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

Proficiency Test Report
AQA 18-01
Methamphetamine

May 2018

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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SUMMARY

AQA 18-01 was conducted in March/April 2018. Three test samples of methamphetamine hydrochloride were sent to forty laboratories. Two laboratories requested two sets of the test samples. Forty-two sets of results were submitted by the due date.

Test samples were prepared at the NMI laboratory in Sydney using methamphetamine hydrochloride synthesised by NMI.

The assigned values 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 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 **1**, **6**, **7**, **9** (reported two results only), **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **35**, **36**, **37**, **38**, **39**, **40**, **41** and **42** returned satisfactory z and E_n-scores for all results.

Laboratories **4**, **23** and **24** returned questionable or unsatisfactory z-scores and E_n-scores for all samples.

Laboratory **2** did not report any quantitative results.

Of the 122 results for which z-scores were calculated, 105 (86%) returned $|z| \leq 2$ indicating a satisfactory performance.

Of the 122 results for which $|E_n|$-scores were calculated, 108 (89%) returned $|E_n| \leq 1$ **i**ndicating 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*

119 results (94%) were reported with an associated expanded uncertainty. Laboratory **4** did not report an uncertainty. This laboratory was not accredited.

Laboratories **1**, **3**, **13**, **27** and **41** reported an identical uncertainty for samples which were of significantly different concentrations.

The magnitude of reported uncertainties was within the range 0.13% to 15% relative.

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

Samples were prepared from methamphetamine hydrochloride approximately 79.5% base (m/m) (sample S1), and from methamphetamine hydrochloride approximately 78.5% base (m/m) (samples S2 and S3), both supplied by the NMI Chemical Reference Materials Laboratory. The study coordinator left Sample S1 uncut, added glucodin in Sample S2 and nicotinamide (niacinamide) in Sample S3.

Only six participants correctly reported both glucodin in Sample S2 and nicotinamide in Sample S3.

1 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:	18 December 2017
Samples dispatched:	9 March 2018
Results due:	20 April 2018
Interim report issued:	7 May 2018

2.2 Participation

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

Forty laboratories agreed to participate and submitted results. These laboratories are listed in Appendix 1. Two laboratories requested two sets of samples to be analysed independently by two analysts..

2.3 Test Material Specification

Three test samples were prepared in March 2018. The starting material for sample S1 was methamphetamine hydrochloride approximately 79.5% base (m/m), and for samples S2 and S3 was methamphetamine hydrochloride approximately 78.5% base (m/m), both synthesised and supplied by the NMI Chemical Reference Materials Laboratory. Glucodin and nicotinamide, purchased from Sigma Aldrich, were used as cutting agents. Sample S1 was left uncut, glucodin was used for Sample S2 and nicotinamide for Sample S3.

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 79.5% Methamphetamine base (m/m).

Sample S2 was prepared to contain 56.8% Methamphetamine base (m/m).

Sample S3 was prepared to contain 39.9% 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 procedure for the preparation of the study samples has been validated in previous studies. No homogeneity testing was conducted for the samples in this proficiency study. Results returned by the participants gave no reason to question the homogeneity of samples.

2.6 Sample Dispatch and Receipt

A set of three test samples, each containing approximately 150 mg of test material, were dispatched on 9 March 2018.

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 20 April 2018, as late results cannot be included in the report; and
- any other comments.

2.8 Interim Report

An interim report was emailed to all participants on 7 May 2018.

3 PARTICIPANT LABORATORY INFORMATION

3.1 Test Method Summaries

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

Table 1 Participant Summary of Test Methods

Lab. Code	Extraction solvent	Internal standard	Calib. points	Technique	Detector	Column
1	Chloroform	Nortriptyline	1	GC	FID	HP5
2						
3	Chloroform	Nortriptyline	1	GC	FID	DB5
4	Ethanol	Propyl paraben	7	UPLC	DAD	BEH Shield RP18
5	ACN/MeOH/H2O	Analog off metamphetamine	7	UPLC	MSMS	C-18 coloumn
6	methanol	Propylparaben	3	UPLC	PDA	ACQUITY C-18
7	D2O	Maleic Acid		QNMR		
8	Methanol	Prazepam	3	UPLC	DAD	Acquity UPLC BEH C18 1,7µ 2,1x150 mm
9	Dissolution in acetonitrile/water	Methoxyphenamine HCl	3	HPLC	DAD	Alltima C-18
10	Methanol		5	HPLC	DAD	Phenomenex C-18-XB
11	Methanol		6	HPLC	UV, 225nm	Phenomenex Luna C18, 0.5% DEA pH 8.5/CH3OH 40:60, 1mL/min
12	Isooctane + Ammonium Hydroxide	Dodecane	3	GC	FID	HP-1MS
13	Methanol	Diazepam	6	GC	FID	J&W 128-5512
14	Chloroform	Nortriptyline		GC	FID	HP5
15	Chloroform	Nortriptyline	1	GC	FID	HP5
16	Water	None	4	HPLC	PDA	C18
17	Chloroform	Nortriptyline	Single	GC	FID	HP5
18	Purified Water	Phentermine	1	LC	DAD	Agilent Zorbax SB-C8
19	D2O	maleic acid		1H QNMR	Bruker AVIII 600 with QNP probe	
20	Methanol	Strychnine	6	UPLC	PDA	Acquity UPLC BEH Phenyl 1.8 um, 2.1 x 100mm
21	Chloroform	Nortriptyline	1	GC	FID	HP5
22	Chloroform	Nortriptyline	1	GC	FID	DB-5MS
23	water/acetonitrile/ n10 sulphuric acid 90:10:1		3	HPLC	Diode Array	Shimpack XR-ODS
24	Methanol		1	HPLC	DAD	Zorbax XDB-C18 (4,6x150 mm)
25	Water		6	UPLC	DAD	Acquity UPLC® BEH C18 1.7µm 2.1 x 100mm Column
26	Chloroform	Nortriptyline	1	GC	FID	HP5
27	Chloroform	Nortriptyline	1	GC	FID	HP5
28	water		3	LC	UV DAD	Silica

Lab. Code	Extraction solvent	Internal standard	Calib. points	Technique	Detector	Column
29	acetonitrile/ammonium acetate solution in water, diethylamine		3	HPLC	DAD	RP18 100mm x 4.6mm x5 micron
30	Chloroform	Nortriptyline	1	GC	FID	HP5
31	Chloroform	Nortriptyline	1	GC	FID	HP5
32	Methanol		5	HPLC	DAD	C18 column
33	Water		4	HPLC	UV-DAD	Zorbax RX-SIL
34	Chloroform	Nortriptyline	1	GC	FID	HP5
35	CHLOROFORM	NORTRIPTYLINE	1	GC	FID	HP5
36	Acetic acid/acetonitrile/water (4/20/76, v/v/v)		5	HPLC	UV DAD	POROSHELL 120 EC-C18
37	Water		6	UPLC	DAD	Acquity UPLC® BEH C18 1.7µm 2.1 x 100 mm Column
38	Methanol:KOH buffer (50:50)	Methoxyphenamine	3	UPLC	DAD	Acquity BEH C18
39	Methanol	Procaine	4	HPLC	DAD	HP5
40	ethyl acetate	Diphenylamine	5	GC	FID	HP1
41	Acetonitrile/Water 20:80		3	HPLC	DAD	Luna 2.5µ C18(2)-HST 100 x 3.00mm
42	Purified Water	Phentermine	1	UHPLC	DAD	Agilent Zorbax SB-C8

3.2 Reported Basis of Participants' Measurement Uncertainty Estimates

Participant returns as received 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	Control Samples – Reference Material	Recoveries of SS Instrument Calibration Masses and volumes	Eurachem/CITAC Guide
2				
3		Duplicate Analysis		Eurachem/CITAC Guide
4				
5	Top Down - precision and estimates of the method and laboratory bias	Reference Material		
6	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
7	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
8	Standard deviation of replicate analyses multiplied by 2 or 3	Duplicate Analysis	Standard Purity Homogeneity of sample	
9	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Duplicate Analysis	Recoveries of SS Matrix Effects Standard Purity Masses and volumes Homogeneity of sample	ISO/GUM
10		Duplicate Analysis		Eurachem/CITAC Guide
11	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate Analysis		Eurachem/CITAC Guide
12	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Control Samples – Certified Reference Material Duplicate Analysis	Recoveries of SS Matrix Effects Standard Purity Instrument Calibration Masses and volumes Homogeneity of sample	Eurachem/CITAC Guide
13	Estimating Measurement Uncertainity by black box by pairs of values			ISO/GUM
14	Top Down - precision and estimates of the method and laboratory bias	Duplicate Analysis		
15	Pooled standard deviation	Duplicate Analysis	Recoveries of SS Standard Purity Homogeneity of sample	NARL
16				
17	Top Down - precision and estimates of the method and laboratory bias	Duplicate Analysis	Recoveries of SS Masses and volumes	Eurachem/CITAC Guide

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation		Guide Document for Estimating MU
		Precision	Method Bias	
18	Top Down - precision and estimates of the method and laboratory bias	Control Samples - SS Duplicate Analysis	Laboratory bias from PT Recoveries of SS	Eurachem/CITAC Guide
19	Standard deviation of replicate analyses multiplied by 2 or 3	Duplicate Analysis	Instrument Calibration Masses and volumes	
20	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
21	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Certified Reference Material	Recoveries of SS Masses and volumes	Eurachem/CITAC Guide
22	Top Down - reproducibility (standard deviation) from PT studies used directly	Duplicate Analysis	Laboratory bias from PT studies Instrument Calibration Homogeneity of sample Masses and volumes	Eurachem/CITAC Guide
23	Professional Judgement	Control Samples – Certified Reference Material Duplicate Analysis	Standard Purity Instrument Calibration	ISO/GUM
24	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
25	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate Analysis	Laboratory bias from PT studies Standard Purity Homogeneity of sample Masses and volumes Instrument Calibration	Nata Technical Note 33
26	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Recoveries of SS Standard Purity	Eurachem/CITAC Guide
27	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Certified Reference Material	Recoveries of SS Masses and volumes	Eurachem/CITAC Guide
28	repeatability, sample heterogeneity (ENFSI qantitative sampling guideline)	Control Samples – Reference Material Duplicate Analysis	Homogeneity of sample	Eurachem/CITAC Guide
29	uncertainty budget	Control Samples – Reference Material	Standard Purity Instrument Calibration Masses and volumes	current SOP for uncertainty of measurement in drugs analysis
30	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	Eurachem/CITAC Guide

