	Methoxyphenamine	3	UPLC	PDA	Acquity UPLC BEH C18
4	Methanol		5	HPLC	DAD	C18
5	Deuterium oxide	maleic acid		1H QNMR	Bruker AVIII 600 with BBFO probe	N/A
6	Methanol	Strychnine	6	UPLC	FID	Waters Acquity UPLC BEH Phenyl 1.8um, 2.1 mm x 100 mm
7	Methanol	NO	1	HPLC	DAD	Zorbax XDB-C18 (4,6x150 mm)
8	Isooctane + Ammonium Hydroxide	Dodecane	3	GC	FID, MS	HP-1MS
9	Methanol	Procaine	4	HPLC	DAD	HP5
10	ethyl acetate	diphenylamine	5	GC	FID	HP1
11	Dissolution in acetonitrile/water	Methoxyphenamine HCl	3	HPLC	DAD	Alltima C-18
12	Water/Acetonitril e (80:20)	None	2	HPLC	UV/Vis	C18
13	Purified Water	Phentermine	1	LC	DAD	Agilent Zorbax SB-C8
14	methanol	propylparaben	3	UPLC	PDA	ACQUITY C-18
15	Purified Water	Phentermine	1	LC	DAD	Agilent Zorbax SB-C8
16	Methanol	Methamphet-amine D11	6	GC	MS	Rxi-5Sil MS 30mx0.25mmlDx0.25um
17	Water	None	4	HPLC	PDA	C18
18	MilliQ water	None	6	UPLC	UV	Acquity UPLC® BEH C18 1.7 µm 2.1 x 100 mm
19	water	None	5	HPLC	UV DAD	Silica
20	Acetonitrile, ammonium acetate, diethylamine & water	None	3	HPLC	Diode Array	LiChrospher RP-18 (5µm)
21	Water	-	4	HPLC	DAD	Zorbax RX-sil
22	Ethanol	Propylparaben	7	UPLC	DAD	BEH Shield RP18
23	Methanol	None	5	HPLC	DAD	Phenomenex C-18-XB
24	D2O	Maleic acid		QNMR		NA
25	Water	N/A	6	LC	DAD	UPLC BEH C18 1.7uM
26	acetic acid/ACN/water (4/20/76 V/V/V)	No ISTD	5	HPLC	UV DAD	POROSHELL 120 EC-C18

3.2 Reported Basis of Participants' Measurement Uncertainty Estimates

Participant returns are listed in Table 2.

Table 2 Reported Basis of Uncertainty Estimate

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation		Guide Document for Estimating MU
		Precision	Method Bias	
1	Top Down - precision and estimates of the method and laboratory bias			
2	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate Analysis		Eurachem/CITAC Guide
3	Top Down - reproducibility (standard deviation) from PT studies used directly	Control Samples – Reference Material Duplicate Analysis	Standard Purity Masses and volumes	Eurachem/CITAC Guide
4	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Control Samples – Reference Material	Laboratory bias from PT studies Instrument Calibration Masses and volumes	ISO/GUM
5	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)			
6	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Control Samples – Duplicate Analysis	Laboratory bias from PT studies Standard Purity Instrument Calibration Masses and volumes Homogeneity of sample	Nata Technical Note 33
7	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Certified Reference Material Duplicate Analysis	Laboratory bias from PT studies Standard Purity Instrument Calibration	Nordtest Report TR537
8	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Control Samples – Certified Reference Material Duplicate Analysis	Recoveries of SS Standard Purity Matrix Effects Instrument Calibration Masses and volumes Homogeneity of sample	Eurachem/CITAC Guide
9	Top Down - precision and estimates of the method and laboratory bias	Control Samples	Laboratory bias from PT studies Recoveries of SS Standard Purity Matrix Effects Instrument Calibration Masses and volumes Homogeneity of sample	EA-4/16: 2003 and ILAG G-17:2002
10	Standard deviation of replicate analyses multiplied by 2 or 3	Control Samples – reference material	Standard Purity	
11	Bottom up (ISO/GUM, Fish bone/ Cause and effect diagram)	Duplicate Analysis	Recoveries of SS Standard Purity Matrix Effects Instrument Calibration Masses and volumes	ISO/GUM
12	Standard deviation of replicate analyses multiplied by 2 or 3	Control Samples – Reference Material Duplicate Analysis	Standard Purity Masses and volumes	Eurachem/CITAC Guide
13	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Spiked sample Duplicate Analysis	Laboratory bias from PT studies	Eurachem/CITAC Guide

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation		Guide Document for Estimating MU
		Precision	Method Bias	
14	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Certified Reference Material Duplicate Analysis	Standard Purity Instrument Calibration Masses and volumes Homogeneity of sample	Nata Technical Note 33
15	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Spiked sample Duplicate Analysis	Laboratory bias from PT studies	Eurachem/CITAC Guide
16	Standard deviation of replicate analyses multiplied by 2 or 3	Duplicate Analysis	Masses and volumes	ISO/GUM
17				
18	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate Analysis	Instrument Calibration Masses and volumes Homogeneity of sample	Nata Technical Note 33
19	repeatability, sample heterogeneity (ENFSI quantitative sampling guideline)	Control Samples – Reference Material Duplicate Analysis	Homogeneity of sample	Eurachem/CITAC Guide
20	Uncertainty Budget Method	Control Samples – Reference Material Duplicate Analysis	Standard Purity Instrument Calibration Masses and volumes	Internal document
21	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Sample from police case. Duplicate Analysis	Laboratory bias from PT studies	Nordtest Report TR537
22				
23				
24	Top Down - precision and estimates of the method and laboratory bias	Control Samples – previously analysed real seizure samples Duplicate Analysis	Matrix Effects Instrument Calibration Masses and volumes Homogeneity of sample	Eurachem/CITAC Guide
25	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate Analysis	Standard Purity Matrix Effects Instrument Calibration Masses and volumes Homogeneity of sample	Nata Technical Note 33
26	Accuracy Profile - based on intermediate precision and repeatability	Reference Material	Standard Purity	ISO 5725-2 and ISO/TS 21748

3.3 Details of Participant Calibration Standard

Participant returns as received are listed in Table 3.

Table 3 Participant Calibration Standard

Lab. Code	Reference Standard*	Purity (%)
1	Sigma Aldrich	100
2	NMI	99.8
3	NMI	99.8
4	NMI	99.8
5	Sigma Aldrich Prod. no. 92816	99.98 ± 0.13
6	NMI	99.8
7	Lipomed	99.47
8	NMI	99.8 +/- 1.9
9	Lipomed	99.467 +/- 0.015
10	LGC	99.8
11	NMI	99.8
12	Sigma Aldrich	>98
13	Lipomed	99.940 ± 0.006
14	NMI	99.8
15	Lipomed	99.940 ± 0.006
16	Lipomed	99.5788
17	In house synthesis	100.6
18	NMI	99.8
19	Lipomed	99,5
20	NMI	99.8
21	Sigma	100
22	Euromedex	99.5
23	Sigma	99.9
24	-	-
25	NMI	99.8
26	LIPOMED	99.47

*Some data has been edited to preserve confidentiality

3.4 Participants' Comments

The study manager welcomes comments or suggestions from participants as it provides information which will improve future studies. All returns are listed as received in Table 4 along with the study manager's response, where appropriate.

Table 4 Participant Comments

Lab. Code	Participant comments	Study co-ordinator response
11	Local illicit "ICE" seizures usually contain very high purity of methamphetamine hydrochloride (over 90% w/w). The determined purity of the test sample in this study is below those of our daily encountered samples.	The study coordinator provides a range of samples of different purity. In this study all samples were cut, while in the previous study Sample S1was uncut (high purity).
16	It would appear the samples for this study have been delayed in transit - perhaps at customs. Would perhaps be useful to have a larger time window for completion and submission of test results	The turn-around-time (TAT) for Controlled drugs PT is set to 6 weeks from dispatch of samples which is two weeks longer than all the other PT programs. Even with a longer TAT, the study coordinator acknowledges extra delays in transit for some countries and that is why sometimes the TAT is modified after the start of the program.
18	I believe this is a fair and true study.	Thank you.

4 PRESENTATION OF RESULTS AND STATISTICAL ANALYSIS

4.1 Results Summary

Participant results are listed in Tables 5 to 7 with resultant summary statistics: mean, median, maximum, minimum, robust average, robust standard deviation (Robust SD) and robust coefficient of variation (Robust CV).

Bar charts of results and performance scores are presented in Figures 2 to 5.

An example chart with interpretation guide is shown in Figure 1.

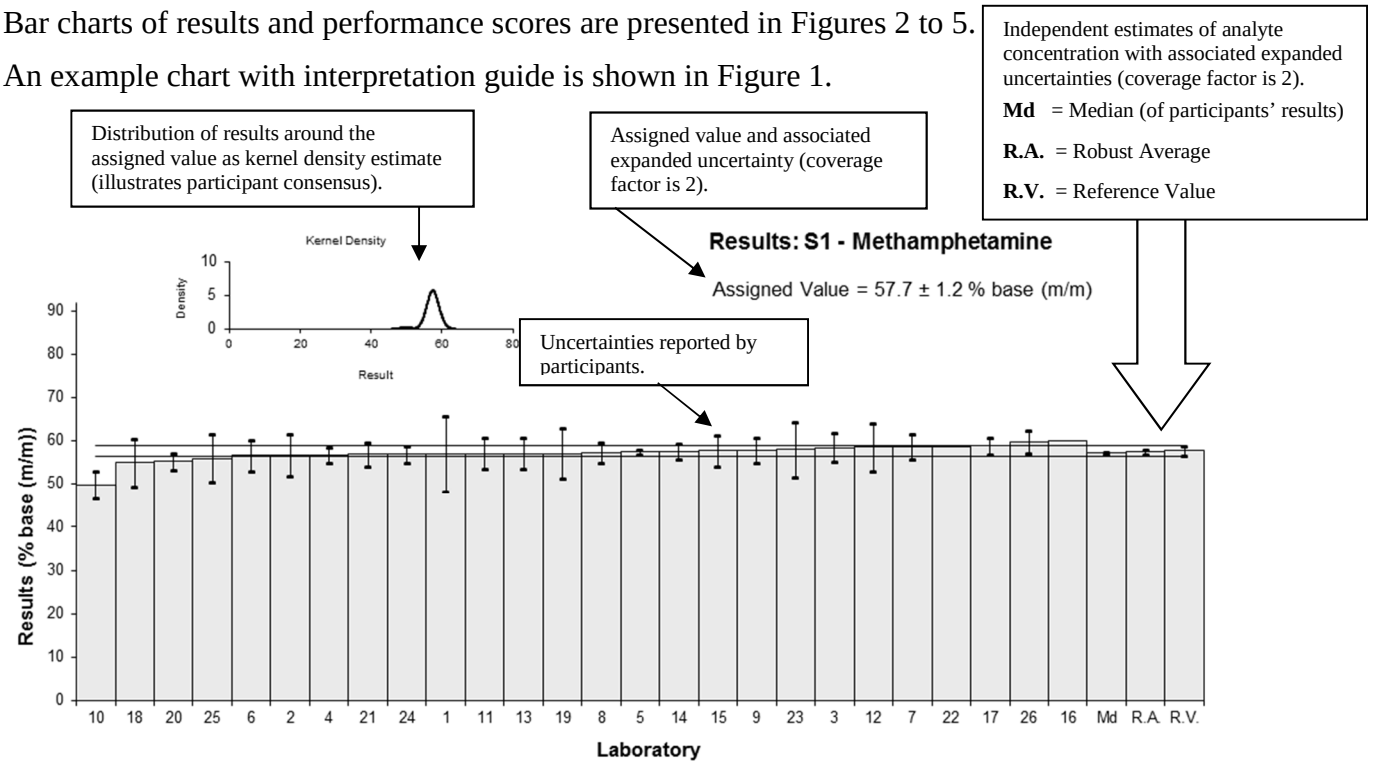


Figure 1 Guide to Presentation of Results

4.2 Assigned Value

Assigned value is defined as: 'the value attributed to a particular quantity and accepted, sometimes by convention, as having an uncertainty appropriate for a given purpose'.[4]

