Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

Proficiency Test Final Report
AQA 20-01
MDMA and Methamphetamine

November 2020

ACKNOWLEDGMENTS

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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 20-01 MDMA and Methamphetamine commenced in February 2020. Sample sets each containing three 3,4-methylenedioxymethamphetamine (MDMA) hydrochloride samples and one methamphetamine hydrochloride sample were sent to thirty-nine laboratories, with two laboratories requesting two sets of test samples to be analysed by different analysts. All participants returned results.

Samples were prepared at the Sydney NMI laboratory. For Sample S1, MDMA hydrochloride approximately 79% base (m/m) supplied by the Australian Federal Police (AFP) was used. For Samples S2 and S3, MDMA hydrochloride approximately 78.5% base (m/m) synthesised by the Chemical Reference Materials Section, NMI was used. For Sample S4, methamphetamine hydrochloride around 80% base (m/m) supplied by the AFP was used.

The assigned values for Samples S1 and S4 were the reference values determined by quantitative nuclear magnetic resonance spectroscopy (qNMR) with maleic acid (NMI certified reference material QNMR010) as the 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 (Batch No.: 10-Q-02).

The assigned values for Samples S2 and S3 were 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 MDMA and methamphetamine in samples typical of a routine seizure.*

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

Of 160 results for which z-scores were calculated, 138 (86%) returned a satisfactory z-score of $|z| \leq 2.0$, indicating a satisfactory performance.

Of 160 results for which E_n-scores were calculated, 131 (82%) returned a satisfactory E_n-score of $|E_n| \leq 1.0$, indicating agreement of the participant's results with the assigned value within their respective expanded uncertainties.

Laboratories **1**, **3** (only 1 result submitted), **5**, **6**, **7**, **8**, **9**, **11**, **13**, **15**, **18**, **19**, **20**, **22**, **23**, **25**, **29**, **30**, **31**, **36**, **39** and **40** returned satisfactory z- and E_n-scores for all samples.

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

Of 160 reported results, 156 (98%) were reported with an associated expanded measurement uncertainty. Laboratory **37** did not report any uncertainties; this laboratory was not accredited.

The magnitudes of reported uncertainties were within the range 0.1% to 15% relative.

- *Test the ability of participants to identify cutting agents commonly found in controlled drug preparation.*

Sample S1 was cut with cellulose, Samples S2/3 were cut with caffeine and glucose, and Sample S4 was cut with procaine hydrochloride. Thirty-nine participants (95%) reported on the identity of at least one cutting agent in the samples.

Laboratories **8** and **9** correctly identified all cutting agents added to the samples in this study.

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 the: '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;
- inorganic analytes in soil, water, food and pharmaceuticals;
- controlled drug assay and clandestine laboratory; and
- allergens in food.

1.2 Study Aims

The aims of the study were to:

- assess the proficiency of laboratories measuring 3,4-methylenedioxymethamphetamine (MDMA) and 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 cutting agents 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[1] 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:	3 February 2020
Samples dispatched:	23 March 2020
Results due:	5 October 2020
Interim report issued:	7 October 2020

2.2 Participation

Thirty-nine laboratories registered to participate, with two laboratories requesting two sets of samples to be analysed independently by different analysts. All participants submitted results.

2.3 Test Material Specification

Four test samples were prepared in March 2020. The starting material for Sample S1 was MDMA hydrochloride approximately 79% base (m/m) supplied by the Australian Federal Police (AFP). The starting material for Samples S2 and S3 was MDMA hydrochloride approximately 78.5% base (m/m) synthesised by the Chemical Reference Materials Section, NMI. The starting material for Sample S4 was methamphetamine hydrochloride approximately 80% base (m/m) supplied by the AFP.

Cellulose and caffeine purchased from Sigma Aldrich, glucodin purchased from a local pharmacy, and procaine hydrochloride purchased from Ajax Finechem were used as cutting agents. Sample S1 was cut with cellulose, Samples S2 and S3 were blind duplicates cut with caffeine and glucodin, and Sample S4 was cut with procaine hydrochloride.

The MDMA and methamphetamine were ground and sieved through a 180 µm sieve. The cutting agents were processed similarly. Test samples were 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 approximately 63% MDMA base (m/m).

Sample S2 was prepared to contain approximately 31% MDMA base (m/m).

Sample S3 was identical to Sample S2 (duplicate).

Sample S4 was prepared to contain approximately 46% methamphetamine base (m/m).

2.4 Laboratory Code

Each participant was 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 substance 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 samples has been validated in previous studies. No homogeneity testing was conducted in this proficiency study. Results returned by participants gave no reason to question the homogeneity of the test samples.

2.6 Sample Dispatch and Receipt

A set of four test samples, each containing approximately 150 mg of test material, was dispatched to each participant on 23 March 2020.

The following items were also sent with the samples:

- a 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:

- one result for each sample as % m/m drug (either MDMA or methamphetamine) as base;
- an estimate of the expanded uncertainty associated with the result as % m/m drug (either MDMA or methamphetamine) as base;
- brief detail on how the uncertainty was calculated, e.g. uncertainty budget method;
- identity of the cutting agents in all four samples, if part of routine analysis;
- source and stated purity of the analytical reference standard used;
- brief summary of the quantitative method used; and
- the completed results sheet by 31 July 2020.

The results due date was changed from 31 July 2020 to 5 October 2020. Due to the exceptional international circumstances occurring over the course of this study, some participants were not able to report results as originally scheduled. Therefore, the results turnaround time was extended by 2 months.