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation		Guide Document for Estimating MU
		Precision	Method Bias	
31	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Control Samples – Reference Material	Standard Purity Matrix Effects Masses and volumes Homogeneity of Sample	Eurachem/CITAC Guide
32	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
33	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Real samples from police case	Laboratory bias from PT studies	Nordtest Report TR537
34	Bottom Up (ISO/GUM, fish bone/ cause and effect diagram)	Duplicate Analysis	Standard Purity	Eurachem/CITAC Guide
35	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material	Standard Purity Matrix effects	Eurachem/CITAC Guide
36	Accuracy profile - based on intermediate precision and repeatability	Control Samples – Reference material	Standard Purity	ISO 5725-2 & ISO/TS 21748
37	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material Duplicate analysis	Laboratory bias from PT studies Standard Purity Instrument Calibration Masses and volumes Homogeneity of sample	Nata Technical Note 33
38	Top Down - reproducibility (standard deviation) from PT studies used directly	Control Samples – Reference Material Duplicate Analysis	Standard Purity Masses and volumes	Eurachem/CITAC Guide
39	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
40	Standard deviation of replicate analyses multiplied by 2 or 3	Control Samples – Reference Material		
41	Top Down - precision and estimates of the method and laboratory bias	Control Samples – Reference Material	Standard Purity Instrument Calibration Masses and volumes Homogeneity of sample	Eurachem/CITAC Guide
42	Top Down - precision and estimates of the method and laboratory bias	Control Samples – SS Duplicate Analysis	Laboratory bias from PT studies Recoveries of SS	Eurachem/CITAC Guide

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	CRM	99.2
2		
3	In-house reference standard	99.2
4	Euromedex	98.5
5	Sigma Aldrich	100%
6	NMI	99.8
7		
8	LGC	100 +/- 0,5 %
9	NMI	99.8
10	Sigma	99.9
11	NMI	99.8
12	NMI	80.1
13	LIPOMED methampetamine	98.5
14	NMI	99.2
15	In-house reference standard	99.20
16	In house synthesis of MA	99.8
17	JKM	99.21
18	Lipomed	99.467 ± 0.015
19	Sigma Aldrich Prod. no. 92816	99.98±0.13%
20	NMI	99.8
21	JKM	99.2
22	TRC	99.2
23	LGC	99.7
24	Lipomed	99.47%
25	NMI	99.8
26	Lipomed	99.20%
27	JKM	99.2
28	Lipomed	99.5
29	NMI	99.8
30	JKM HQ (Meth)	99.2
31	Methamphetamine	99.2
32	NMI	99.8

Lab. Code	Reference Standard*	Purity (%)
33	Methamphetamine HCl (M8750 Sigma)	100 % (as chloride)
34	In-house reference standard	99.2
35	JKM	99.2
36	LIPOMED	99.467
37	NMI	99.8
38	NMI	99.8 ± 1.9
39	Lipomed	99,467 +/- 0,015 %
40	Lipomed	99.467
41	Sigma aldrich	100
42	Lipomed	99.467 ± 0.015

*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
2	Our laboratory does not quantify methylamphetamine and so no purity results have been submitted. Qualitatively the presence of methylamphetamine was confirmed in all three samples by GCMS

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 4.

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

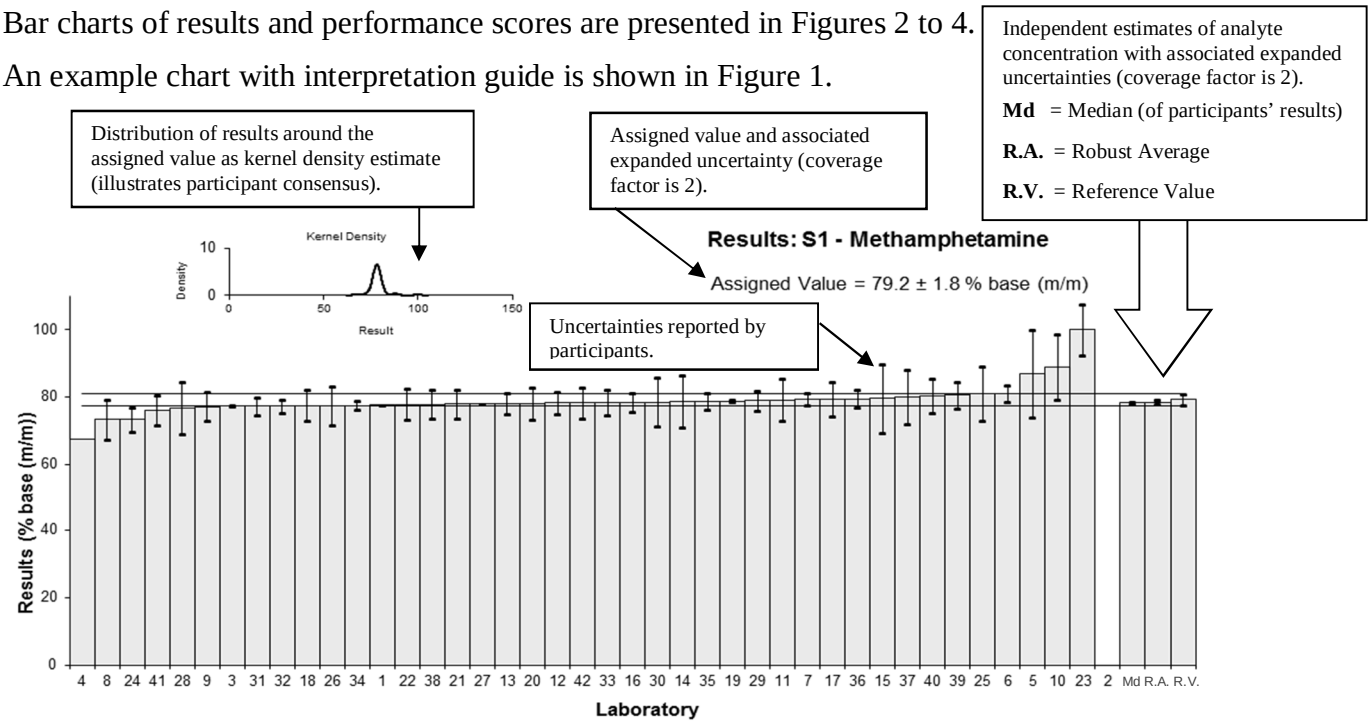


Figure 1 Guide to Presentation of Results

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 Between-Laboratory Coefficient of Variation

The between-laboratory coefficient of variation is a measure of the between laboratory variation that in the judgement of the study coordinator would be expected from participants given the analyte concentration. It is important to note this is not the coefficient of variation of participants' results.

4.4 Target Standard Deviation

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

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

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 participant's 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)