For a proficiency test, the assigned value is the best available measurement of the true concentration of an analyte in the test sample.

4.3 Performance Coefficient of Variation (PCV)

The performance coefficient of variation (PCV) is a measure of the between laboratory variation that in the judgement of the study organiser would be expected from participants given the sample concentration. It is important to note that this is a performance measure set by the study coordinator; it is not the coefficient of variation of participant results.

4.4 Target Standard Deviation

The target standard deviation (σ) is the product of the assigned value (*X)* and the performance laboratory coefficient of variation (PCV) as presented in Equation 1. This value is used for calculation of participant z-score.

$$\sigma = X * PCV \qquad \textit{Equation 1}$$

4.5 z-Score

For each participant result a z-score is calculated according to Equation 2 below:

$$z = \frac{(\chi - X)}{\sigma} \qquad \textit{Equation 2}$$

where:

z is z-score

χ is participants' result

X is the study assigned value

σ is the target standard deviation from Equation 1

A z-score with absolute value (|z|):

- $|z| \leq 2$ is satisfactory;
- $2 < |z| < 3$ is questionable;
- $|z| \geq 3$ is unsatisfactory.

4.6 E_n-Score

The E_n-score is complementary to the z-score in assessment of laboratory performance. E_n-score includes measurement uncertainty and is calculated according to Equation 3 below:

$$E_n = \frac{(\chi - X)}{\sqrt{U_\chi^2 + U_X^2}} \qquad \textit{Equation 3}$$

where:

E_n is E_n-score

χ is a participants' result

X is the assigned value

U_χ is the expanded uncertainty of the participants' result

U_X is the expanded uncertainty of the assigned value

An E_n-score with absolute value ($|E_n|$):

- $|E_n| \leq 1$ is satisfactory;
- $|E_n| > 1$ is unsatisfactory.

4.7 Traceability and Measurement Uncertainty

Laboratories accredited to ISO/IEC Standard 17025:2017[5] must establish and demonstrate the traceability and measurement uncertainty associated with their test results. Guidelines for quantifying uncertainty in analytical measurement are described in the Eurachem /CITAC Guide. [6]

5 TABLES AND FIGURES

Table 5

Sample Details

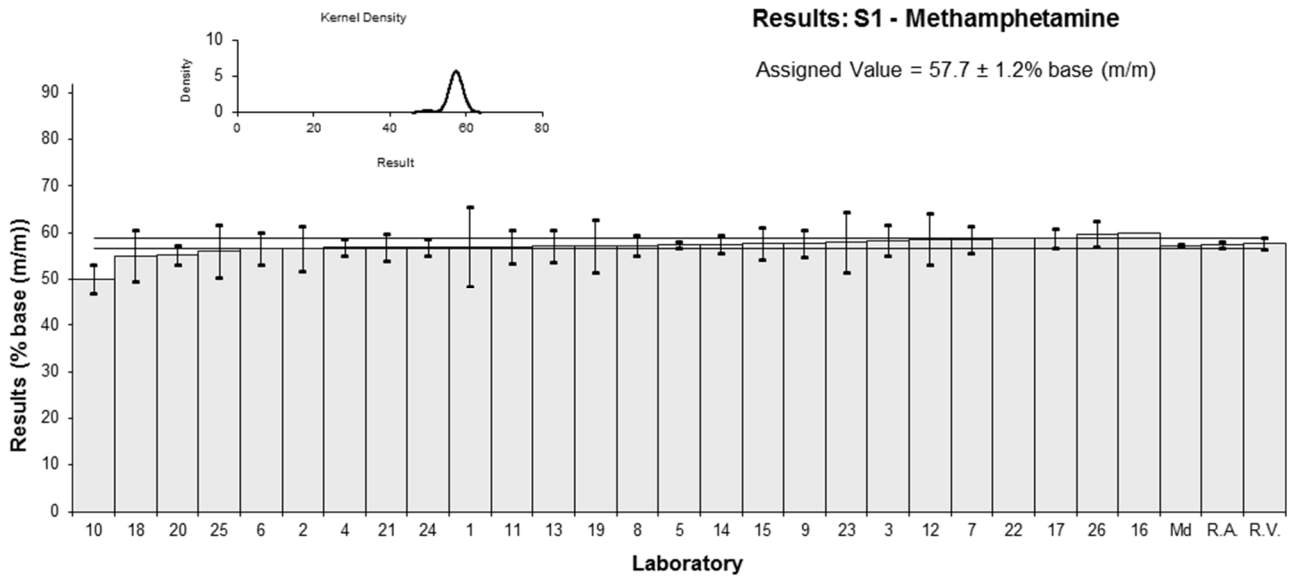
Sample No.	S1
Matrix.	Powder
Analyte.	Methamphetamine
Units	% base (m/m)

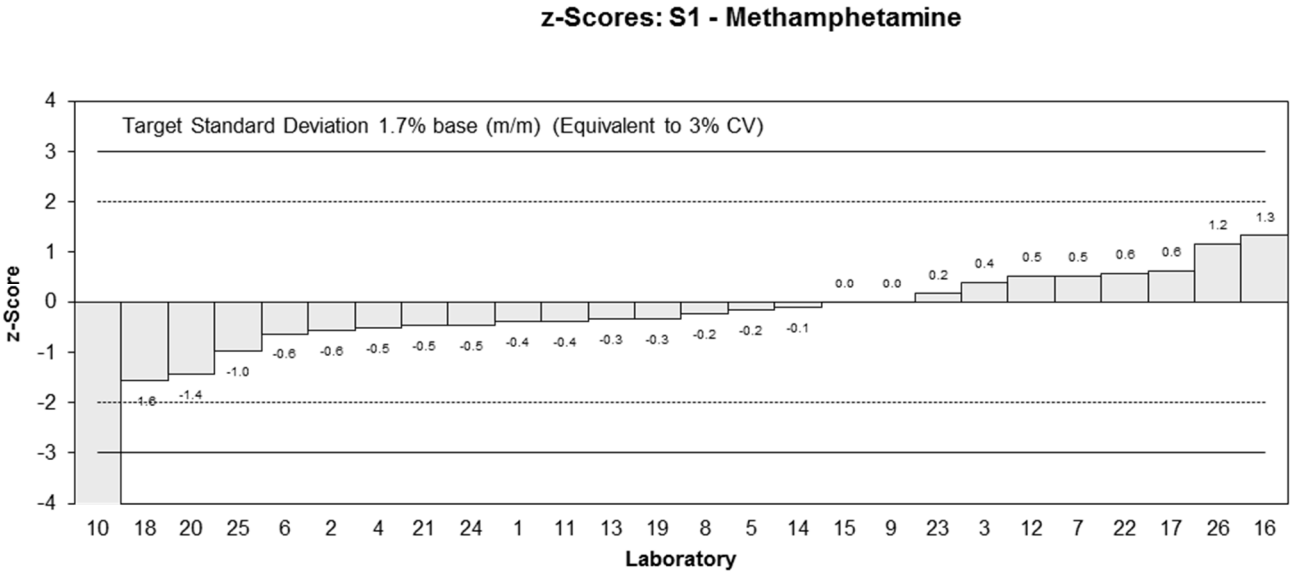
Participant Results

Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	57	8.6	-0.40	-0.08
2	56.7	4.8	-0.58	-0.20
3	58.4	3.3	0.40	0.20
4	56.8	1.8	-0.52	-0.42
5	57.4	0.6	-0.17	-0.22
6	56.6	3.5	-0.64	-0.30
7	58.6	2.93	0.52	0.28
8	57.3	2.3	-0.23	-0.15
9	57.7	2.9	0.00	0.00
10	49.9	3.2	-4.51	-2.28
11	57.0	3.6	-0.40	-0.18
12	58.6	5.519	0.52	0.16
13	57.1	3.5	-0.35	-0.16
14	57.5	1.9	-0.12	-0.09
15	57.7	3.5	0.00	0.00
16	60	NR	1.33	1.92
17	58.8	2.0	0.64	0.47
18	55	5.5	-1.56	-0.48
19	57.1	5.7	-0.35	-0.10
20	55.2	2.0	-1.44	-1.07
21	56.9	2.8	-0.46	-0.26
22	58.7	NR	0.58	0.83
23	58	6.4	0.17	0.05
24	56.9	1.88	-0.46	-0.36
25	56	5.6	-0.98	-0.30
26	59.7	2.7	1.16	0.68

Statistics

Assigned Value	57.7	1.2
Reference Value	57.7	1.2
Robust Average	57.4	0.6
Median	57.2	0.3
Mean	57.2	
N	26	
Max.	60	
Min.	49.9	
Robust SD	1.2	
Robust CV	2.1%	


Kernel Density
Density
Result
Results: S1 - Methamphetamine
Assigned Value = 57.7 ± 1.2% base (m/m)
Results (% base (m/m))
Laboratory
10 18 20 25 6 2 4 21 24 1 11 13 19 8 5 14 15 9 23 3 12 7 22 17 26 16 Md R.A. R.V.