2.8 Interim Report

An interim report was emailed to all participants on 7 October 2020.

3 PARTICIPANT LABORATORY INFORMATION

3.1 Test Methods Reported by Participants

Participants were requested to provide information about their test methods. Responses as received are presented in Table 1.

Table 1 Summary of Participants' Test Methods

Lab. Code	Analyte	Extraction Solvent	Internal Standard	Calib. Points	Technique	Detector	Column
1	All	Chloroform	Nortriptyline	1	GC	FID	HP5
2	All	Chloroform	Nortriptyline	1	GC	FID	DB5
3	Methamphetamine	Dissolution in acetonitrile/water	Methoxyphenamine HCl	3	HPLC	DAD	Alltima C-18
4	All	Chloroform	Nortriptyline	1	GC	FID	HP5
5	All	Purified water	Phentermine	1	LC	DAD	Agilent Zorbax SB-C8
6	All	Methanol:KOH buffer (50:50)	Methoxyphenamine	3	UPLC	PDA	Acquity UPLC BEH C18
7	All	methanol	propylparaben	3	UPLC	PDA	ACQUITY C-18
8	All	Milli-Q Water	N/A	6	UPLC	DAD	Acquity UPLC BEH C18 2.1 x 100 mm
9	All	Isooctane + Ammonium Hydroxide	Dodecane	3	GC	FID, MS	HP-1MS
10	MDMA	water	N/A	4 or 1	HPLC / UPLC	PDA	C18
	Methamphetamine			1	UPLC		
11	All	Chloroform	Nortriptyline	1	GC	FID	HP5
12	All	Chloroform	Nortriptyline	1	GC	FID	HP5
13	All	MeOH	Strychnine	6	UHPLC	PDA	Phenyl 1.8um 2.1x100mm
14	MDMA	Methanol	N/A	6	HPLC	UV, 285nm	Luna C-18, 0.5% DEA, pH 8.5 : CH3OH, 40:60
	Methamphetamine					UV, 258nm	
15	All	deuterium oxide	maleic acid		1H QNMR	Bruker AVIII 600 with BBFO probe	N/A
16	All	Methanol	None	5	HPLC	DAD	Phenomenex C-18-XB
17	MDMA	Methanol	Selegiline	4	HPLC	DAD	C18
	Methamphetamine		None				
18	MDMA	KH2PO4 buffer	3-phenyl-1-propylamine	1	HPLC	DAD	Zorbax Sil (150mm x 4.6mm, 5micron)
	Methamphetamine	purified water		5			

Lab. Code	Analyte	Extraction Solvent	Internal Standard	Calib. Points	Technique	Detector	Column
19	All	Chloroform	Nortriptyline	1	GC	FID	HP5
20	All	Chloroform	Nortriptyline	1	GC	FID	HP5
21	All	Chloroform	Nortriptyline	1	GC	FID	HP5
22	All	Chloroform	Nortriptyline	1	GC	FID	HP-ULTRA2
23	All	Acetonitrile ammonium acetate, diethylamine & water	None	3	HPLC	Diode-array	LiChrospher 100-5 RP18
24	All	Chloroform	Nortriptyline	1	GC	FID	HP5
25	All	Chloroform	Nortriptyline	1	GC	FID	HP5
26	All	Methanol		5	HPLC	DAD	C18 column
27	All	D2O	Maleic acid	NA	QNMR		NA
28	All	Chloroform	Nortriptyline	1	GC	FID	HP5
29	All	Milli-Q Water	N/A	6	UPLC	DAD	Acquity UPLC BEH C18 2.1 x 100 mm
30	All	Purified water	Phentermine	1	LC	DAD	Agilent Zorbax SB-C8
31	All	Chloroform	Nortriptyline	1	GC	FID	HP5
32	MDMA	ACN/MeOH/H2O	Analog of MDMA	7	UPLC	MSMS	C-18 column
	Methamphetamine		Analog of methamphetamine				
33	All	Chloroform	Nortriptyline	1	GC	FID	HP5
34	All	water	none	4	HPLC	DAD	Zorbax RX-sil
35	All	ethyl acetate	diphenylamine	5	GC	FID	HP1
36	All	Methanol	Diazepam	6	GC	FID	128-5512 DB-5ms
37	All	methanol	NO	1	HPLC	DAD	zorbax eclipse XDB-C18 (4.6x150mm)
38	All	Water	None	3	HPLC	Diode Array	Shimpack XR-ODS
39	MDMA	hexane	eicosane	4	GC	FID	HP1
	Methamphetamine	D2O	calcium formate	2	NMR (400mHz)		
40	All	acetic acid, acetonitrile, water	No IS	4	HPLC	UV-DAD	Poroshell 120 EC-C18
41	MDMA	Methanol	PPA	5	GC	FID	Hp-5 30mx0.32mm 0.25um