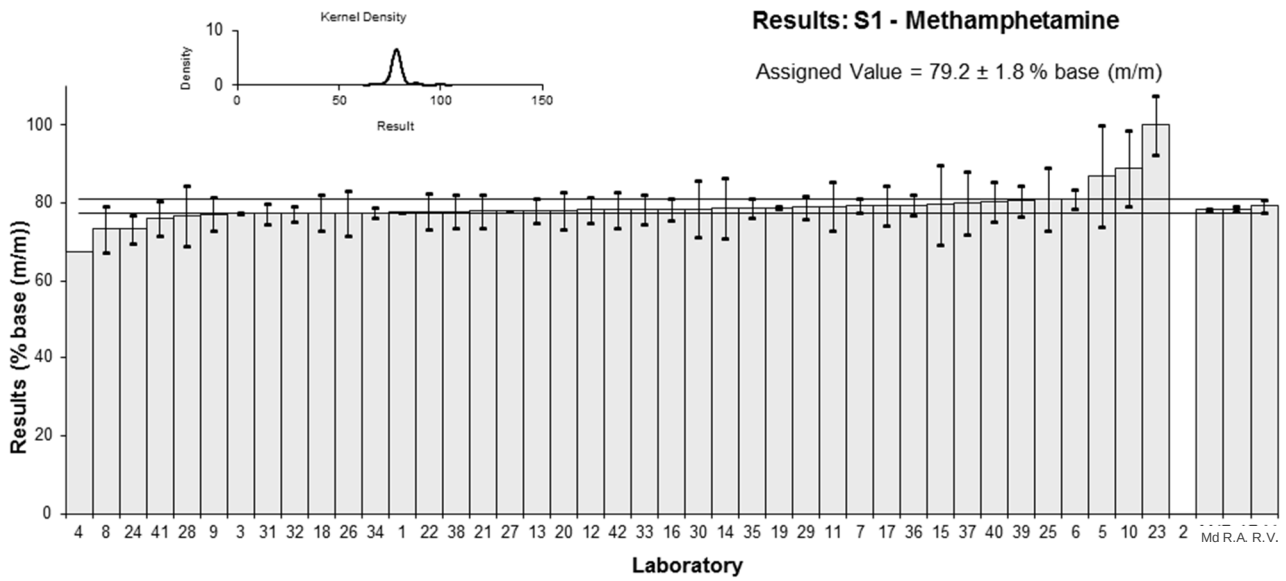
Participant Results

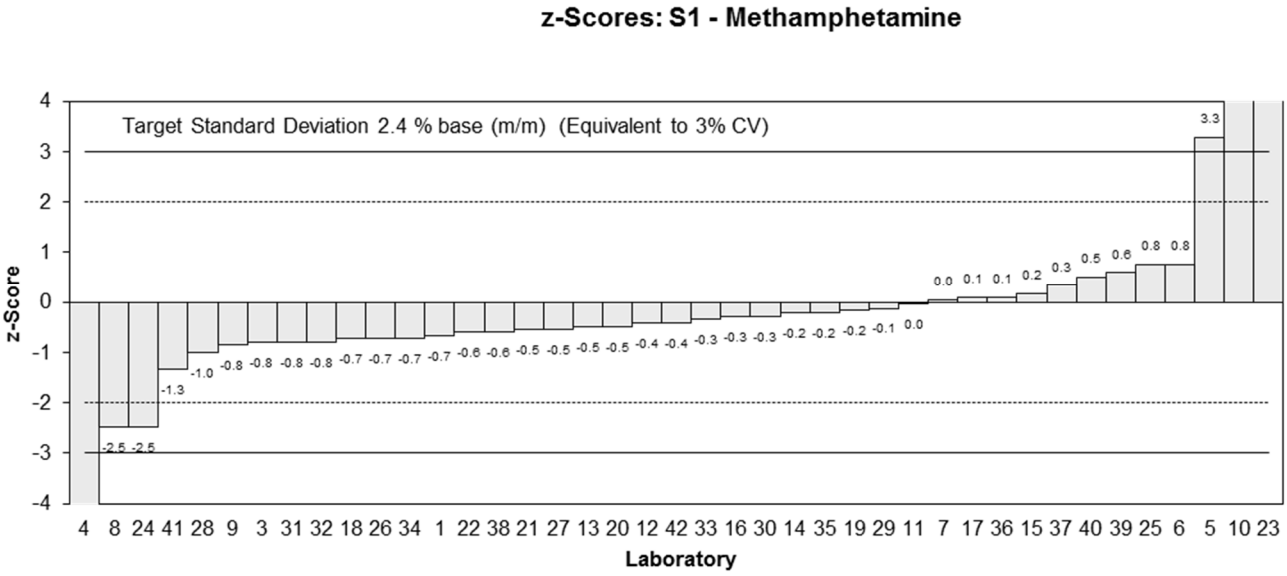
Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	77.6	0.1	-0.67	-0.89
2	NT	NT		
3	77.3	0.1	-0.80	-1.05
4	67.5	NR	-4.92	-6.50
5	87	13.1	3.28	0.59
6	81.0	2.5	0.76	0.58
7	79.3	1.74	0.04	0.04
8	73.3	6	-2.48	-0.94
9	77.2	4.4	-0.84	-0.42
10	89	9.79	4.12	0.98
11	79.1	6.3	-0.04	-0.02
12	78.2	3.2	-0.42	-0.27
13	78	3.1	-0.51	-0.33
14	78.7	7.9	-0.21	-0.06
15	79.6	10.3	0.17	0.04
16	78.5	2.8	-0.29	-0.21
17	79.4	5.0	0.08	0.04
18	77.5	4.7	-0.72	-0.34
19	78.8	0.4	-0.17	-0.22
20	78.0	4.9	-0.51	-0.23
21	77.9	4.2	-0.55	-0.28
22	77.8	4.7	-0.59	-0.28
23*	100	7.50	8.75	2.70
24	73.32	3.67	-2.47	-1.44
25	81	8.1	0.76	0.22
26	77.5	5.8	-0.72	-0.28
27	77.9	0.1	-0.55	-0.72
28	76.8	7.7	-1.01	-0.30
29	78.9	3.0	-0.13	-0.09
30	78.5	7.2	-0.29	-0.09
31	77.3	2.7	-0.80	-0.59
32	77.3	2.0	-0.80	-0.71
33	78.4	3.9	-0.34	-0.19
34	77.5	1.36	-0.72	-0.75
35	78.7	2.6	-0.21	-0.16
36	79.43	2.6	0.10	0.07
37	80	8.0	0.34	0.10
38	77.8	4.2	-0.59	-0.31
39	80.6	4	0.59	0.32
40	80.4	5.1	0.51	0.22
41	76	4.5	-1.35	-0.66
42	78.2	4.7	-0.42	-0.20

*After the release of the interim report, laboratory 23 indicated that their results are reported as HCl instead of free base.

Statistics

Assigned Value	79.2		1.8
Reference Value	79.2		1.8
Robust Average	78.5		0.6
Median	78.2		0.4
Mean	78.9		
N	41		
Max.	100		
Min.	67.5		
Robust SD	1.6		
Robust CV	2.0%		


Kernel Density
Density
Result
Results: S1 - Methamphetamine
Assigned Value = 79.2 ± 1.8 % base (m/m)
Results (% base (m/m))
Laboratory
4 8 24 41 28 9 3 31 32 18 26 34 1 22 38 21 27 13 20 12 42 33 16 30 14 35 19 29 11 7 17 36 15 37 40 39 25 6 5 10 23 2
Md R.A. R.V.


z-Scores: S1 - Methamphetamine
Target Standard Deviation 2.4 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
4 8 24 41 28 9 3 31 32 18 26 34 1 22 38 21 27 13 20 12 42 33 16 30 14 35 19 29 11 7 17 36 15 37 40 39 25 6 5 10 23

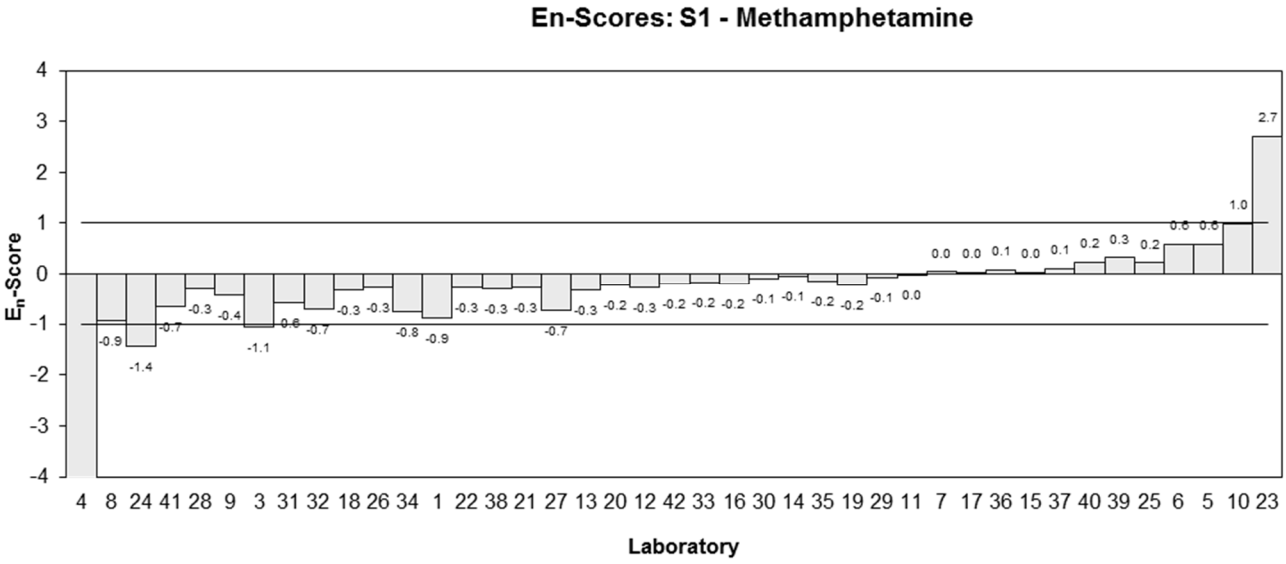

En-Scores: S1 - Methamphetamine
En-Score
Laboratory
4 8 24 41 28 9 3 31 32 18 26 34 1 22 38 21 27 13 20 12 42 33 16 30 14 35 19 29 11 7 17 36 15 37 40 39 25 6 5 10 23