z-Scores: S1 - Methamphetamine
Target Standard Deviation 1.7% base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
10 18 20 25 6 2 4 21 24 1 11 13 19 8 5 14 15 9 23 3 12 7 22 17 26 16
-2.3 -1.6 -1.4 -1.0 -0.6 -0.6 -0.5 -0.5 -0.5 -0.4 -0.4 -0.3 -0.3 -0.2 -0.2 -0.1 0.0 0.0 0.2 0.4 0.5 0.5 0.6 0.6 1.2 1.3

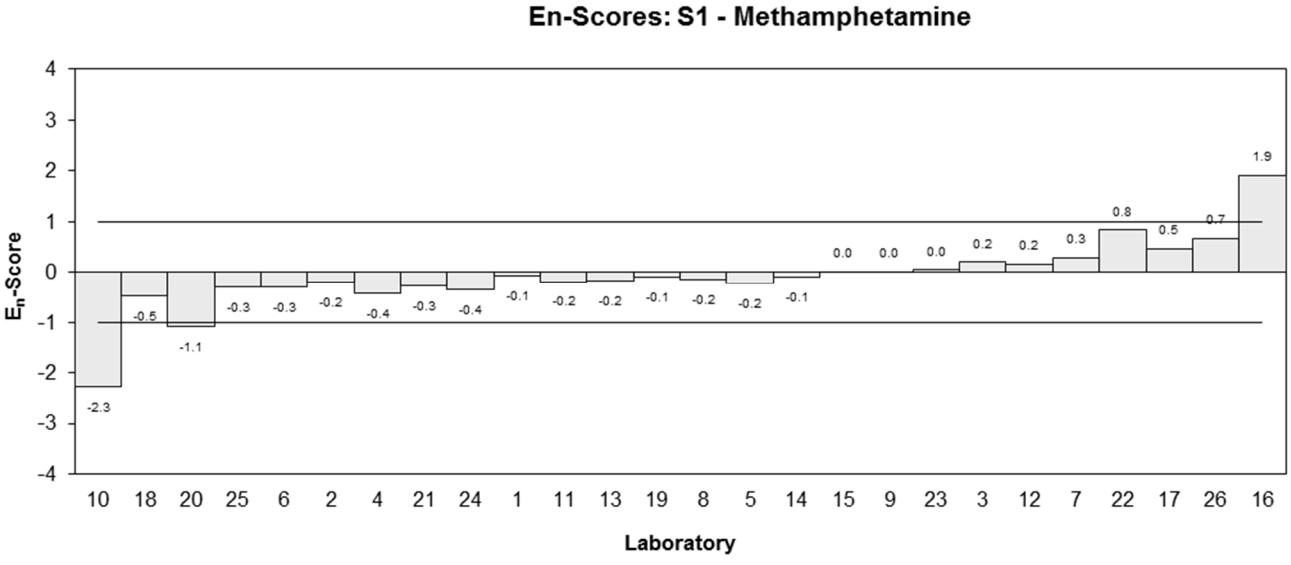

En-Scores: S1 - Methamphetamine
En-Score
Laboratory
10 18 20 25 6 2 4 21 24 1 11 13 19 8 5 14 15 9 23 3 12 7 22 17 26 16
-2.3 -0.5 -1.1 -0.3 -0.3 -0.2 -0.4 -0.3 -0.4 -0.1 -0.2 -0.2 -0.1 -0.2 -0.2 -0.1 0.0 0.0 0.0 0.2 0.2 0.3 0.8 0.5 0.7 1.9

Figure 2

Table 6

Sample Details

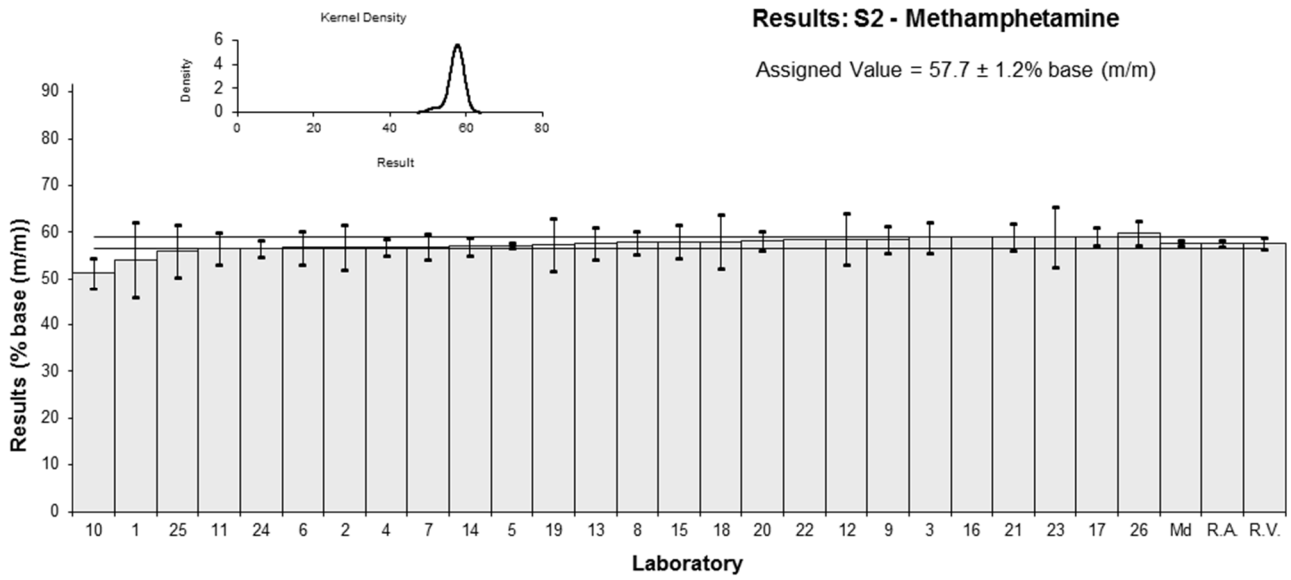
Sample No.	S2
Matrix.	Powder
Analyte.	Methamphetamine
Units	% base (m/m)

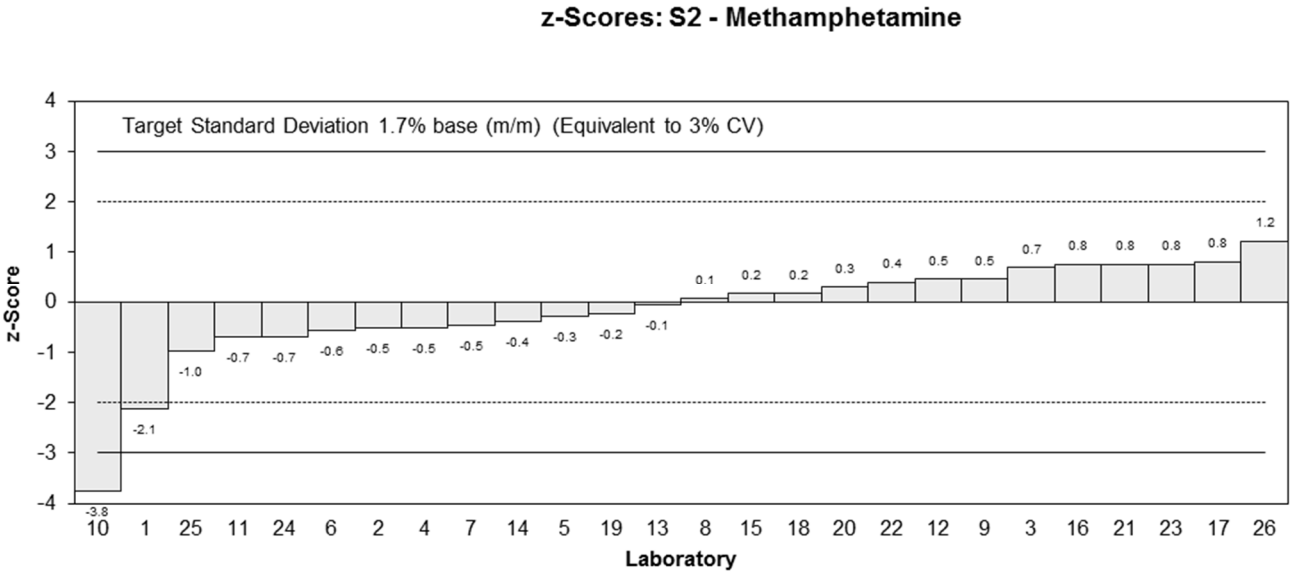
Participant Results

Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	54	8.1	-2.14	-0.45
2	56.8	4.8	-0.52	-0.18
3	58.9	3.2	0.69	0.35
4	56.8	1.9	-0.52	-0.40
5	57.2	0.6	-0.29	-0.37
6	56.7	3.5	-0.58	-0.27
7	56.9	2.84	-0.46	-0.26
8	57.8	2.4	0.06	0.04
9	58.5	2.9	0.46	0.25
10	51.2	3.3	-3.76	-1.85
11	56.5	3.5	-0.69	-0.32
12	58.5	5.519	0.46	0.14
13	57.6	3.5	-0.06	-0.03
14	57.0	1.9	-0.40	-0.31
15	58.0	3.5	0.17	0.08
16	59	NR	0.75	1.08
17	59.1	2.0	0.81	0.60
18	58	5.8	0.17	0.05
19	57.3	5.7	-0.23	-0.07
20	58.2	2.1	0.29	0.21
21	59.0	3.0	0.75	0.40
22	58.4	NR	0.40	0.58
23	59	6.5	0.75	0.20
24	56.5	1.86	-0.69	-0.54
25	56	5.6	-0.98	-0.30
26	59.8	2.7	1.21	0.71

Statistics

Assigned Value	57.7	1.2
Reference Value	57.7	1.2
Robust Average	57.6	0.6
Median	57.7	0.5
Mean	57.4	
N	26	
Max.	59.8	
Min.	51.2	
Robust SD	1.3	
Robust CV	2.3%	


Kernel Density
Density
Result
Results: S2 - Methamphetamine
Assigned Value = 57.7 ± 1.2% base (m/m)
Results (% base (m/m))
Laboratory
10 1 25 11 24 6 2 4 7 14 5 19 13 8 15 18 20 22 12 9 3 16 21 23 17 26 Md R.A. R.V.


z-Scores: S2 - Methamphetamine
Target Standard Deviation 1.7% base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
10 1 25 11 24 6 2 4 7 14 5 19 13 8 15 18 20 22 12 9 3 16 21 23 17 26
-3.8 -2.1 -1.0 -0.7 -0.7 -0.6 -0.5 -0.5 -0.5 -0.4 -0.3 -0.2 -0.1 0.1 0.2 0.2 0.3 0.4 0.5 0.5 0.7 0.8 0.8 0.8 0.8 1.2