3.2 Reported Basis of Participants' Measurement Uncertainty Estimates

Participants were requested to provide information about their basis of measurement uncertainty (MU). Responses as received are presented 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	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - RM	Recoveries of SS	Eurachem/CITAC Guide
2	Pooled Standard Deviation	Standard deviation from PT studies only		NARL
		Duplicate analysis	Homogeneity of sample Standard purity	
3	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Duplicate analysis	Instrument calibration Masses and volumes Matrix effects Recoveries of SS Standard purity	ISO/GUM
4	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Masses and volumes Recoveries of SS	Eurachem/CITAC Guide
5	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
6	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM Duplicate analysis	Masses and volumes Standard purity	Eurachem/CITAC Guide
7	Top Down - precision and estimates of the method and laboratory bias	Control samples - CRM Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Standard purity	Nata Technical Note 33
8	Top Down - precision and estimates of the method and laboratory bias	Control samples Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Standard purity	Nata Technical Note 33
9	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - CRM Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Matrix effects Recoveries of SS Standard purity	Eurachem/CITAC Guide
10	validation			
11	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis		Eurachem/CITAC Guide
12	pooled standard deviation	Duplicate analysis	Homogeneity of sample Recoveries of SS Standard purity	NARL
13	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - CRM Duplicate analysis	Instrument calibration Masses and volumes Matrix effects	ISO/GUM

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation**		Guide Document for Estimating MU
		Precision	Method Bias	
			Recoveries of SS Standard purity	
14	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM Duplicate analysis		Eurachem/CITAC Guide
15	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - CRM Duplicate analysis	Instrument calibration Masses and volumes Standard purity	Nata Technical Note 33
16				
17	Top Down - precision and estimates of the method and laboratory bias	Control samples - Seizures	Instrument calibration Homogeneity of sample Masses and volumes Matrix effects Laboratory bias from PT studies Recoveries of SS Standard purity	EA-4/16: 2003 and ILAG G-17:2002
18	repeatability, sample heterogeneity (ENFSI quantitative sampling guideline)	Control samples - RM Duplicate analysis	Homogeneity of sample	Eurachem/CITAC Guide
19	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Duplicate analysis	Masses and volumes Recoveries of SS Standard purity	Eurachem/CITAC Guide
20	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Instrument calibration Recoveries of SS Standard purity	Eurachem/CITAC Guide
21	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Masses and volumes Recoveries of SS Standard purity	ISO/GUM
22	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Homogeneity of sample Laboratory bias from PT studies	Nata Technical Note 33
23	Uncertainty Budget Method	Control samples - RM Duplicate analysis	Instrument calibration Masses and volumes Standard purity	Internal SOP document
24	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM	Instrument calibration Homogeneity of sample Masses and volumes Matrix effects Standard purity	ASCLD/LAB GUIDANCE ON THE ESTIMATION OF MU-AL-PD-3061 Ver 1.0,2013 , AL-PD-3063 Ver 1.0,2013
25	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples	Homogeneity of sample Masses and volumes Recoveries of SS Standard purity	Eurachem/CITAC Guide
26	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - RM	Instrument calibration Masses and volumes Laboratory bias from PT studies	ISO/GUM

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation**		Guide Document for Estimating MU
		Precision	Method Bias	
27	Top Down - precision and estimates of the method and laboratory bias	Control samples - previously analysed real seizure samples Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Matrix effects	Eurachem/CITAC Guide
28	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Standard purity	Eurachem/CITAC Guide
29	Top Down - precision and estimates of the method and laboratory bias	Control samples Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Standard purity	Nata Technical Note 33
30	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
31	Top Down - precision and estimates of the method and laboratory bias	Control samples	Homogeneity of sample Recoveries of SS Standard purity	Eurachem/CITAC Guide
32	Top Down - precision and estimates of the method and laboratory bias			
33	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Duplicate analysis	Masses and volumes Recoveries of SS Standard purity	Eurachem/CITAC Guide
34	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
35	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM	Standard purity	ISO/GUM
36	Estimating Measurement Uncertainty by black box by pairs of values	Standard deviation from PT studies only		ISO/GUM Guide ENAC G 09 or ISO 21748
37		Control samples - CRM Duplicate analysis	Instrument calibration Laboratory bias from PT studies Standard purity	
38	Professional judgement	Control samples - CRM Duplicate analysis	Standard purity	ISO/GUM
39	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM Duplicate analysis		internal document based on Eurachem/CITAC, ISO/GUM
40	accuracy profile - based on intermediate precision and repeatability	Control samples - CRM	Standard purity	ISO/GUM
41	Standard deviation of replicate analyses multiplied by 2 or 3	Duplicate analysis	Masses and volumes	ISO/GUM

* Some responses have been modified so that the participant cannot be identified.

** CRM = Certified Reference Material; RM = Reference Material; SS = Spiked Samples

3.3 Details of Participants' Calibration Standards

Participants were requested to provide information about their calibration standards. Responses as received are presented in Table 3.