Figure 2

Table 6

Sample Details

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

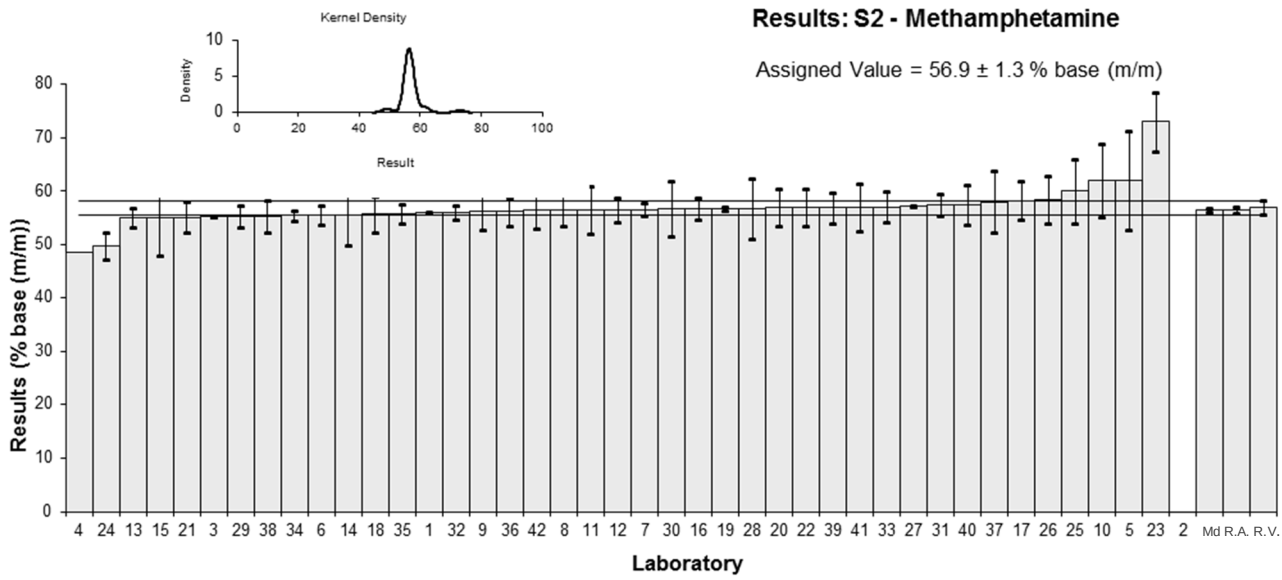
Participant Results

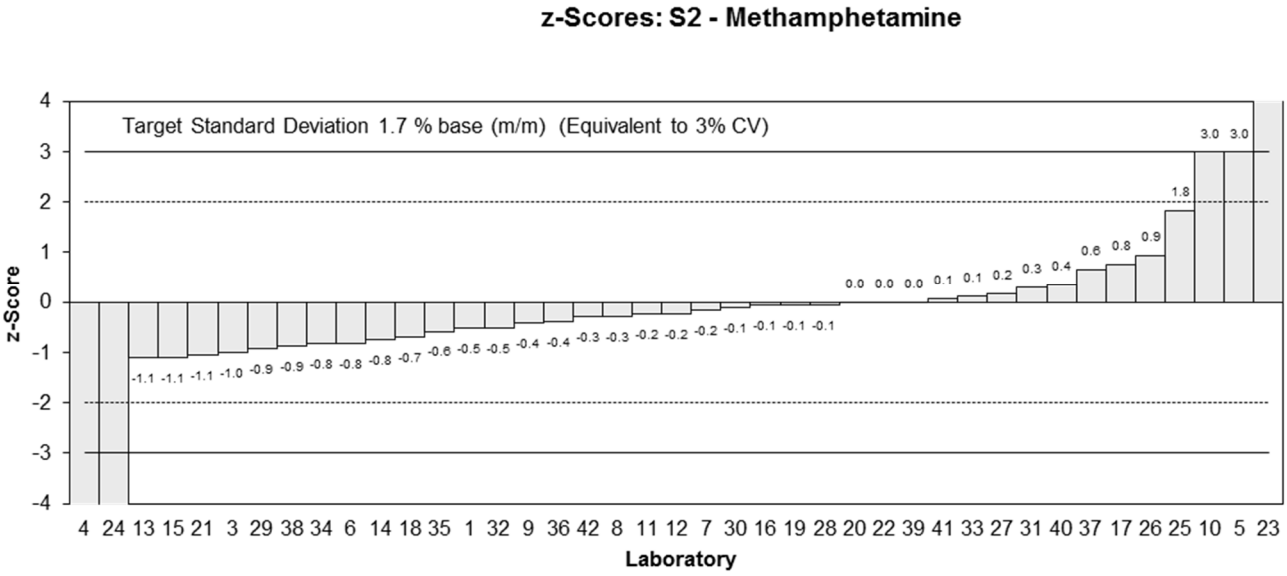
Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	56.0	0.1	-0.53	-0.69
2	NT	NT		
3	55.2	0.1	-1.00	-1.30
4	48.5	NR	-4.92	-6.46
5	62	9.3	2.99	0.54
6	55.5	1.8	-0.82	-0.63
7	56.6	1.25	-0.18	-0.17
8	56.4	3	-0.29	-0.15
9	56.2	3.3	-0.41	-0.20
10	62	6.82	2.99	0.73
11	56.5	4.5	-0.23	-0.09
12	56.5	2.3	-0.23	-0.15
13	55	1.8	-1.11	-0.86
14	55.6	5.6	-0.76	-0.23
15	55.0	7.1	-1.11	-0.26
16	56.8	2.0	-0.06	-0.04
17	58.2	3.6	0.76	0.34
18	55.7	3.4	-0.70	-0.33
19	56.8	0.3	-0.06	-0.07
20	56.9	3.5	0.00	0.00
21	55.1	2.9	-1.05	-0.57
22	56.9	3.5	0.00	0.00
23*	73	5.48	9.43	2.86
24	49.84	2.49	-4.14	-2.51
25	60	6.0	1.82	0.50
26	58.5	4.4	0.94	0.35
27	57.2	0.1	0.18	0.23
28	56.8	5.7	-0.06	-0.02
29	55.3	2.1	-0.94	-0.65
30	56.7	5.2	-0.12	-0.04
31	57.4	2.0	0.29	0.21
32	56.0	1.4	-0.53	-0.47
33	57.1	2.9	0.12	0.06
34	55.5	0.97	-0.82	-0.86
35	55.9	1.8	-0.59	-0.45
36	56.21	2.6	-0.40	-0.24
37	58	5.8	0.64	0.19
38	55.4	3.0	-0.88	-0.46
39	56.9	2.8	0.00	0.00
40	57.5	3.7	0.35	0.15
41	57	4.5	0.06	0.02
42	56.4	3.4	-0.29	-0.14

*After the release of the interim report, laboratory 23 indicated that their results are reported as HCl instead of free base.

Statistics

Assigned Value	56.9	1.3
Reference Value	56.9	1.3
Robust Average	56.5	0.5
Median	56.5	0.4
Mean	56.8	
N	41	
Max.	73	
Min.	48.5	
Robust SD	1.3	
Robust CV	2.3%	


Kernel Density
Density
Result
Results: S2 - Methamphetamine
Assigned Value = 56.9 ± 1.3 % base (m/m)
Results (% base (m/m))
Laboratory
4 24 13 15 21 3 29 38 34 6 14 18 35 1 32 9 36 42 8 11 12 7 30 16 19 28 20 22 39 41 33 27 31 40 37 17 26 25 10 5 23 2 Md R.A. R.V.


z-Scores: S2 - Methamphetamine
Target Standard Deviation 1.7 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
4 24 13 15 21 3 29 38 34 6 14 18 35 1 32 9 36 42 8 11 12 7 30 16 19 28 20 22 39 41 33 27 31 40 37 17 26 25 10 5 23

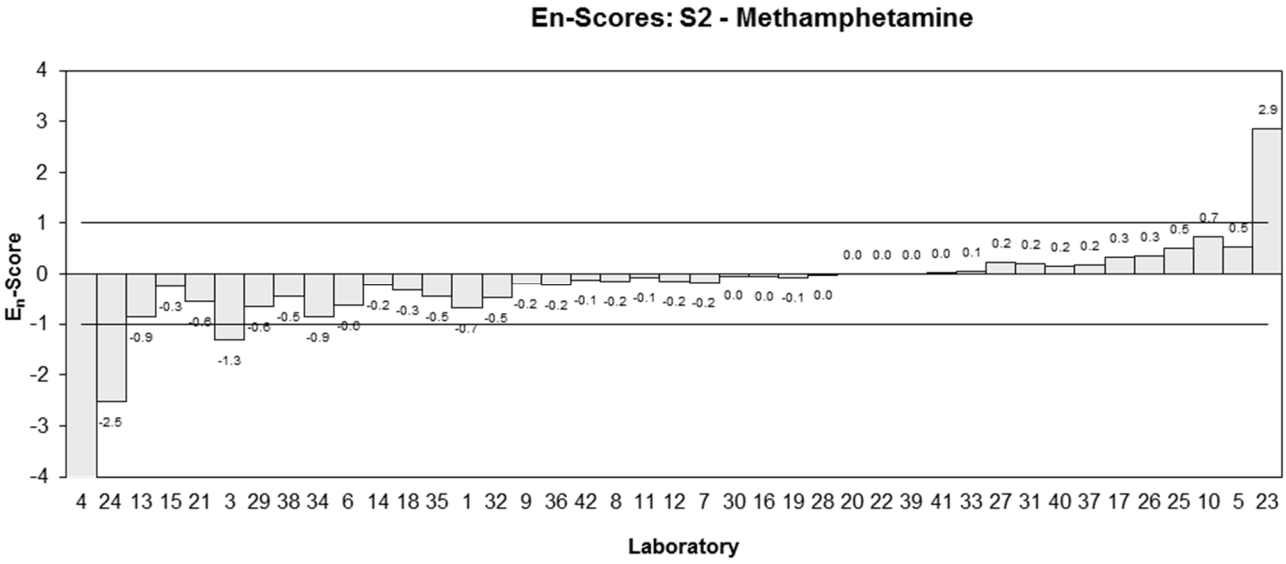

En-Scores: S2 - Methamphetamine
En-Score
Laboratory
4 24 13 15 21 3 29 38 34 6 14 18 35 1 32 9 36 42 8 11 12 7 30 16 19 28 20 22 39 41 33 27 31 40 37 17 26 25 10 5 23