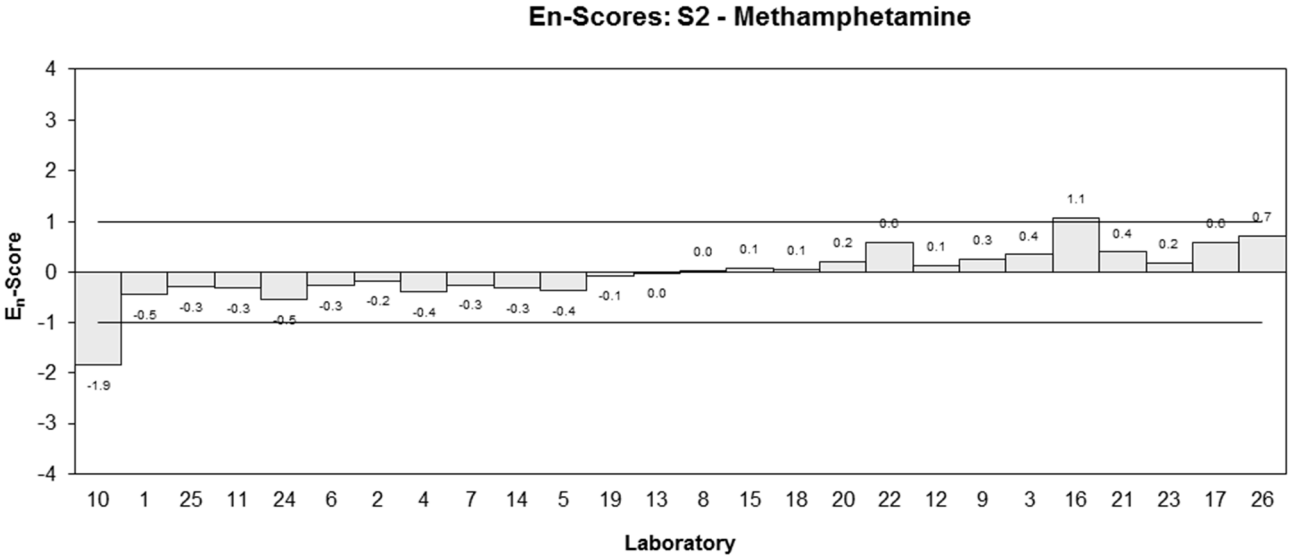

En-Scores: S2 - Methamphetamine
En-Score
Laboratory
10 1 25 11 24 6 2 4 7 14 5 19 13 8 15 18 20 22 12 9 3 16 21 23 17 26
-1.9 -0.5 -0.3 -0.3 -0.5 -0.3 -0.2 -0.4 -0.3 -0.3 -0.4 -0.1 0.0 0.0 0.1 0.1 0.2 0.6 0.1 0.3 0.4 1.1 0.4 0.2 0.6 0.7

Figure 3

Table 7

Sample Details

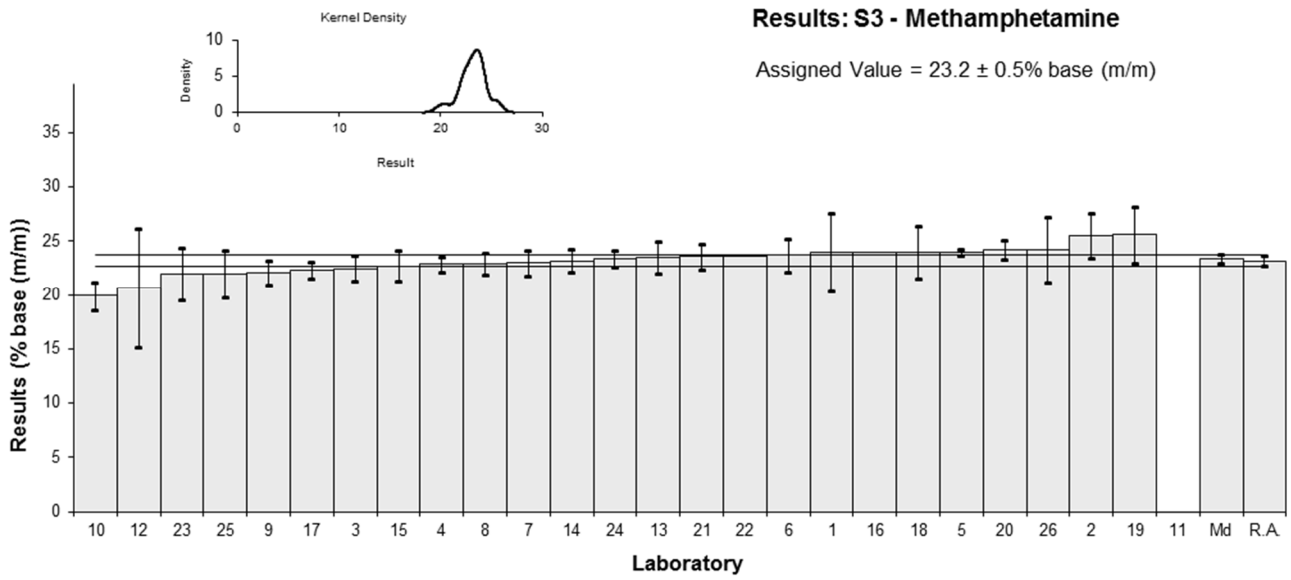
Sample No.	S3
Matrix.	Powder
Analyte.	Methamphetamine
Units	% base (m/m)

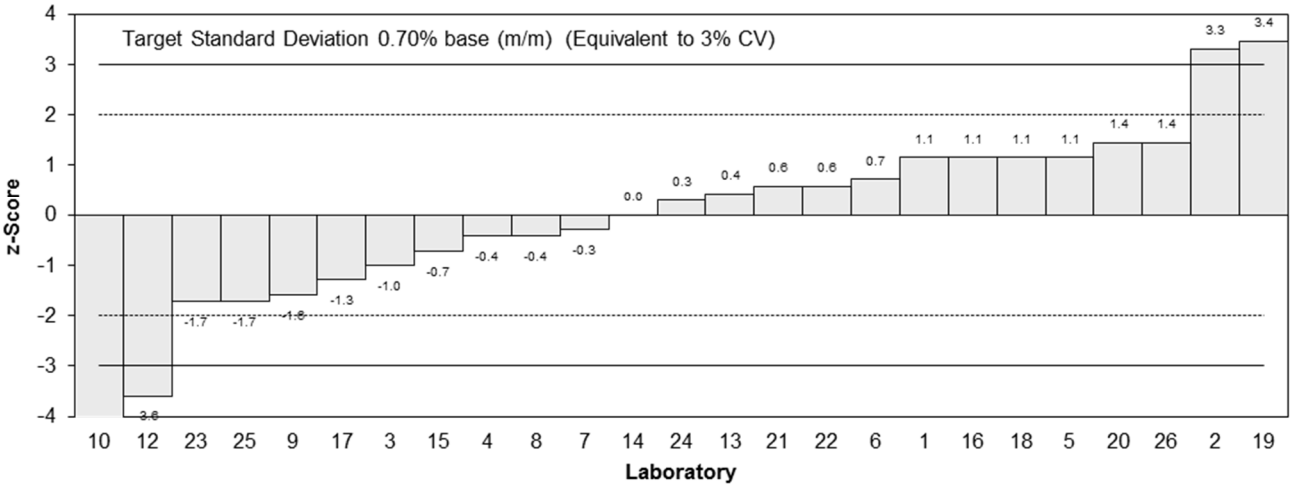
Participant Results

Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	24	3.6	1.15	0.22
2	25.5	2.1	3.30	1.07
3	22.5	1.2	-1.01	-0.54
4	22.9	0.7	-0.43	-0.35
5	24.0	0.3	1.15	1.37
6	23.7	1.5	0.72	0.32
7	23.0	1.15	-0.29	-0.16
8	22.9	1.0	-0.43	-0.27
9	22.1	1.1	-1.58	-0.91
10	19.9	1.3	-4.74	-2.37
11	NR	NR		
12	20.7	5.519	-3.59	-0.45
13	23.5	1.5	0.43	0.19
14	23.2	1.1	0.00	0.00
15	22.7	1.4	-0.72	-0.34
16	24	NR	1.15	1.60
17	22.3	0.8	-1.29	-0.95
18	24	2.4	1.15	0.33
19	25.6	2.6	3.45	0.91
20	24.2	0.9	1.44	0.97
21	23.6	1.2	0.57	0.31
22	23.6	NR	0.57	0.80
23	22	2.4	-1.72	-0.49
24	23.4	0.77	0.29	0.22
25	22	2.2	-1.72	-0.53
26	24.2	3.0	1.44	0.33

Statistics

Assigned Value	23.2	0.5
Robust Average	23.2	0.5
Median	23.4	0.4
Mean	23.2	
N	25	
Max.	25.6	
Min.	19.9	
Robust SD	1.1	
Robust CV	4.7%	


Kernel Density
Density
Result
Results: S3 - Methamphetamine
Assigned Value = 23.2 ± 0.5% base (m/m)
Results (% base (m/m))
Laboratory
10 12 23 25 9 17 3 15 4 8 7 14 24 13 21 22 6 1 16 18 5 20 26 2 19 11 Md R.A.


z-Scores: S3 - Methamphetamine
Target Standard Deviation 0.70% base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
10 12 23 25 9 17 3 15 4 8 7 14 24 13 21 22 6 1 16 18 5 20 26 2 19