Table 3 Participant Calibration Standard*

Lab. Code	MDMA		Methamphetamine	
	Reference Standard	Purity (%)	Reference Standard	Purity (%)
1	TRC	95	In-house	99.34
2	TRC Canada	96.54	In-house	99.34
3	NT		USP	100
4	TRC Canada	95	In-house	99.3
5	Lipomed	99.950 +/- 0.050	Lipomed	99.950 +/- 0.050
6	NMI	99.4	NMI	99.8
7	NMI	99.4	NMI	99.8
8	NMI	99.4	NMI	99.8
9	NMI	99.4 +/- 1.5	NMI	99.8 +/- 0.9
10	In-house	96.8	In-house	100.6
11	TRC Canada	95	In-house	99.34
12	TRC-Canada	95	In-house	99.34
13	NMI	99.4	NMI	99.8
14	NMI	97	In house	100
15	Sigma Aldrich	99.98	Sigma Aldrich	99.98
16	LGC	98.54	Sigma	99.9
17	Lipomed	99.788 +/- 0.002	Lipomed	99.467 +/- 0.015
18	Lipomed	99.72	Lipomed	99.5
19	TRC-Canada	95	In-house	99.34
20	TRC Canada	95	In-house	99.34
21	Toronto Research Chemical (TRC)	95	In-house	99.3
22	TRC Canada	95	In-house	99.34
23	NMI	99.4	NMI	99.8
24	TRC Canada	95	In-house	99.34
25	TRC Canada	95	In-house	99.34
26	NMI	99.4	NMI	99.8
27	NA		NA	
28	TRC Canada	95	In-house	99.3
29	NMI	99.4	NMI	99.8
30	Lipomed	99.950 +/- 0.050	Lipomed	99.950 +/- 0.050
31	TRC Canada	95	In-house	99.3
32	In-house	99	Sigma Aldrich	100

Lab. Code	MDMA		Methamphetamine	
	Reference Standard	Purity (%)	Reference Standard	Purity (%)
33	TRC Canada	95	In-house	99.34
34	In-house	100	Sigma	100
35	lipomed	99.95	lipomed	99.987
36	Lipomed HCl MDMA	83.7	Lipomed HCl Methamphetamine	79.5
37				
38	Sigma/Merck	99.5	Sigma/Merck	100
39	In-house	100	-	-
40	Lipomed	99.8	Lipomed	99.47
41	LGC	97.7	NT	

* Some responses have been modified so that the participant cannot be identified.

3.4 Participants' Comments

Participants were invited to comment on the samples, their methodology, the PT study in general and suggestions for future PT studies. Such feedback allows for the improvement of future studies. Participants' comments are presented in Table 4, along with the study coordinator's response where appropriate.

Table 4 Participants' Comments

Lab. Code	Participants' Comments	Study Co-ordinator's Response
3	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. Methamphetamine Methodology: Linear regression	A range of drug purities are selected to cater for the needs of different participant laboratories. In this study, the methamphetamine sample was cut; there have been uncut methamphetamine samples in previous NMI PT studies.
10	insufficient sample for repeat analysis of S2	Most participants use less than 50 mg for each analysis. For security and accountability reasons, NMI PT studies are conducted using the minimum practical amount of controlled substance.
13	Prefer separate proficiencies for distinct analytes eg an annual Amphetamine/Methylamphetamine and an annual MDA/MDMA rather than combined.	Currently, NMI runs amphetamine-type stimulants (ATS) as one PT study annually. We will take your suggestions into account for future controlled drug PT studies.
15	Methodology: Simultaneous observation of analyte and IS peaks in 1H NMR spectrum acquired using QNMR conditions	
16	Methodology: Average of 2 determinations	
22	Methodology: verify with 4 QC different preparation	
27	Methodology: No reference standard involved	
37	Quantitative analysis is based on the use of a historical value obtained from different batches of Certified reference material.	
38	No analysis carried out for inert bulking agents	

Lab. Code	Participants' Comments	Study Co-ordinator's Response
39	Measurement uncertainty methamphetamine: t-test 95% confidence level Measurement uncertainty MDMA: 95% confidence level	
40	Methodology: 5,20,60,100	

4 PRESENTATION OF RESULTS AND STATISTICAL ANALYSIS

4.1 Results Summary

Participant results are listed in Tables 5 to 8 with resultant summary statistics: robust average, median, mean, number of numeric results (N), maximum (Max.), minimum (Min.), 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.