Figure 3

Table 7

Sample Details

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

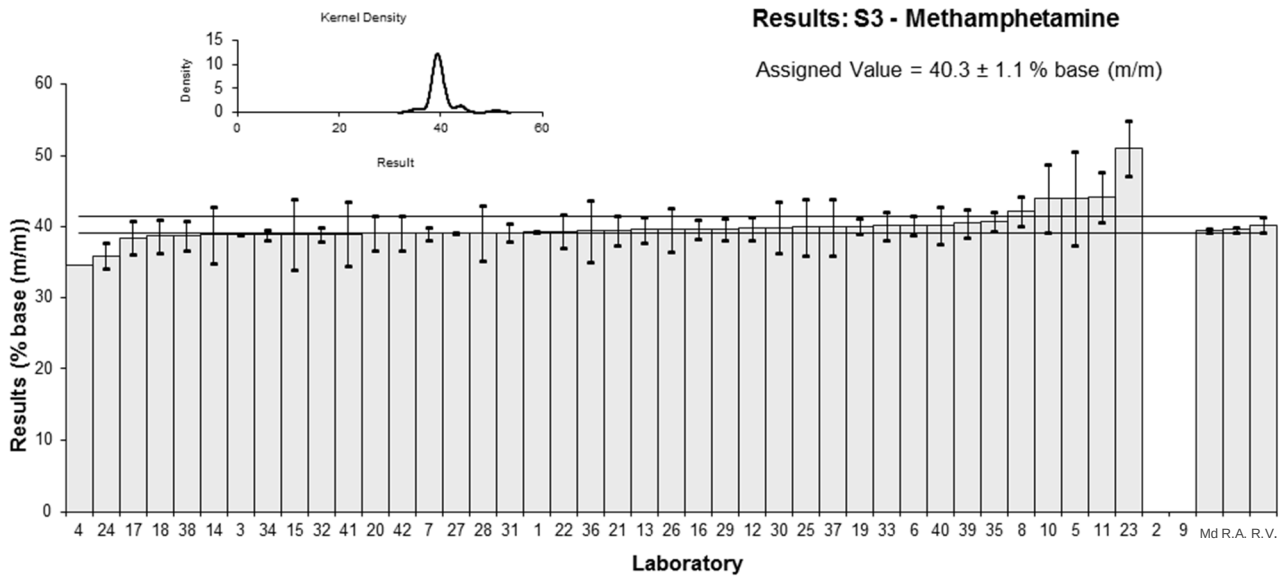
Participant Results

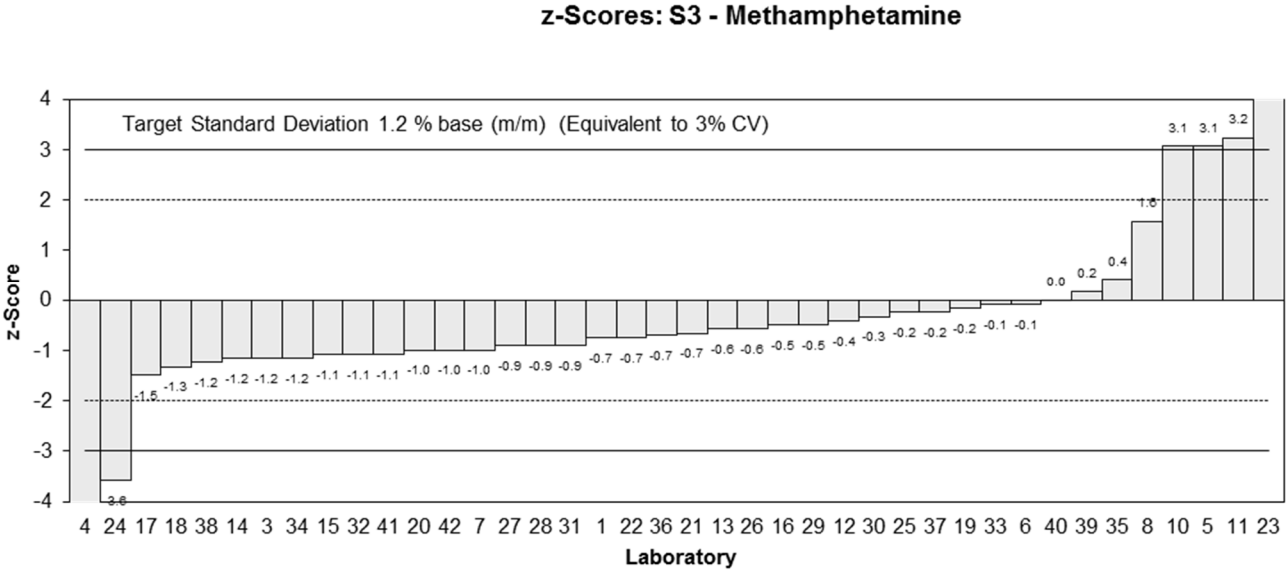
Lab Code	Result	Uncertainty	z-Score	E_n-Score
1	39.4	0.1	-0.74	-0.81
2	NT	NT		
3	38.9	0.1	-1.16	-1.27
4	34.6	NR	-4.71	-5.18
5	44	6.6	3.06	0.55
6	40.2	1.4	-0.08	-0.06
7	39.1	0.86	-0.99	-0.86
8	42.2	2	1.57	0.83
9	NT	NT		
10	44	4.84	3.06	0.75
11	44.2	3.5	3.23	1.06
12	39.8	1.6	-0.41	-0.26
13	39.6	1.8	-0.58	-0.33
14	38.9	3.9	-1.16	-0.35
15	39.0	5.0	-1.08	-0.25
16	39.7	1.4	-0.50	-0.34
17	38.5	2.4	-1.49	-0.68
18	38.7	2.4	-1.32	-0.61
19	40.1	1.1	-0.17	-0.13
20	39.1	2.4	-0.99	-0.45
21	39.5	2.1	-0.66	-0.34
22	39.4	2.4	-0.74	-0.34
23*	51	3.83	8.85	2.69
24	35.96	1.8	-3.59	-2.06
25	40	4.0	-0.25	-0.07
26	39.6	3.0	-0.58	-0.22
27	39.2	0.1	-0.91	-1.00
28	39.2	3.9	-0.91	-0.27
29	39.7	1.5	-0.50	-0.32
30	39.9	3.6	-0.33	-0.11
31	39.2	1.3	-0.91	-0.65
32	39.0	1.0	-1.08	-0.87
33	40.2	2.0	-0.08	-0.04
34	38.9	0.68	-1.16	-1.08
35	40.8	1.3	0.41	0.29
36	39.45	4.3	-0.70	-0.19
37	40	4.0	-0.25	-0.07
38	38.8	2.1	-1.24	-0.63
39	40.5	2	0.17	0.09
40	40.3	2.6	0.00	0.00
41	39	4.5	-1.08	-0.28
42	39.1	2.4	-0.99	-0.45

*After the release of the interim report, laboratory 23 indicated that their results are reported as HCl instead of free base.

Statistics

Assigned Value	40.3	1.1
Reference Value	40.3	1.1
Robust Average	39.6	0.3
Median	39.5	0.2
Mean	40.0	
N	40	
Max.	51	
Min.	34.6	
Robust SD	0.9	
Robust CV	2.3%	


Kernel Density
Density
Result
Results: S3 - Methamphetamine
Assigned Value = 40.3 ± 1.1 % base (m/m)
Results (% base (m/m))
Laboratory
4 24 17 18 38 14 3 34 15 32 41 20 42 7 27 28 31 1 22 36 21 13 26 16 29 12 30 25 37 19 33 6 40 39 35 8 10 5 11 23 2 9 Md R.A. R.V.


z-Scores: S3 - Methamphetamine
Target Standard Deviation 1.2 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
4 24 17 18 38 14 3 34 15 32 41 20 42 7 27 28 31 1 22 36 21 13 26 16 29 12 30 25 37 19 33 6 40 39 35 8 10 5 11 23

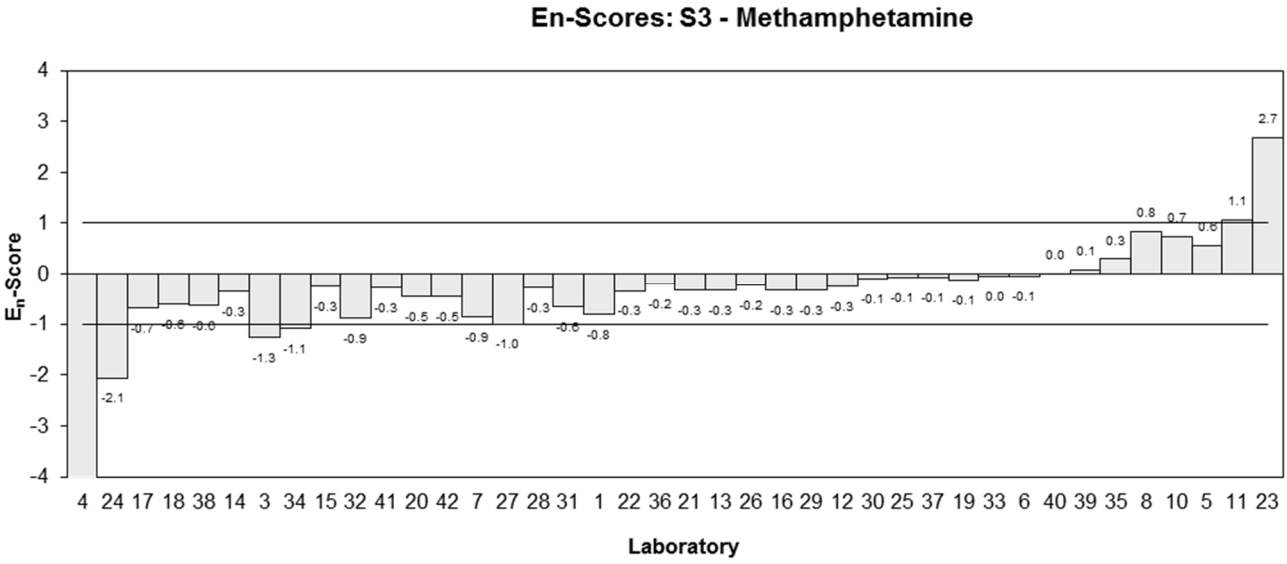

En-Scores: S3 - Methamphetamine
En-Score
Laboratory
4 24 17 18 38 14 3 34 15 32 41 20 42 7 27 28 31 1 22 36 21 13 26 16 29 12 30 25 37 19 33 6 40 39 35 8 10 5 11 23

Figure 4

Table 8 Participants' identification of cutting agents

Lab Code	Cutting agents		
	S1	S2	S3
1	-		Niacinamide
2			
3			Niacinamide
4		Glucose : 22,6 %	Nicotinamide
5			Nicotinmide
6			
7		Glucose	Nicotinamide
8		Mannose	Nicotinamide
9			
10			Nicotinamide
11			
12		Vitamin B8 (Inositol)	Nicotinamide
13			Niacinamide
14			Niacinamide
15		-	Niacinamide
16			Nicotinamide
17			Niacinamide
18	-	-	Nicotinamide (screened positive)
19	At least two minor impurities (total <2%) with similar structural features, possibly ephedrine isomers	Glucose	Nicotinamide
20			Nicotinamide
21			Niacinamide
22			Niacinamide
23	amphetamine (trace)		Nicotinamide
24			Nicotinamide
25		D-Glucose	Nicotinamide
26	-	-	Niacinamide
27			Niacinamide
28			
29			Nicotinamide
30	-	-	Niacinamide
31			Niacinamide
32		Glucose	Niacinamide

Lab Code	Cutting agents		
	S1	S2	S3
33			Possibly nicotinamide
34			Niacinamide
35			Niacinamide
36		Glucose	
37		Dextrose	Nicotinamide
38			Nicotinamide
39			Nicotinamide
40			
41		Glucose	Niacinamide
42	-	-	Nicotinamide (screened positive)

6 DISCUSSION OF RESULTS

6.1 Assigned Value

A reference value was obtained for all samples using the quantitative nuclear magnetic resonance spectrometry (QNMR) measurement method described in Appendix 3.
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 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.