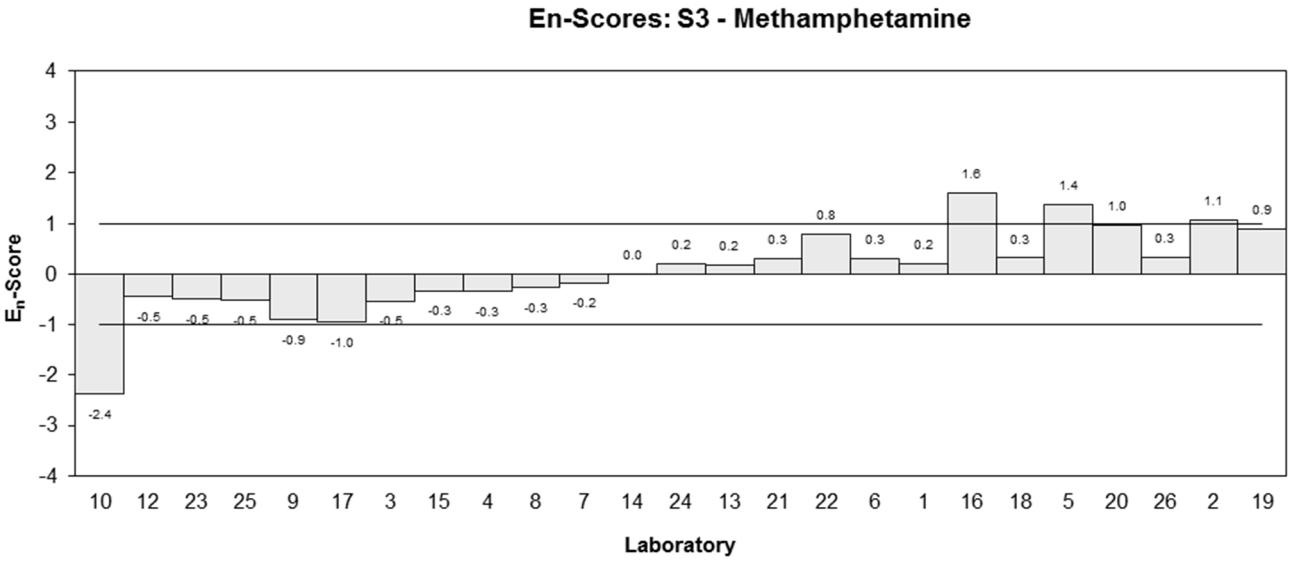

En-Scores: S3 - Methamphetamine
En-Score
Laboratory
10 12 23 25 9 17 3 15 4 8 7 14 24 13 21 22 6 1 16 18 5 20 26 2 19

Figure 4

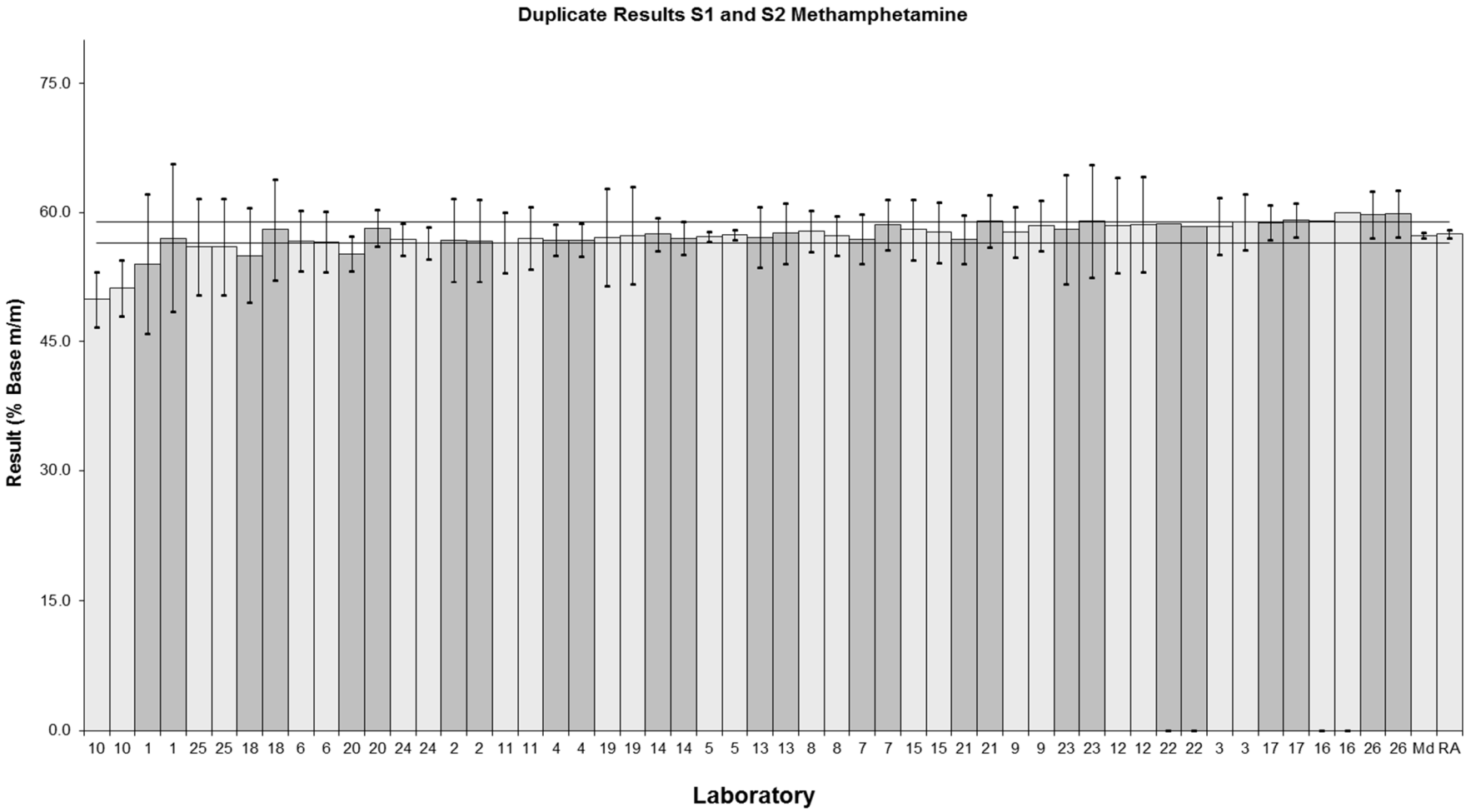


Figure 5 Results for duplicate samples S1 and S2
Horizontal lines (solid) are the upper and lower 95% confidence interval of the assigned value.

Table 8 Participants' identification of cutting agents

Lab Code	Cutting agents		
	S1	S2	S3
1	Caffeine	Caffeine	
2			
3	Caffeine	Caffeine	Methylsulfonylmethane
4	Caffeine	Caffeine	Dimethylsulfone
5	Caffeine (28.3% m/m)	Caffeine (28.8% m/m)	Dimethylsulfone (70.1% m/m)
6	Caffeine	Caffeine	Dimethylsulfone
7	Caffeine	Caffeine	Dimethylsulfone
8	Caffeine	Caffeine	Dimethylsulfone
9	Caffeine	Caffeine	Dimethylsulfone
10	Caffeine 25.1%	Caffeine 25.5%	
11	Caffeine	Caffeine	
12	Caffeine	Caffeine	Dimethylsulfone ($DMSO_2$)
13	Caffeine	Caffeine	Dimethylsulfone
14	caffeine	caffeine	
15	Caffeine	Caffeine	Dimethylsulfone
16	Caffeine	Caffeine	Dimethylsulfone
17	Caffeine	Caffeine	Dimethylsulfone
18	Caffeine	Caffeine	Dimethylsulfone
19	caffeine	caffeine	
20	Caffeine	Caffeine	Dimethylsulphone
21	Caffeine	Caffeine	
22	Caffeine	Caffeine	Dimethylsulfone
23	Caffeine	Caffeine	Methylsulfonylmethane
24	Caffeine	Caffeine	Dimethylsulfone
25	Caffeine	Caffeine	Dimethylsulfone
26	Caffeine	Caffeine	

6 DISCUSSION OF RESULTS

6.1 Assigned Value

A reference value was obtained for identical Samples S1 and S2 using the quantitative nuclear magnetic resonance spectrometry (QNMR) measurement method described in Appendix 2. Maleic acid (NMI certified reference material QNMR010) was used as internal standard. The measured reference value was in agreement with the gravimetric preparation value and the robust average of participants' results, within their respective associated uncertainties.
The uncertainty of the reference value was estimated in accordance with the ISO GUM[7] by combining standard uncertainty terms for method precision, sample homogeneity, weighing of sample, preparation and addition of standard solution, the very small uncertainties in molecular weights and an estimate of potential bias made by comparing the results from different NMR signals.
The reference value was used as the assigned value for these samples.

Traceability: The measurements of the reference values for Samples S1 and S2 were made using QNMR and are traceable to the SI through Australian Standards for mass via balance calibration certificates and the purity of the NMI maleic acid certified reference material QNMR010.2018.01.

The assigned value for Sample S3 is the robust average of the results reported participants. The robust average and associated expanded uncertainties were calculated using the procedure described in 'ISO 13528:2015, Statistical methods for use in proficiency testing by interlaboratory comparisons'.[8] The calculation procedure for the expanded uncertainty for Sample S3 is presented in Appendix 1.

Traceability: The consensus of participants' results is not traceable to any external reference, so although expressed in SI units, metrological traceability has not been established.

6.2 Measurement Uncertainty Reported by Participants

Participants were asked to report an estimate of the expanded measurement uncertainty associated with their results and the basis of this uncertainty estimate (Table 2).

It is a requirement of the ISO Standard 17025[5] that laboratories have procedures to estimate the uncertainty of chemical measurements and to report this uncertainty in specific circumstances, including 'when the client's instruction so requires.' From 1 July 2012 this is also a requirement of ASCLD/Lab-International accreditation program.

71 results (92%) were reported with an associated expanded uncertainty. Laboratories **16** and **22** did not report an uncertainty. These laboratories were not accredited.

Laboratory **12** reported an identical uncertainty for samples which were of significantly different concentrations.

The magnitude of reported uncertainties was within the range 1% to 27% relative.

Sixty-one of 71 (86%) expanded uncertainties were between 3% and 10% relative to the result. Laboratories reporting uncertainties smaller than 3% or larger than 10% relative may wish to consider whether these estimates are realistic or fit for purpose.

Laboratories having a satisfactory z-score and an unsatisfactory E_n-score are likely to have underestimated the expanded uncertainty associated with the result.

In some cases the results were reported with an inappropriate number of significant figures. The recommended format is to write the uncertainty to no more than two significant figures

and then to write the result with the corresponding number of decimal places (for example instead of 58.5 ± 5.519% the recommended format is 58.5 ± 5.5%).[6]

6.3 z-Score

A target standard deviation equivalent to 3% CV was used to calculate z-scores. Target SDs, the between-laboratory coefficient of variation predicted by the Thomson - Horwitz equation[9] and the between-laboratories coefficient of variation obtained in this study are presented in Table 9.

Table 9 Target standard deviations, coefficient of variations from predictive model and between laboratories

Sample	Analyte	Assigned value (% base m/m)	Target SD (as PCV)	Thompson Horwitz CV	Between laboratories CV
S1/S2	Methamphetamine	57.7	3%	2.2%	2.1%, 2.3%
S3	Methamphetamine	23.2	3%	2.5%	4.7%

A summary of z-scores by laboratory is presented in Figure 6.