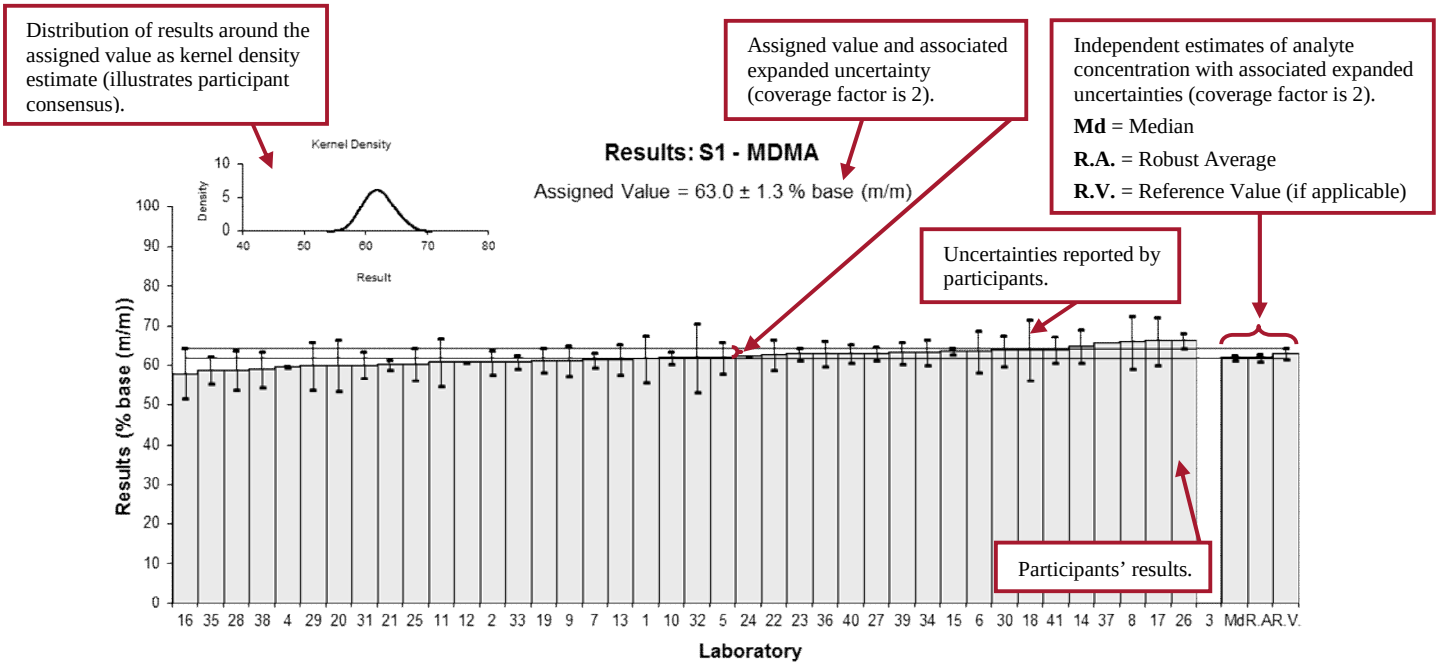


Figure 1 Guide to Presentation of Results

4.2 Assigned Value

The assigned value is defined as the: 'value attributed to a particular property of a proficiency test item'.[1] In this study, the property is the % base (m/m) of MDMA or methamphetamine in the test samples. Assigned values for Samples S1 and S4 were reference values determined by quantitative nuclear magnetic resonance spectroscopy (qNMR) (Appendix 1). Assigned values for Samples S2 and S3 were the robust averages of participants' results, and the expanded uncertainties were estimated from the associated robust SDs (Appendix 2).

4.3 Robust Average and Robust Standard Deviation

The robust averages and associated expanded MUs, and robust SDs (a measure of the variability of participants' results) were calculated using the procedure described in ISO 13528:2015.[5]

4.4 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 CV of participants' results. By setting a fixed value for the PCV, the participants' performance can be compared from study to study.

4.5 Target Standard Deviation

The target standard deviation (σ) is the product of the assigned value (X) and the PCV, as presented in Equation 1. This value is used for calculation of z-scores.

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

4.6 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 a participant's result

X is the assigned value

σ is the target standard deviation from Equation 1

For a z-score with absolute value (|z|):

- $|z| \leq 2.0$ is satisfactory;
- $2.0 < |z| < 3.0$ is questionable;
- $|z| \geq 3.0$ is unsatisfactory.

4.7 E_n-Score

The E_n-score is complementary to the z-score in assessment of laboratory performance. The 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 participant's 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

For an E_n-score with absolute value ($|E_n|$):

- $|E_n| \leq 1.0$ is satisfactory;
- $|E_n| > 1.0$ is unsatisfactory.

4.8 Traceability and Measurement Uncertainty

Laboratories accredited to ISO/IEC 17025 must establish and demonstrate the traceability and measurement uncertainty associated with their test results.[6]

Guidelines for quantifying uncertainty in analytical measurement are described in the Eurachem/CITAC Guide.[7]