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.

119 results (94%) were reported with an associated expanded uncertainty. Laboratory **4** did not report an uncertainty. This laboratory was not accredited.

Laboratories **1**, **3**, **13**, **27** and **41** reported an identical uncertainty for samples which were of significantly different concentrations.

The magnitude of reported uncertainties was within the range 0.13% to 15% relative.

Ninety-two of 119 (79%) 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 49.84 ± 2.49% the recommended format is 49.8 ± 2.5%).[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 Thomson - Horwitz equation[8] and 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 CV)	Thompson Horwitz CV	Between laboratories CV
S1	Methamphetamine	79.2	3%	2.0%	2.0%
S2	Methamphetamine	56.9	3%	2.2%	2.3%
S3	Methamphetamine	40.3	3%	2.3%	2.3%

A summary of z-scores by laboratory is presented in Figure 5.

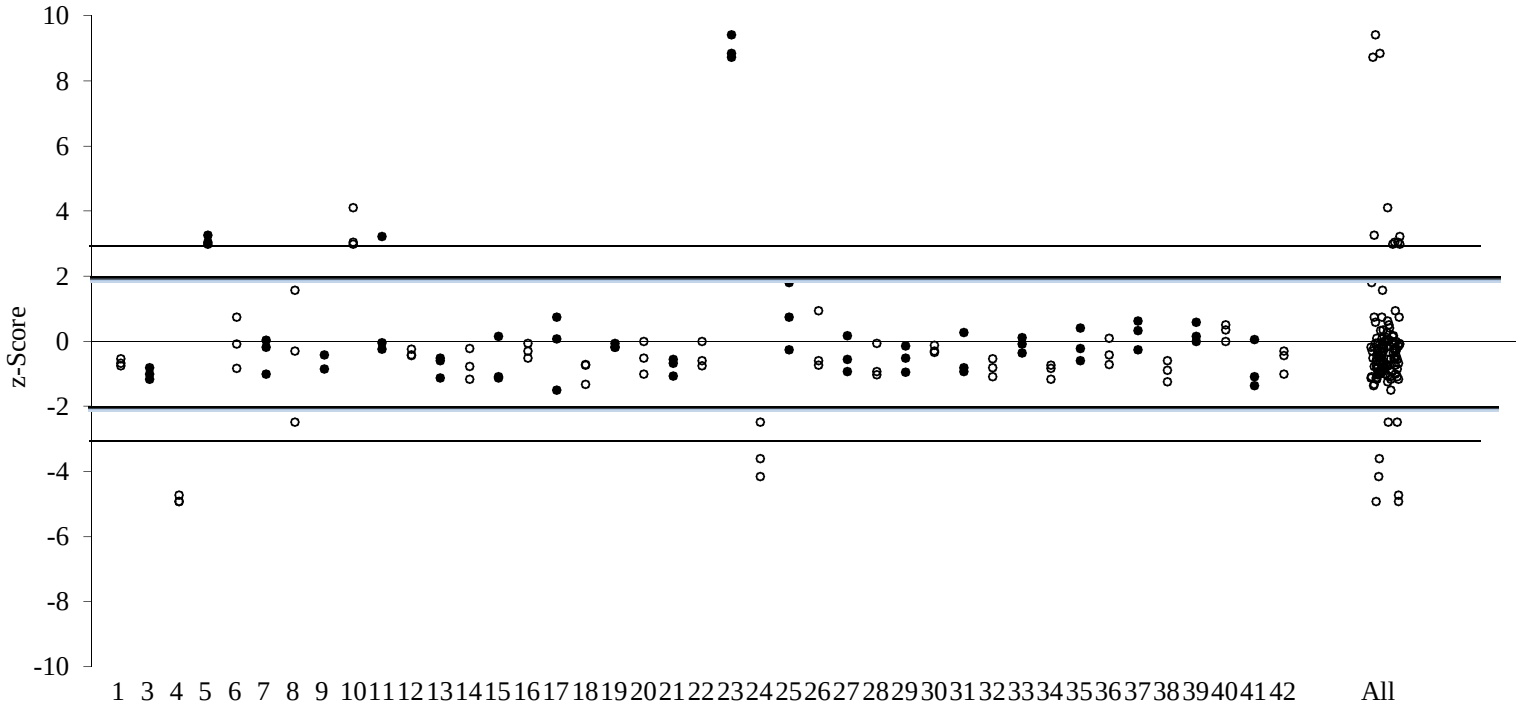


Figure 5 Summary of participants' z-score.

105 of 122 numeric results (86%) returned a satisfactory z-score with $|z| \leq 2$**.**

- Thirty-four participants (81%) - **1**, **3**, **6**, **7**, **9** (only two results submitted) **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **34**, **35**, **36**, **37**, **38**, **39**, **40**, **41** and **42** returned satisfactory scores for all three samples;
- Seven participants returned at least one questionable or unsatisfactory z-score;
- Laboratories **4**, **5**, **10**, **23** and **24** returned questionable or unsatisfactory z-scores for all test samples demonstrating an unsatisfactory performance. Laboratories **4** and **24** reported results for all test samples lower than the assigned value (negative bias), while laboratories **5** and **10** reported all results higher than the assigned value (positive bias). These laboratories may need to investigate the source of bias.
  After the release of the interim report, laboratory **23** indicated that they reported methamphetamine as HCl salt and not as free base.

6.4 E_n-Score

The dispersal of participants' E_n-scores is graphically presented in Figure 6. 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.

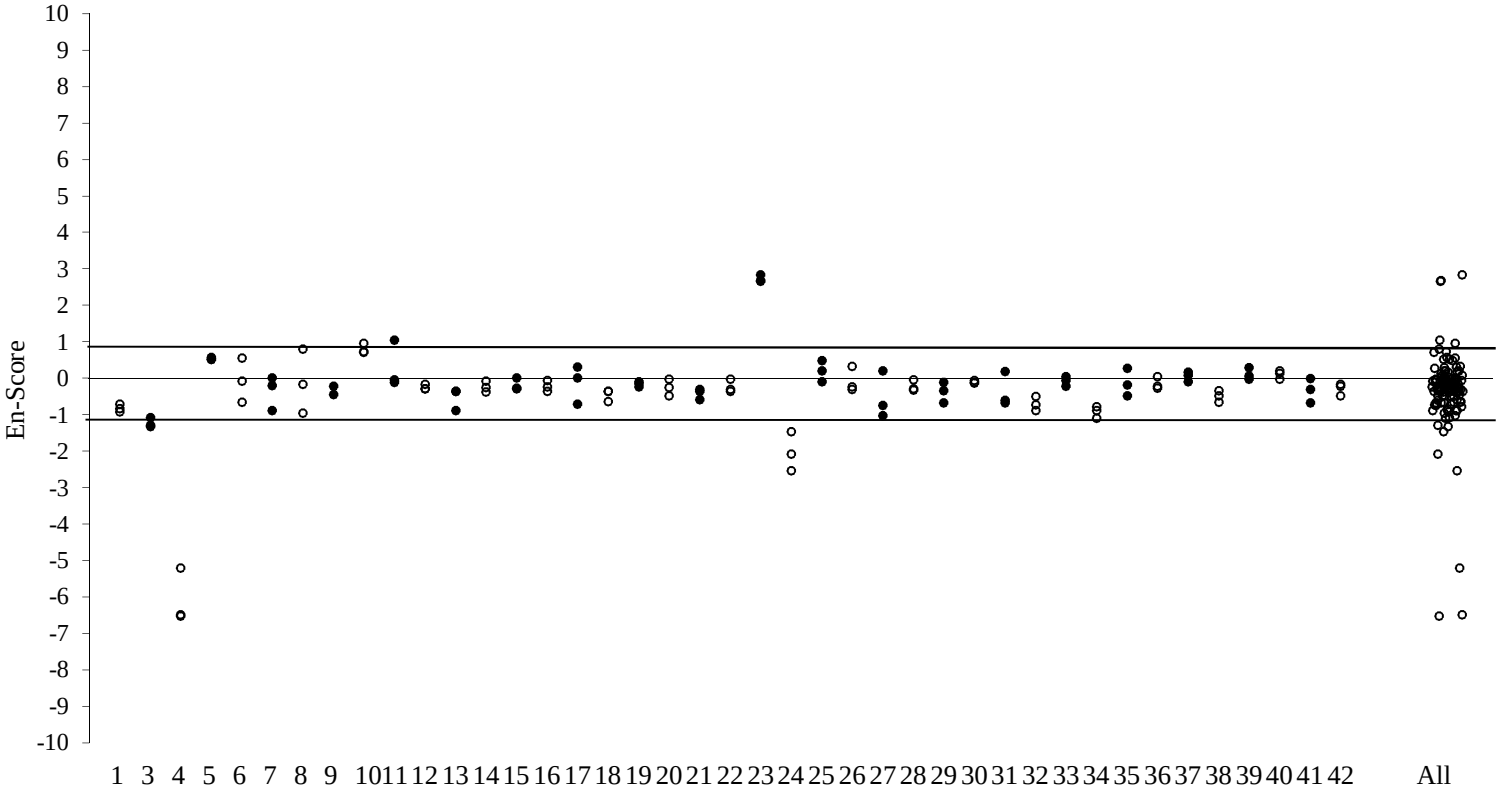


Figure 6 Summary of participants' E_n-Score

108 of 122 numeric results (89%) returned a satisfactory E_n-score with $|E_n| \leq 1$.

- Thirty-five participants (83%) – **1**, **5**, **6**, **7**, **8**, **9** (only reported two results), **10**, **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**, **21**, **22**, **25**, **26**, **27**, **28**, **29**, **30**, **31**, **32**, **33**, **35**, **36**, **37**, **38**, **39**, **40**, **41** and **42** returned satisfactory scores for all three samples;
- Two laboratories returned at least one questionable E_n-score; and
- Laboratories **3**, **4**, **23**, **24** returned $|E_n| > 1$ for all samples.