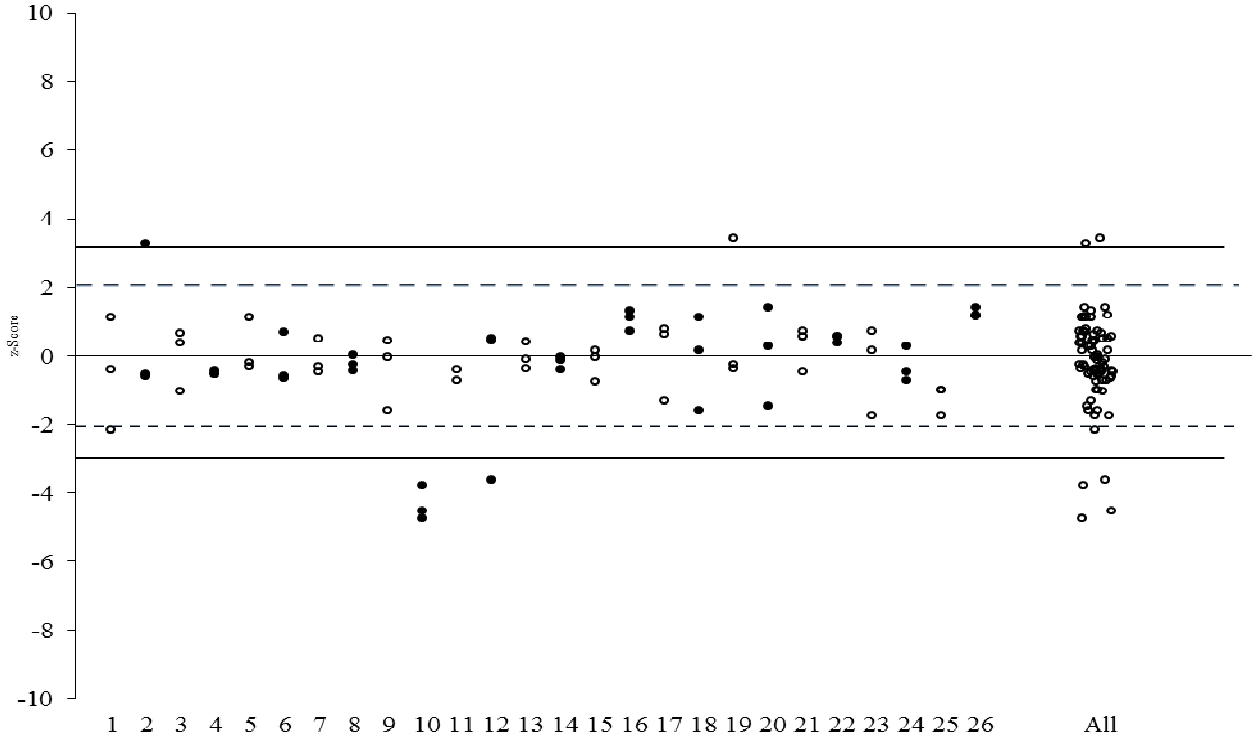


Figure 6 Summary of participants' z-score.

70 of 77 numeric results (91%) returned a satisfactory z-score with $|z| \leq 2$**.**

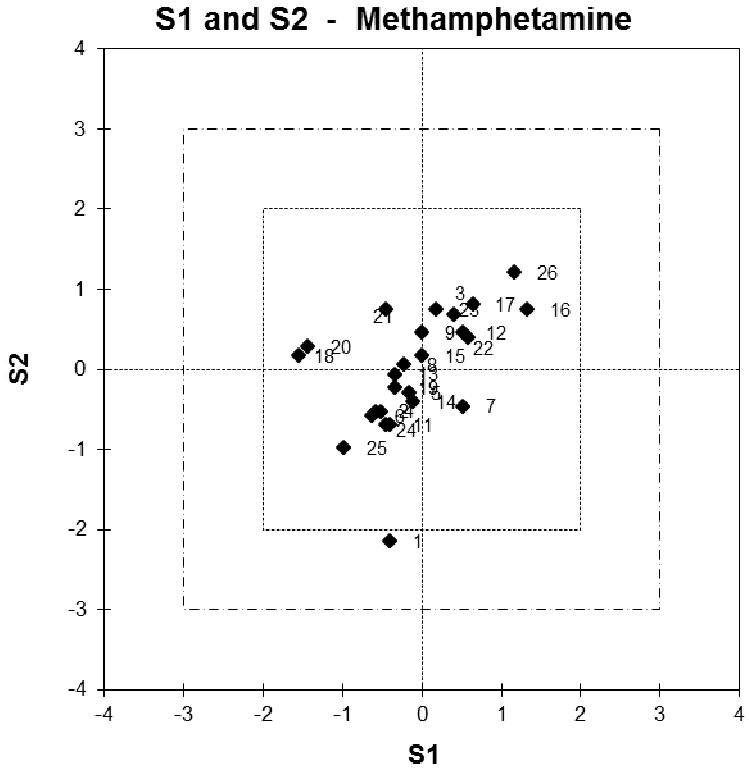
- Twenty-one participants (81%) - **3**, **4**, **5**, **6**, **7**, **8**, **9**, **11**(only two results submitted), **13**, **14**, **15**, **16**, **17**, **18**, **20**, **21**, **22**, **23**, **24**, **25** and **26** returned satisfactory scores for all three samples;
- Four participants returned at least one questionable or unsatisfactory z-score;

- Laboratory **10** returned unsatisfactory z-scores for all test samples demonstrating an unsatisfactory performance. Results for all test samples were lower than the assigned value (negative bias).

6.4 Z-Score scatter plot

Samples S1 and S2 were blind duplicates. A scatter plot was used for the evaluation of the participants' within-laboratory repeatability (Figure 7).

Most laboratories are plotted in the upper-right or lower-left quadrants. Points close to the diagonal axis demonstrate excellent repeatability while points close to zero demonstrate excellent repeatability and accuracy.



Laboratory 10 is off scale.

Figure 7 z-scores scatter plot

6.5 E_n-Score

The dispersal of participants' E_n-scores is graphically presented in Figure 8. Where a laboratory did not report an expanded uncertainty with a result, an expanded uncertainty of zero (0) was used to calculate the E_n-score.

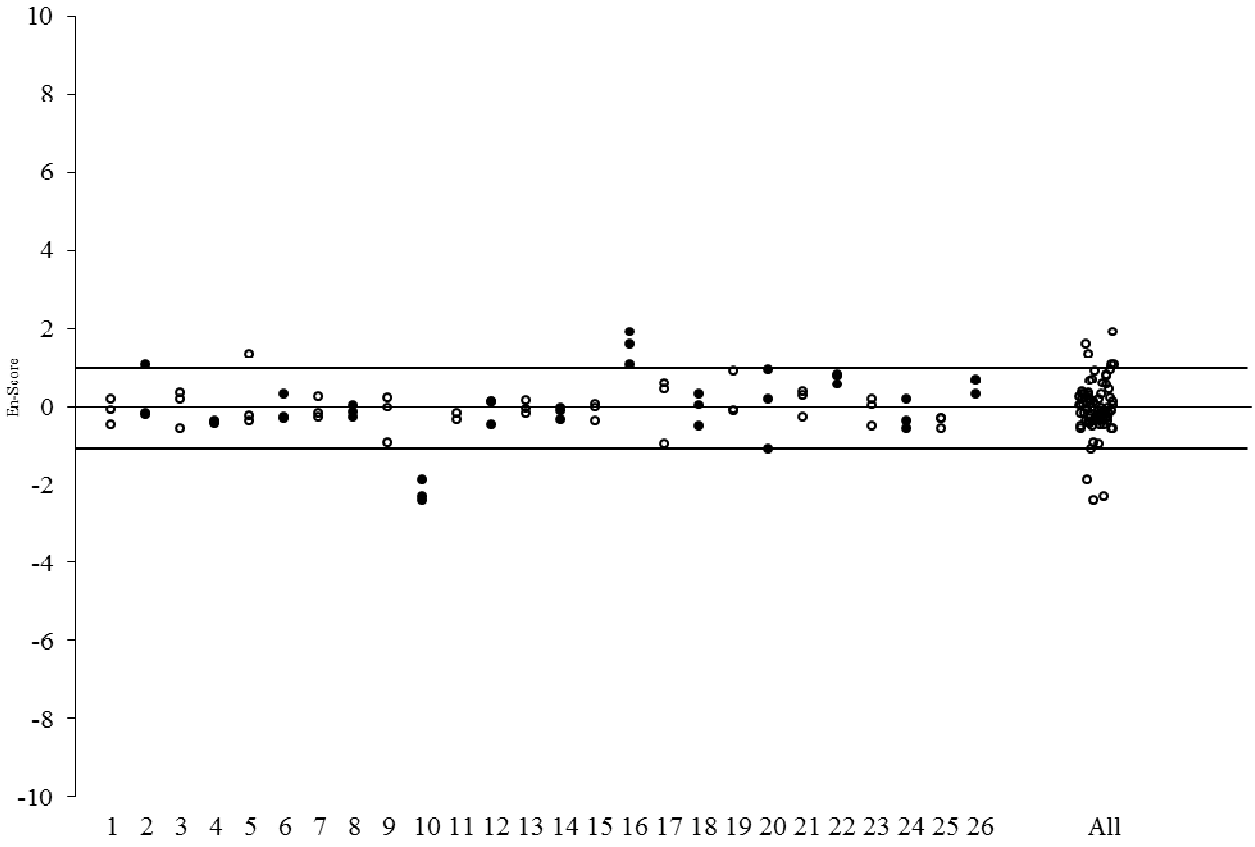


Figure 8 Summary of participants' E_n-Score

68 of 77 numeric results (88%) returned a satisfactory E_n-score with $|E_n| \leq 1$**.**

- Twenty-one participants (81%) – **1**, **3**, **4**, **6**, **7**, **8**, **9, 11** (only reported two results), **12**, **13**, **14**, **15**, **17**, **18**, **19**, **21**, **22**, **23, 24, 25** and **26** returned satisfactory scores for all three samples;
- Three laboratories returned at least one questionable E_n-score; and
- Laboratories **10** and **16** returned $|E_n| > 1$ for all samples.

6.6 Identification of Cutting Agent

Twenty-five laboratories (96%) reported on the identity of the cutting agents in Samples S1 and S2 and eighteen (72%) in Sample S3 and the findings are presented in Table 8.

Samples were methamphetamine hydrochloride approximately 80% base (m/m) supplied by the Australian Federal Police (AFP).

Caffeine was used to prepare Samples S1 and S2. Twenty-five laboratories reported on the diluent and correctly identified it.