5 TABLES AND FIGURES

Table 5

Sample Details

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

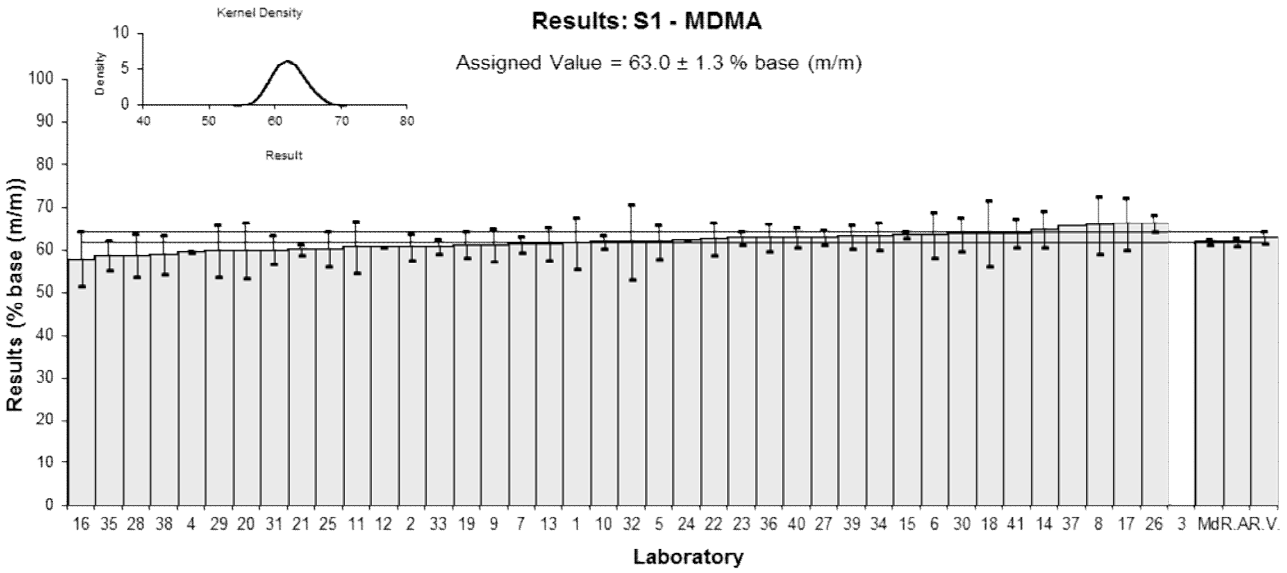
Participant Results

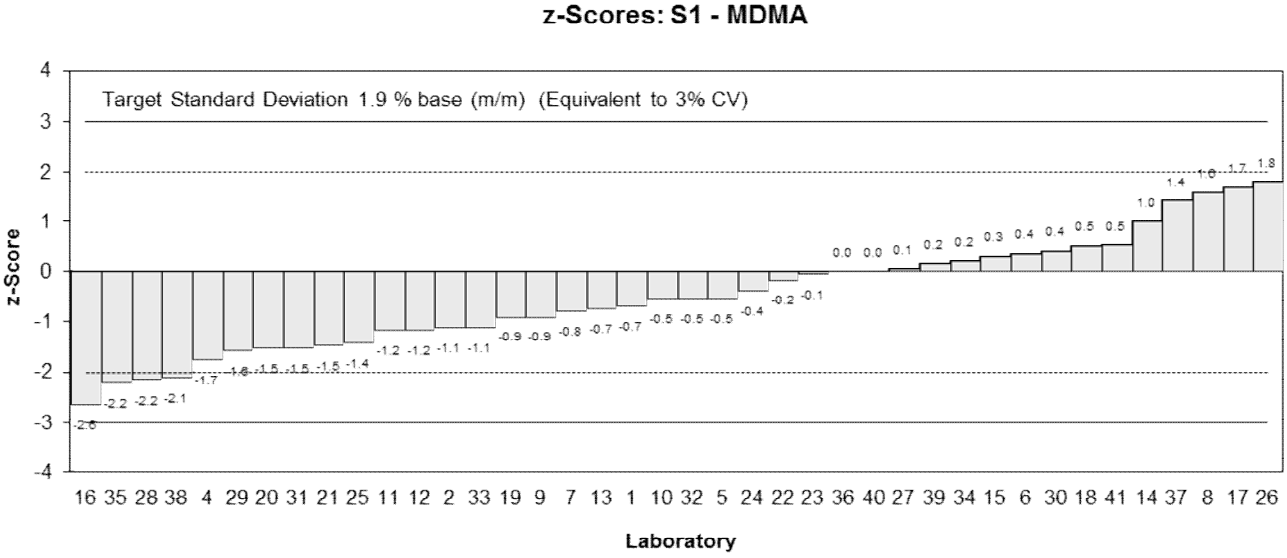
Lab. Code	Result	Uncertainty	z-Score	E_n-Score
1	61.7	5.9	-0.69	-0.22
2	60.9	3	-1.11	-0.64
3	NR	NR		
4	59.7	0.1	-1.75	-2.53
5	62	3.8	-0.53	-0.25
6	63.7	5.3	0.37	0.13
7	61.50	1.80	-0.79	-0.68
8	66	6.6	1.59	0.45
9	61.3	3.7	-0.90	-0.43
10	62	1.5	-0.53	-0.50
11	60.8	6.1	-1.16	-0.35
12	60.8	0.09	-1.16	-1.69
13	61.6	3.8	-0.74	-0.35
14	64.9	4.2	1.01	0.43
15	63.6	0.8	0.32	0.39
16	58	6.38	-2.65	-0.77
17	66.2	6.0	1.69	0.52
18	64	7.6	0.53	0.13
19	61.3	3	-0.90	-0.52
20	60.1	6.5	-1.53	-0.44
21	60.2	1.2	-1.48	-1.58
22	62.7	3.82	-0.16	-0.07
23	62.9	1.5	-0.05	-0.05
24	62.3	0.1114	-0.37	-0.54
25	60.3	4.1	-1.43	-0.63
26	66.4	2	1.80	1.43
27	63.1	1.6	0.05	0.05
28	58.9	4.9	-2.17	-0.81
29	60	6	-1.59	-0.49
30	63.8	3.9	0.42	0.19
31	60.1	3.3	-1.53	-0.82
32	62	8.7	-0.53	-0.11
33	60.9	1.7	-1.11	-0.98
34	63.4	3.2	0.21	0.12
35	58.8	3.5	-2.22	-1.12
36	63	3.1	0.00	0.00
37	65.7	NR	1.43	2.08
38	59	4.43	-2.12	-0.87
39	63.3	2.7	0.16	0.10
40	63	2.2	0.00	0.00
41	64.01	3.37	0.53	0.28

Statistics

Assigned Value*	63.0	1.3
Reference Value	63.0	1.3
Robust Average	62.0	0.9
Median	62.0	0.7
Mean	62.1	
N	40	
Max.	66.4	
Min.	58	
Robust SD	2.2	
Robust CV	3.5%	

* Assigned value is the reference value, determined by qNMR.