6.5 Identification of Cutting Agent

Thirty-six laboratories (86%) reported on the identity of the cutting agents in each test sample and the findings are presented in Table 8.

Sample S1 was methamphetamine hydrochloride approximately 79.5% base (m/m), while Samples S2 and S3 were methamphetamine hydrochloride approximately 78.5% base (m/m), both supplied by the NMI Chemical Reference Materials Laboratory.

Sample S1 was left uncut.

Glucodin was used to prepare Sample S2. Ten laboratories reported on the diluent and six correctly identified glucose.

Nicotinamide (niacinamide) was used to prepare Sample S3. Thirty-five laboratories correctly identified the cutting agent.

Two laboratories reported traces of impurities in sample S1 as cutting agents. A cutting agent is commonly a cheaper compound added to dilute the drug sample, whereas minor impurities

typically arise either as by-products from undesirable side reactions during the synthesis process or unreacted starting materials/intermediates.

6.6 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	5 6 7 9 12 13 16 17 20 21 22 25 29 30 32 33 37 38 39 41
Yes to ASCLD/Lab International	1 3 15 18 26 27 30 31 34 35 42
Other (Unspecified)	14
No	4 8 10 19 23 24 28 36 40

Sample Mass Used (mg)	Laboratory Code
4-10	7 8 13 27
11-30	1 3 6 9 10 11 12 14 15 17 18 19 21 22 25 26 29 30 31 34 35 36 37 38 40 42
31-50	4 5 18 20 23 24 28 30 33 39
51-100	4 32
101-150	16 36 41

Instrument Used for quantification	Laboratory Code
GC-FID	1 3 12 13 14 15 17 21 22 26 27 30 31 34 35 40
UPLC-MS(MS)	5
HPLC(UPLC)-DAD	4 6 7 8 9 10 11 16 18 19 20 23 24 25 28 29 32 33 36 37 38 39 41 42
QNMR	7 19

Sources of Calibration Standard	Laboratory Code
NMI Australia	6 9 11 12 14 20 25 29 32 37 38
Lipomed	13 18 24 26 28 36 39 40 42
Sigma Aldrich	5 10 19 33 41
Other	1 3 4 8 15 16 17 21 22 23 27 30 31 34 35

Plots of extraction solvent vs z-score, measurement instrument vs z-score and calibration standard vs z-score are presented in Figures 7, 8 and 9. HPLC(UPLC)-DAD was the most common method used, and was also the most variable in the results submitted by participants. Chloroform was the most common solvent used, and also gave the most consistent and accurate results. No trends were identified in the calibration standards used.