Dimethylsulfone (DMS or MMS) was used to prepare Sample S3. Eighteen laboratories reported the diluent and correctly identified it.

6.7 Participants' Analytical Methods

Participants were requested to analyse the samples using their normal test methods and to report a single result for each sample as they would normally report to a client. Results reported in this way reflect the true variability of results reported to laboratory clients. The method descriptions provided by participants are presented in Table 1.

A summary of accreditation status, participants' methods and reference standards is presented below.

Accredited	Laboratory Code
Yes to ISO 17025	1 2 3 4 6 8 9 11 12 14 17 18 19 20 21 24 25 26 (Qualitative only)
Other (Unspecified)	13 15 20
No	5 7 10 16 22 23

Sample Mass Used (mg)	Laboratory Code
4-10	24
11-30	2 3 5 8 10 11 12 13 14 15 18 20 23 25 26
31-50	1 6 7 9 13 15 16 19 21 22
51-100	4
101-150	17 20

Instrument Used for quantification	Laboratory Code
GC-FID	8 10
GC-MS	8 16
UPLC-MS(MS)	1
HPLC(UPLC)-DAD	2 3 4 7 9 11 12 13 14 15 17 18 19 20 21 22 23 25 26
HPLC-FLD	6
QNMR	5 24

Sources of Calibration Standard	Laboratory Code
NMI Australia	2 3 4 6 8 11 14 18 20 25
Lipomed	7 9 13 15 16 19 26
Sigma Aldrich	1 5 12 21 23
Other	10 17 22

Plots of extraction solvent vs z-score, measurement instrument vs z-score and calibration standard vs z-score are presented in Figures 9 to 11. A variety of solvents and calibration standards were used. HPLC (UPLC)-DAD was the most common measurement technique with the participants. No trends were identified.

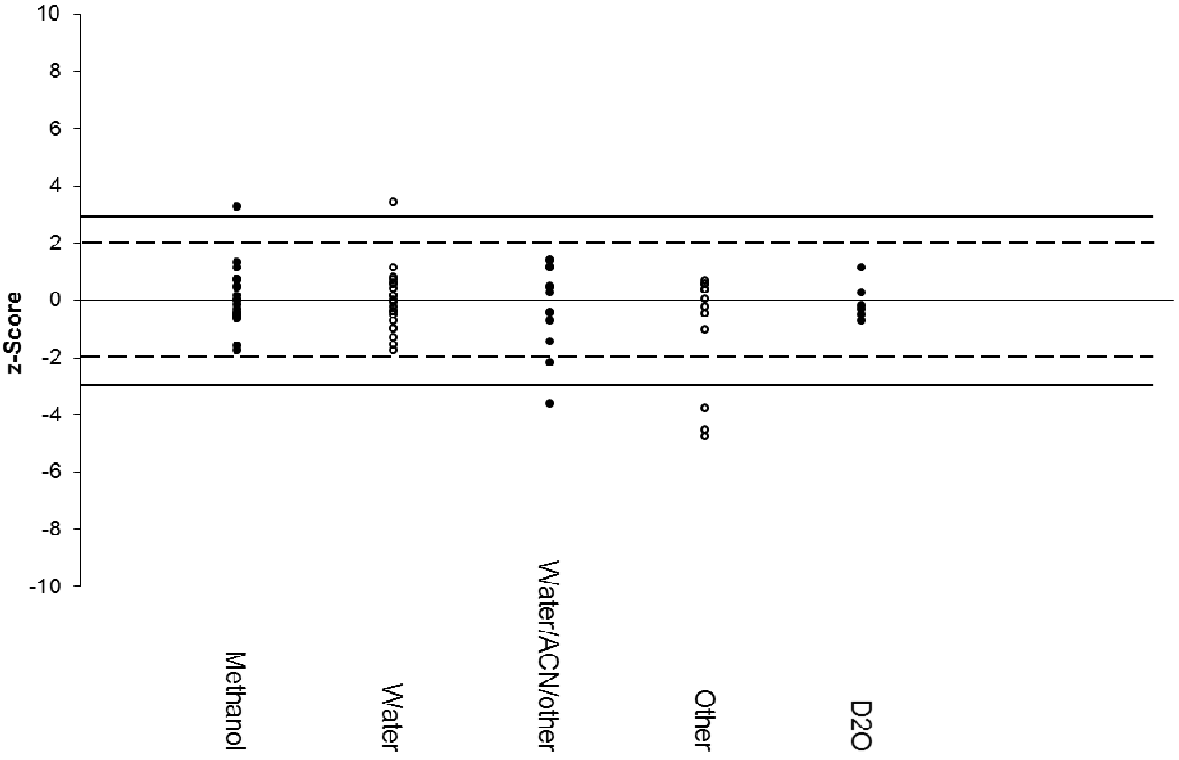


Figure 9 Extraction solvent vs z-score

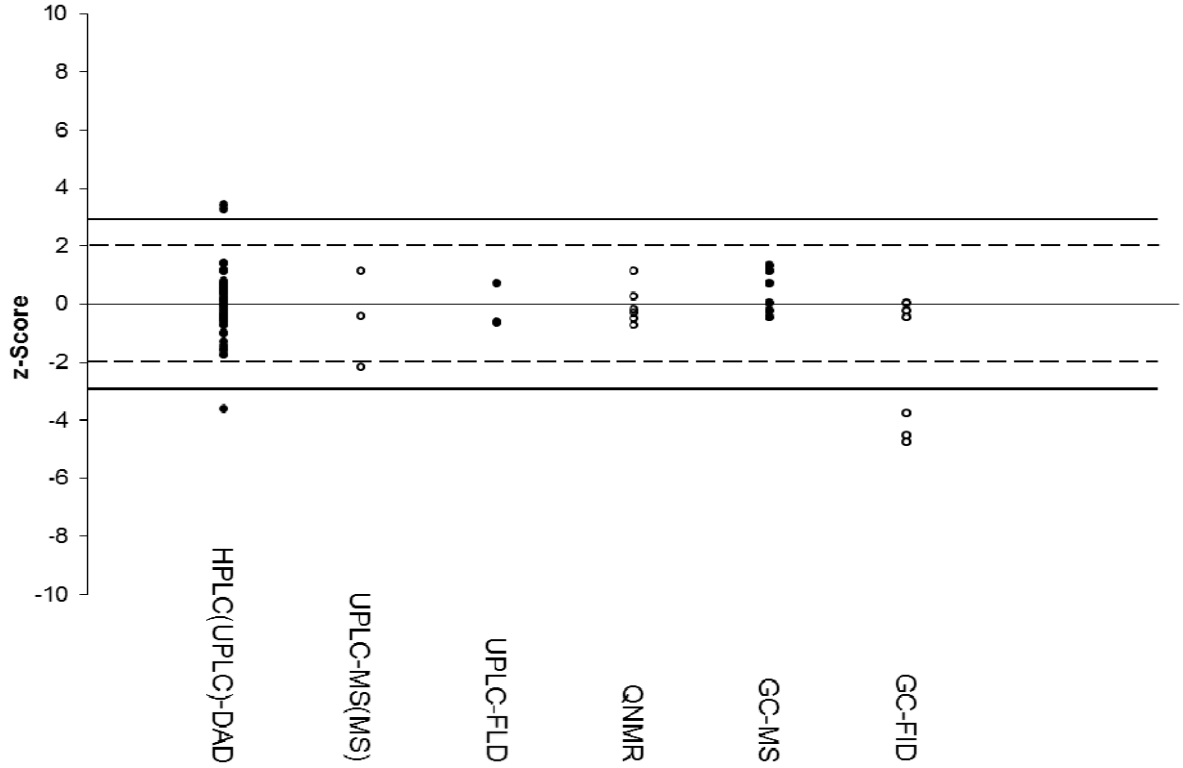


Figure 10 Measurement instrument vs z-score

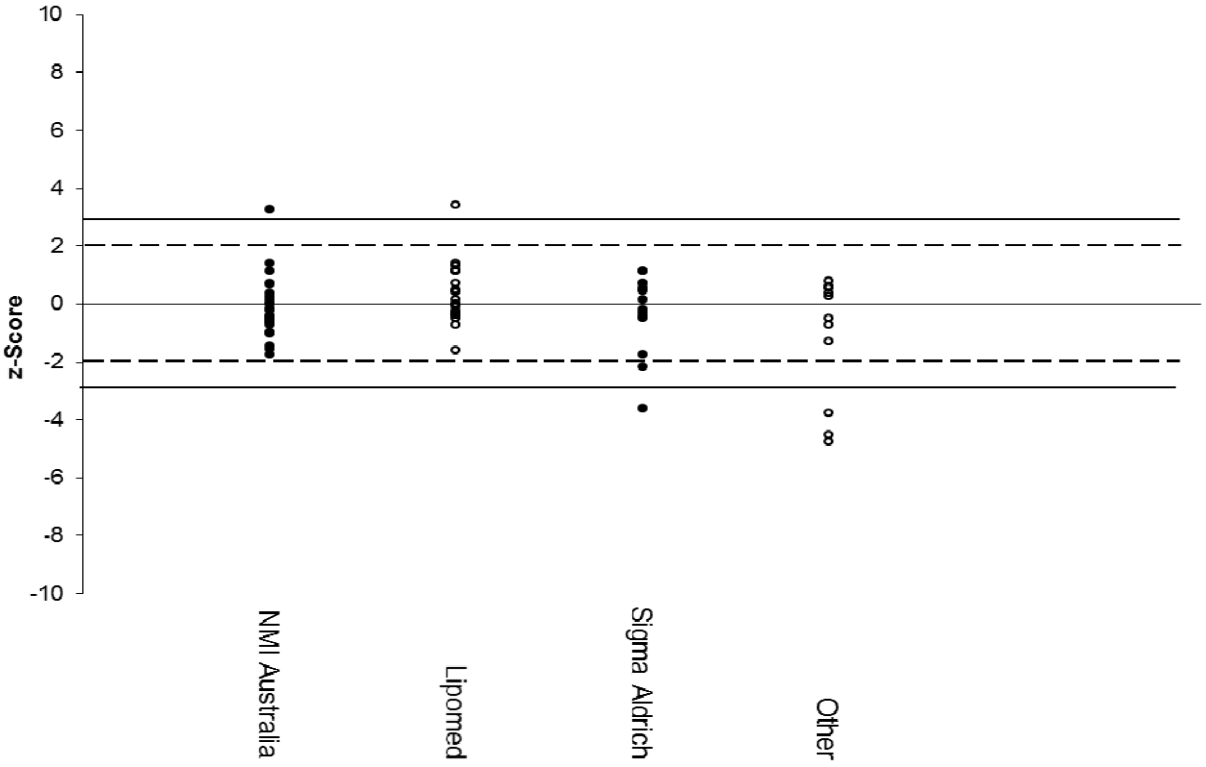


Figure 11 Calibration standard vs z-score

6.8 Summary of Participation and Performance in Methamphetamine Studies

Overall percentages of satisfactory z-scores and E_n-scores obtained by laboratories since 2009 are presented in Figure 12. The proportion of satisfactory z-scores and E_n-scores over 10 years has increased with an average of 82% and 77% respectively.