Kernel Density
Density
Result
Results: S1 - MDMA
Assigned Value = 63.0 ± 1.3 % base (m/m)
Results (% base (m/m))
16 35 28 38 4 29 20 31 21 25 11 12 2 33 19 9 7 13 1 10 32 5 24 22 23 36 40 27 39 34 15 6 30 18 41 14 37 8 17 26 3 MdR AR V
Laboratory


z-Scores: S1 - MDMA
Target Standard Deviation 1.9 % base (m/m) (Equivalent to 3% CV)
z-Score
16 35 28 38 4 29 20 31 21 25 11 12 2 33 19 9 7 13 1 10 32 5 24 22 23 36 40 27 39 34 15 6 30 18 41 14 37 8 17 26
Laboratory

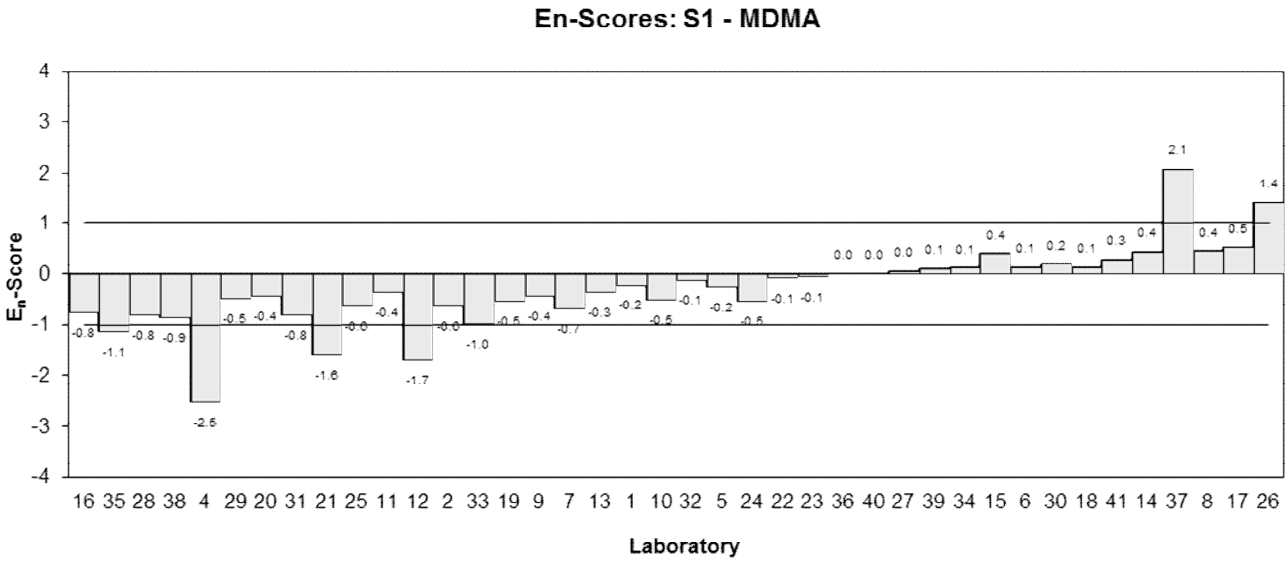

En-Scores: S1 - MDMA
En-Score
16 35 28 38 4 29 20 31 21 25 11 12 2 33 19 9 7 13 1 10 32 5 24 22 23 36 40 27 39 34 15 6 30 18 41 14 37 8 17 26
Laboratory