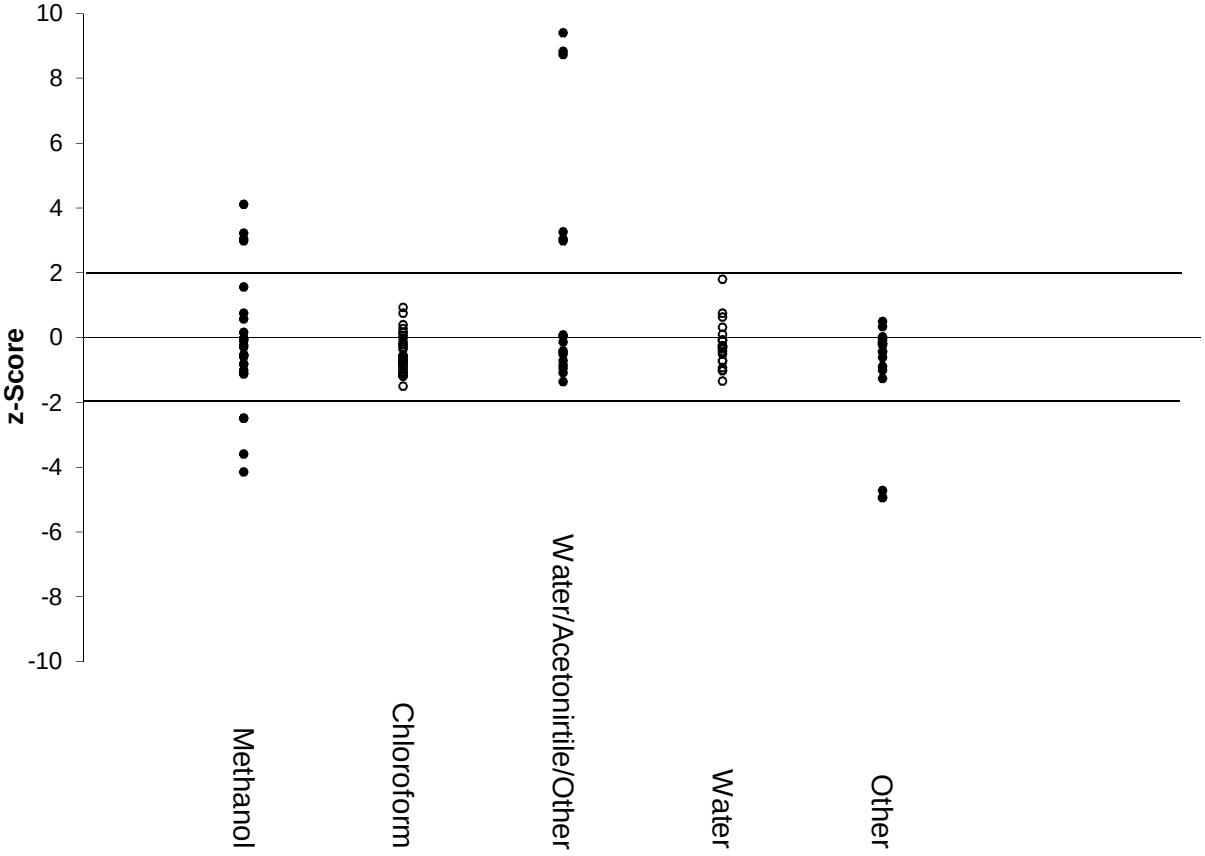


Figure 7 Extraction solvent vs z-score

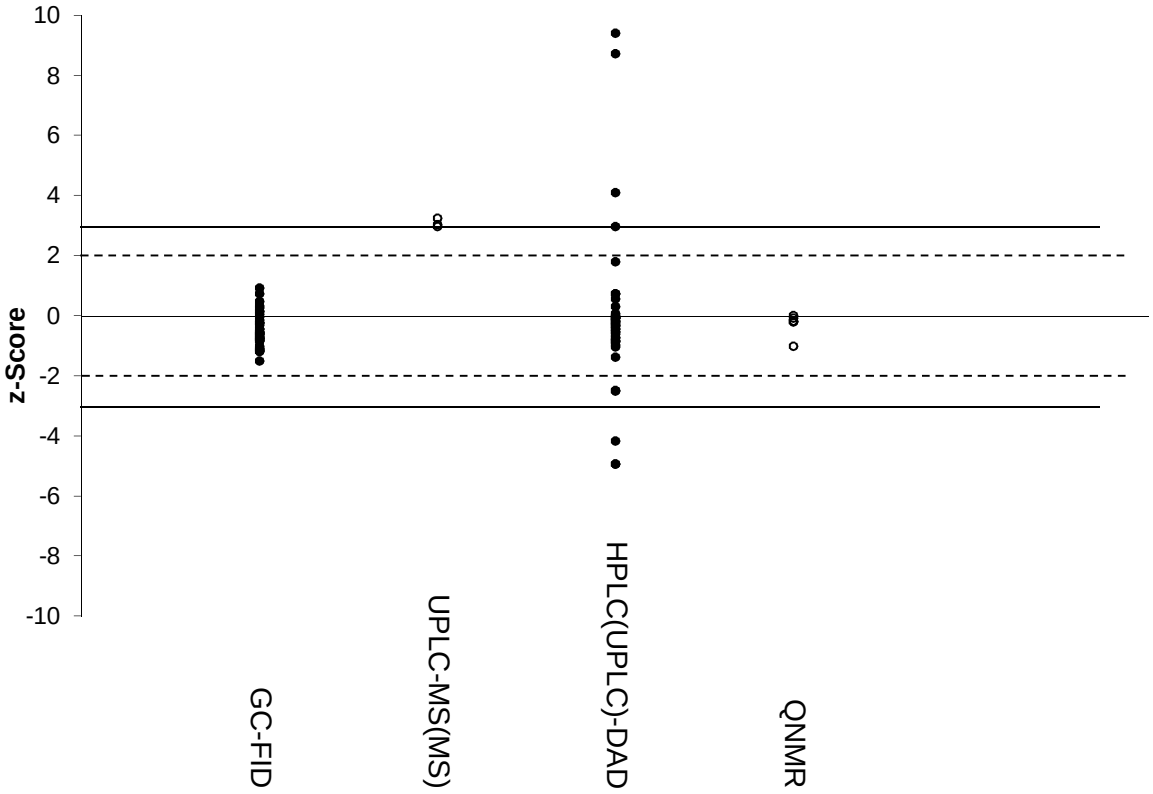


Figure 8 Measurement instrument vs z-score

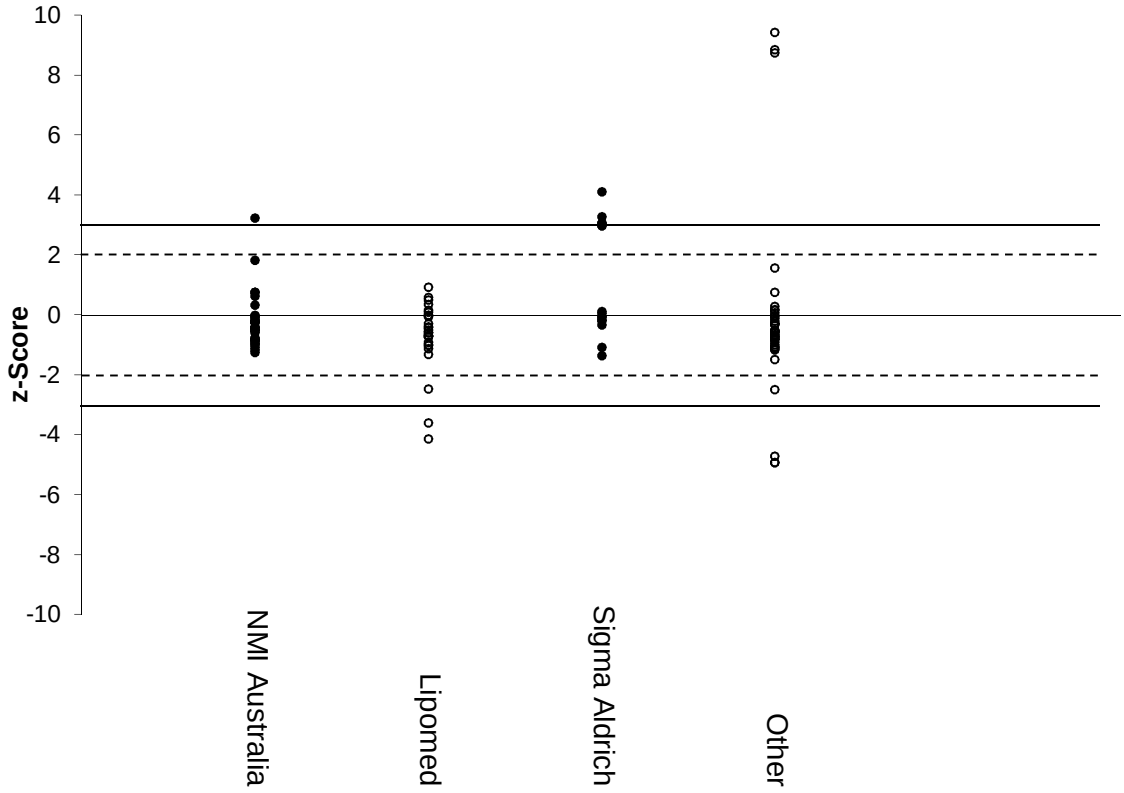


Figure 9 Calibration standard vs z-score

6.7 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 10. The proportion of satisfactory z-scores and E_n-scores over 8 years on average is 81% and 76% respectively.

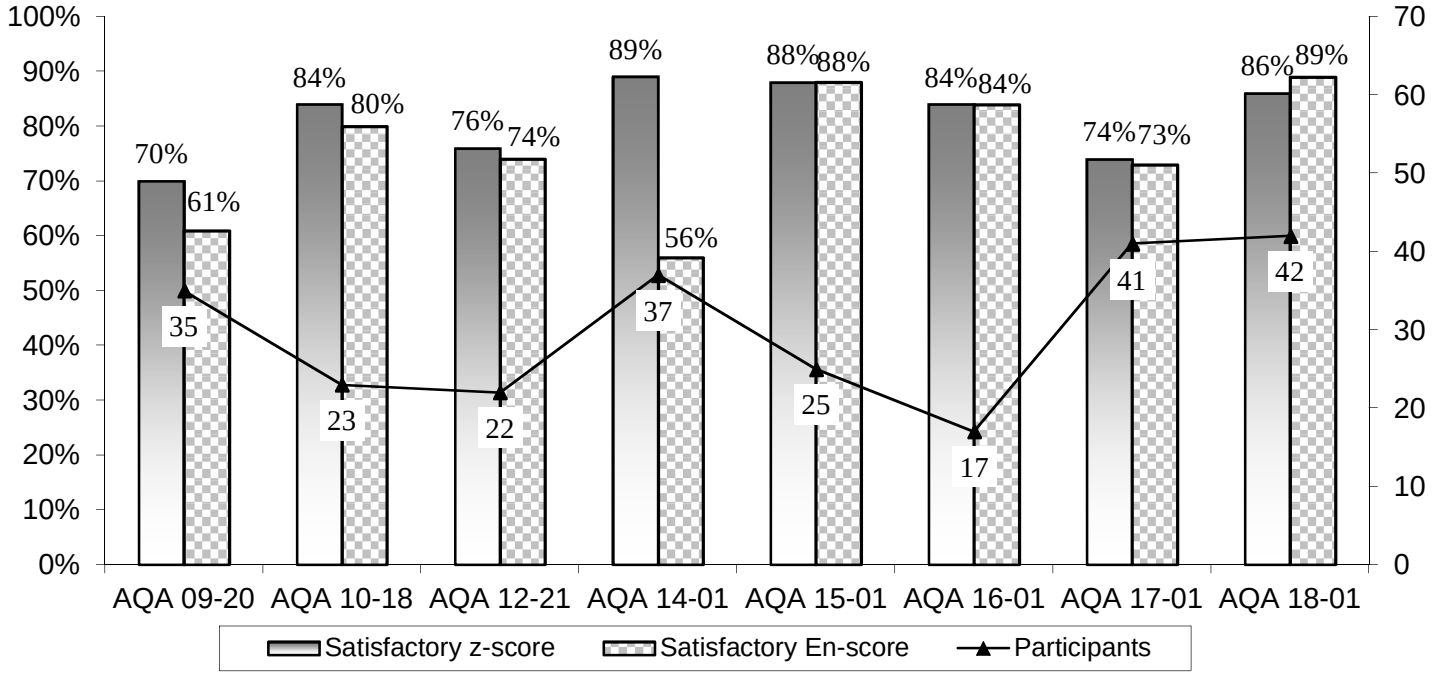


Figure 10 Summary of participants' performance since 2009

7 REFERENCES

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

[2] NMI 2016, *Chemical Proficiency Testing Study Protocol*, viewed 3 May 2018, http://www.measurement.gov.au.

[3] NMI 2016, *Chemical Proficiency Testing Statistical Manual*, viewed 3 May 2018, <http://www.measurement.gov.au >.

[4] Thompson, M., Ellison, SLR. & 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 May 2017, <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 Lowthian, P.J., A Horwitz-like function describes precision in a proficiency test, Analyst, 120, 271-272, 1995.

APPENDIX 1 - PARTICIPANT LABORATORIES

ACT Government Analytical Laboratory ACT	Central Customs Laboratory and Scientific Service Korea Customs Service, KOREA
CHU Nantes, FRANCE	CHEMCENTRE WA
Department of Chemistry, Alor Star, MALAYSIA	Department of Chemistry Sarawak, MALAYSIA
Department of Chemistry, Johor, MALAYSIA	Department of Chemistry, Bintulu Sarawak, MALAYSIA
Department of Chemistry, Kuching Sarawak, MALAYSIA	Department of Chemistry, Kelantan, MALAYSIA
Department of Chemistry, Melaka, MALAYSIA	Department of Chemistry, Selangor, MALAYSIA
Department of Chemistry, Perak, MALAYSIA	Department of Chemistry, Pahang, MALAYSIA
Department of Chemistry, Sabah, MALAYSIA	Department of Chemistry, Pulau Pinang, MALAYSIA
Environmental Science and Research Ltd, Mt. Albert Science Centre, NEW ZEALAND	Department of Chemistry, Terengganu, MALAYSIA
Forensic & Analytical Science Services, NSW	Eurofins Forensic Services Limited Middlesex, UK
Forensic Science SA	Forensic Institute, Odense Syddansk Universitet, DENMARK
Government Laboratory, HONG KONG	Forensic Science Services TAS
Health Sciences Authority, SINGAPORE	I.N.C.C., BELGIUM
Instituto Nacional de Toxicologia y Ciencias Forenses Madrid, SPAIN	Instituto Nacional de Toxicologia y Ciencias Forenses Barcelona, SPAIN
Laboratoire Toxlab s.a.s., FRANCE	Lancashire Constabulary Headquarters, UK
National Criminal Investigation Service/Kripos, NORWAY	National Measurement Institute NSW
NBI - Laboratories, FINLAND	PJGN/IRCGN/ASQ, FRANCE
Queensland Health Forensic and Scientific Services QLD	Scottish Police Authority Forensic Services Dundee, UK
University of Copenhagen, DENMARK	University of Aarhus, Institut of Forensic Medicine DENMARK
University of New South Wales School of Chemical Engineering, NSW	Victoria Police Forensic Services Dept. VIC

APPENDIX 2 - 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 S2 as % base (m/m)

No. results (p)	41
Robust average	56.52
$S_{rob\ average}$	1.26
$u_{rob\ average}$	0.246
k	2
$U_{rob\ average}$	0.49

The robust average for Sample S2 is 56.5 ± 0.5% Methamphetamine base (m/m).

APPENDIX 3 – REFERENCE VALUE

A reference value was obtained for all samples. Five sample bottles from Sample S1 and S3, and four bottles from Sample S2 were selected at random for the purpose of assigning a reference value. The bottles selected for S2 were done 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.

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 by accurately weighing 20 mg of sample and dissolving in 900 µL of internal standard solution (245 mg of maleic acid in 36.45 mL (40.359 g) of D_2O). 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 average of NMR responses at 1.15 ppm, 2.58 ppm, 2.93 ppm and 3.44 ppm.

The average mass fractions (Tables 12, 13 and 14) determined for Sample S1, S2 and S3 were used as the reference values and the assigned values for the PT study. The standard uncertainties on the mass fraction reference values were 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

Bottle Fill No.	Methamphetamine (% base m/m)
101	78.5
115	79.3
116	79.4
127	79.2
129	79.5
136	78.5
139	79.3
Mean	79.2
CV	1.1%

Reference value 79.2 ± 1.8% 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[10] equation (k = 2.09).

Table 13 Reference value for Sample S2

Bottle Fill No.	Methamphetamine (% base m/m)	
	Replicate 1	Replicate 2
206	56.8	56.6
213	57.1	56.8
250	57.6	56.7
255	57.2	56.1
Mean	56.9	
CV	1.1%	

Reference value 56.9 ± 1.3% 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[10] equation (k = 2.10).

Table 14 Reference value for Sample S3

Bottle Fill No.	Methamphetamine (% base m/m)
314	40.1
320	40.0
330	40.5
347	40.8
351	40.1
Mean	40.3
CV	1.2%

Reference value 40.3 ± 1.1% 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[10] equation (k = 2.16).

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

APPENDIX 4 - 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
$\|E_n\|$	Absolute value of an E_n-score
FID	Flame Ionization 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
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