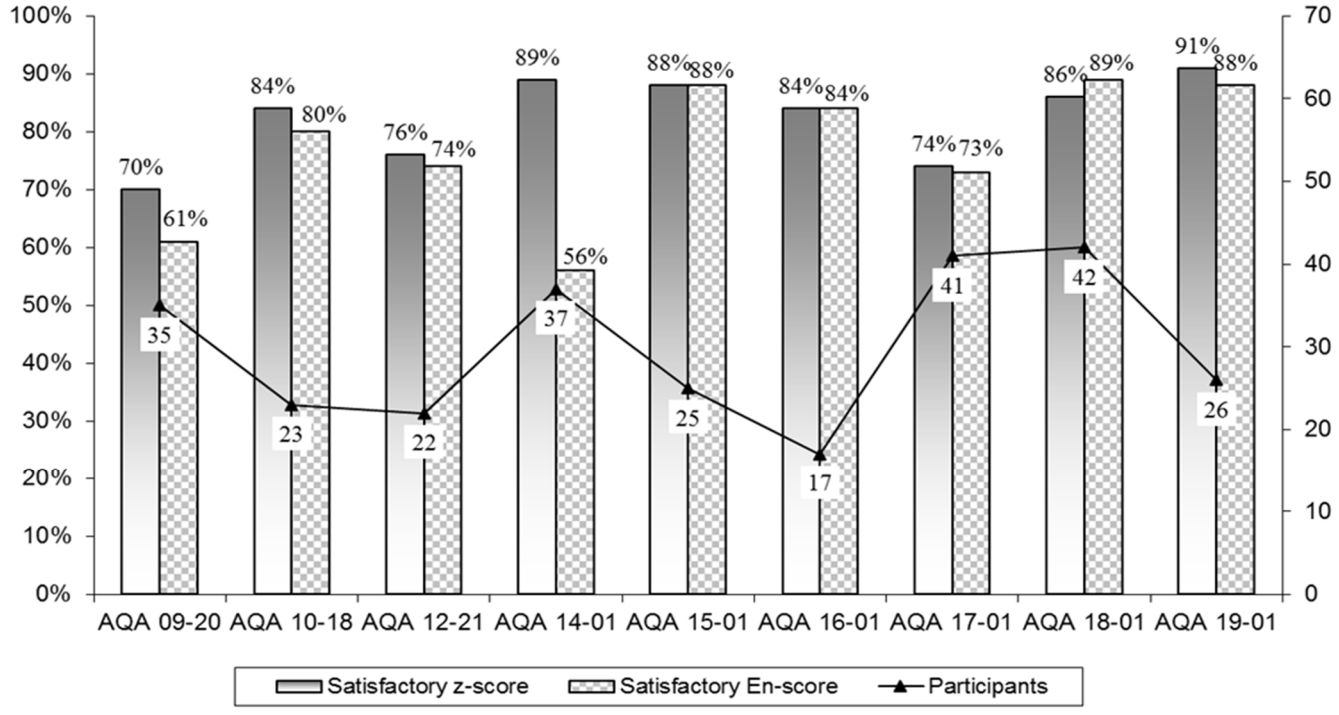


Figure 12 Summary of participants' performance since 2009

7 REFERENCES

[1] ISO/IEC 17043 2010, *Conformity assessment – General requirements for proficiency testing*.

[2] NMI 2016, *Chemical Proficiency Testing Study Protocol*, viewed 18 June 2019, <http://www.measurement.gov.au>.

[3] NMI 2016, *Chemical Proficiency Testing Statistical Manual*, viewed 18 June 2019, <http://www.measurement.gov.au >.

[4] Thompson, M., Ellison, S.L.R. & Wood, R. 2006. 'The international harmonized protocol for proficiency testing of (chemical) analytical laboratories', *Pure Appl. Chem*, vol 78, pp 145-196.

[5] ISO/IEC 17025 2017, *General requirements for the competence of testing and calibration laboratories.*

[6] Eurachem 2012, *Quantifying Uncertainty in Analytical Measurement*, 3rd edition, viewed 10 June 2019, <http://www.eurachem.org/images/stories/Guides/pdf/QUAM2012_P1.pdf>.

[7] ISO/IEC 98-3 2008, *Uncertainty of measurement – Part 3 Guide to the expression of uncertainty in measurement*.

[8] ISO/IEC 13528 2015, *Statistical methods for use in proficiency testing by interlaboratory comparisons.*

[9] Thompson M. and Lowthian, P.J. 1995, 'A Horwitz-like function describes precision in a proficiency test', *Analyst*, vol 120, pp 271-272

[10] Thompson, M. and Fearn, T.,2001 A new test for sufficient homogeneity, *Analyst*, vol 126, pp 1414-1417.

APPENDIX 1 - MEASUREMENT UNCERTAINTY OF THE ROBUST AVERAGE

When the robust average is calculated using the procedure described in 'ISO13528:2015, Statistical methods for use in proficiency testing by interlaboratory comparisons – Annex C'[8], the uncertainty is estimated as:

$$u_{rob\ average} = 1.25 * S_{rob\ average} / \sqrt{p} \qquad \text{Equation 4}$$

where:

$u_{rob\ average}$	robust average standard uncertainty
$S_{rob\ average}$	robust average standard deviation
p	number of results

The expanded uncertainty ($U_{rob\ average}$) is the standard uncertainty multiplied by a coverage factor of 2 at approximately 95% confidence level.

A worked example is set out below in Table 10.

Table 10 Uncertainty of assigned value for Sample S3 as % base (m/m)

No. results (p)	25
Robust average	23.23
$S_{rob\ average}$	1.07
$u_{rob\ average}$	0.268
k	2
$U_{rob\ average}$	0.535

The robust average for Sample S3 is 23.2 ± 0.5% Methamphetamine base (m/m).

APPENDIX 2 – REFERENCE VALUE AND HOMOGENEITY TESTING

Five sample bottles from each of Samples S1 and S2 (duplicate) were selected at random for the purpose of assigning a reference value. Samples were analysed in duplicate.

Measurements were made using quantitative nuclear magnetic resonance spectrometry (QNMR) with maleic acid as internal standard. A Certified Reference Material of maleic acid was obtained from NMI Chemical Reference Materials. The purity data supplied with the material is shown in Table 11 and is traceable to the SI unit for mass, the kilogram (kg), through QNMR. Internal standard solutions were prepared gravimetrically in D_2O.

Table 11 NMI Reference Standard

	Supplier	Catalogue / Lot No	Purity (95% confidence)
Maleic acid	NMI Chemical Reference Materials	QNMR010.2018.01	98.8 ± 0.12 %

Samples were prepared gravimetrically by accurately weighing 20 mg of sample, dissolving in 650 µL of internal standard solution (12.9 mg/g for S1/S2) and accurately weighing the final solution. Samples were analysed on a Bruker 500 MHz Ascend NMR spectrometer, using a QNMR relaxation time of 25 s. The mass fraction of methamphetamine was determined from the NMR response at 1.15 ppm.

The average of mass fractions determined for Samples S1 and S2 (Table 12), was used as the reference value and the assigned value for the PT study. The standard uncertainty on the mass fraction reference value was estimated in accordance with the ISO GUM by combining standard uncertainty terms for method precision, sample homogeneity, weighing of sample, preparation and addition of standard solution, the very small uncertainties in molecular weights and an estimate of potential bias made by comparing the results from different NMR signals.

Table 12 Reference value for Sample S1/S2

Bottle Fill No.	Methamphetamine (% base m/m)	
	Replicate 1	Replicate 2
115	57.0	56.6
116	58.2	57.5
127	57.5	57.4
129	57.4	58.0
136	58.0	57.8
203	57.9	57.6
219	57.9	57.8
227	57.9	58.1
239	58.5	57.8
248	57.8	57.6
Mean	57.7	
CV	0.73%	

Reference value 57.7 ± 1.2% methamphetamine base (m/m)[a]

[a] The uncertainty is an expanded uncertainty at 95% confidence level. A coverage factor k was calculated using the effective degrees of freedom derived from the Welch-Satterthwaite[9] equation (k = 2.1).

The measured reference value was in agreement with the gravimetric preparation value and the robust average of participants' results, within their respective associated uncertainties.

Homogeneity check was based on that described by Thompson and Fearn[10] which is also the procedure described in the International Protocol.[4]

Thompson and Fearn Homogeneity Tests for duplicate pair Samples S1 and S2

Test	Test Value	Critical Value	Result
Cochran	0.28	0.60	Pass
S_a/σ	0.17	0.5	Pass
s^2_{sam}	0.096	0.59	Pass

Samples were found to be sufficiently homogeneous for use in a proficiency test with a target standard deviation of 3%.

APPENDIX 3 - ACRONYMS AND ABBREVIATIONS

ASCLD	American Society of Crime Laboratory Directors
CITAC	Cooperation on International Traceability in Analytical Chemistry
CRM	Certified Reference Material
CV	Coefficient of Variation
DAD	Diode Array Detector
DMS	Dimethyl sulfone
$\|E_n\|$	Absolute value of an E_n-score
FID	Flame Ionization Detector
FLD	Fluorescence Detector
GC	Gas Chromatography
GC-MS	Gas Chromatography Mass Spectrometry
GUM	Guide to the expression of uncertainty in measurement
HPLC	High Performance Liquid Chromatography
ISO	International Standards Organisation
LC	Liquid Chromatography
Max	Maximum value in a set of results
Md	Median
Min	Minimum value in a set of results
NATA	National Association of Testing Authorities
NMI	National Measurement Institute Australia
NR	Not Reported
NT	Not Tested
PCV	Performance Coefficient of Variation
PDA	Photodiode Array
PT	Proficiency Test
QNMR	Quantitative Nuclear Magnetic Resonance
Robust CV	Robust Coefficient of Variation
Robust SD	Robust Standard Deviation
SI	International System of Units
Target SD (σ)	Target standard deviation
UPLC	Ultra Performance Liquid Chromatography
UV	Ultraviolet
$\|z\|$	Absolute value of a z-score

END OF REPORT