Figure 2

Table 6

Sample Details

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

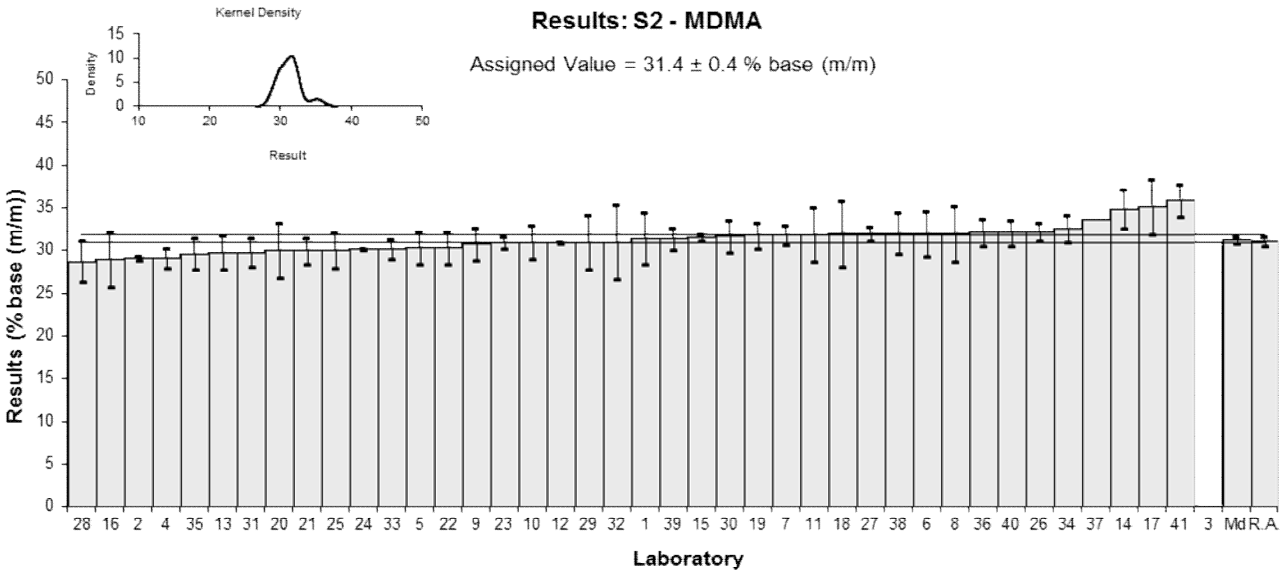
Participant Results

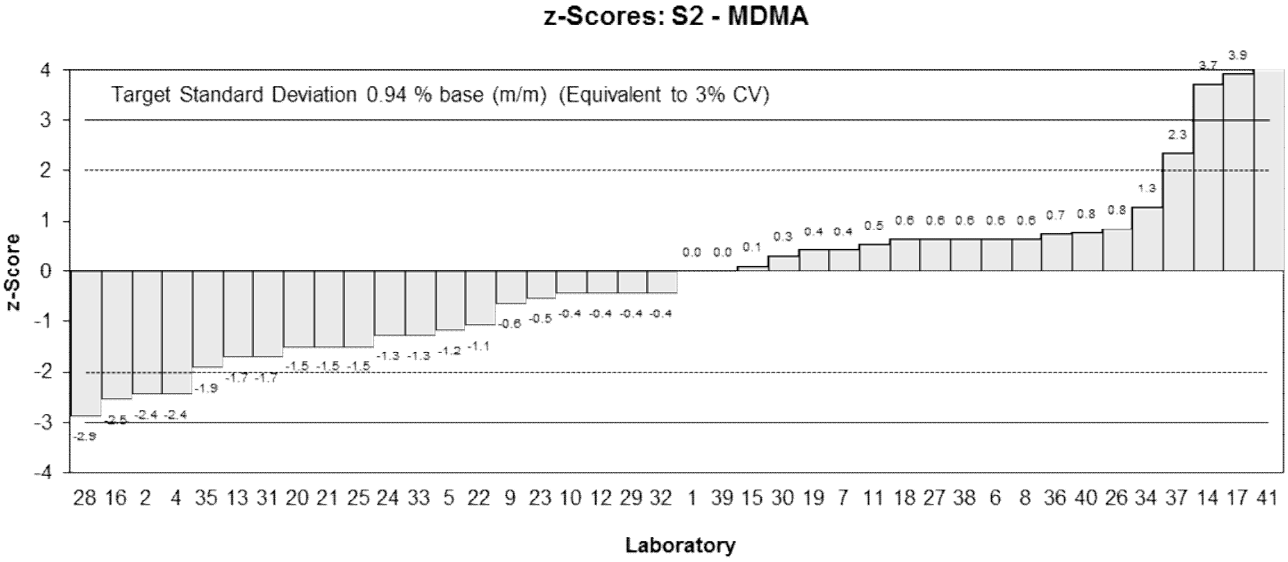
Lab. Code	Result	Uncertainty	z-Score	E_n-Score
1	31.4	3	0.00	0.00
2	29.1	0.21	-2.44	-5.09
3	NR	NR		
4	29.1	1.1	-2.44	-1.97
5	30.3	1.9	-1.17	-0.57
6	32	2.6	0.64	0.23
7	31.80	1.10	0.42	0.34
8	32	3.2	0.64	0.19
9	30.8	1.9	-0.64	-0.31
10	31	2	-0.42	-0.20
11	31.9	3.2	0.53	0.16
12	31	0.09	-0.42	-0.98
13	29.8	1.9	-1.70	-0.82
14	34.9	2.3	3.72	1.50
15	31.5	0.4	0.11	0.18
16	29	3.19	-2.55	-0.75
17	35.1	3.2	3.93	1.15
18	32	3.8	0.64	0.16
19	31.8	1.5	0.42	0.26
20	30	3.2	-1.49	-0.43
21	30	1.5	-1.49	-0.90
22	30.4	1.86	-1.06	-0.53
23	30.9	0.7	-0.53	-0.62
24	30.2	0.1114	-1.27	-2.89
25	30	2	-1.49	-0.69
26	32.2	1	0.85	0.74
27	32	0.8	0.64	0.67
28	28.7	2.4	-2.87	-1.11
29	31	3.1	-0.42	-0.13
30	31.7	1.9	0.32	0.15
31	29.8	1.6	-1.70	-0.97
32	31	4.3	-0.42	-0.09
33	30.2	1.1	-1.27	-1.03
34	32.6	1.6	1.27	0.73
35	29.6	1.8	-1.91	-0.98
36	32.1	1.6	0.74	0.42
37	33.6	NR	2.34	5.50
38	32	2.4	0.64	0.25
39	31.4	1.3	0.00	0.00
40	32.13	1.51	0.77	0.47
41	35.89	1.89	4.77	2.32

Statistics

Assigned Value*	31.4	0.4
Robust Average	31.1	0.5
Median	31.2	0.4
Mean	31.3	
N	40	
Max.	35.89	
Min.	28.7	
Robust SD	1.4	
Robust CV	4.4%	

* Assigned value is the robust average of the combined results of duplicate Samples S2 and S3.


Kernel Density
Density
Result
Results: S2 - MDMA
Assigned Value = 31.4 ± 0.4 % base (m/m)
Results (% base (m/m))
28 16 2 4 35 13 31 20 21 25 24 33 5 22 9 23 10 12 29 32 1 39 15 30 19 7 11 18 27 38 6 8 36 40 26 34 37 14 17 41 3 Md R.A.
Laboratory


z-Scores: S2 - MDMA
Target Standard Deviation 0.94 % base (m/m) (Equivalent to 3% CV)
z-Score
28 16 2 4 35 13 31 20 21 25 24 33 5 22 9 23 10 12 29 32 1 39 15 30 19 7 11 18 27 38 6 8 36 40 26 34 37 14 17 41
Laboratory

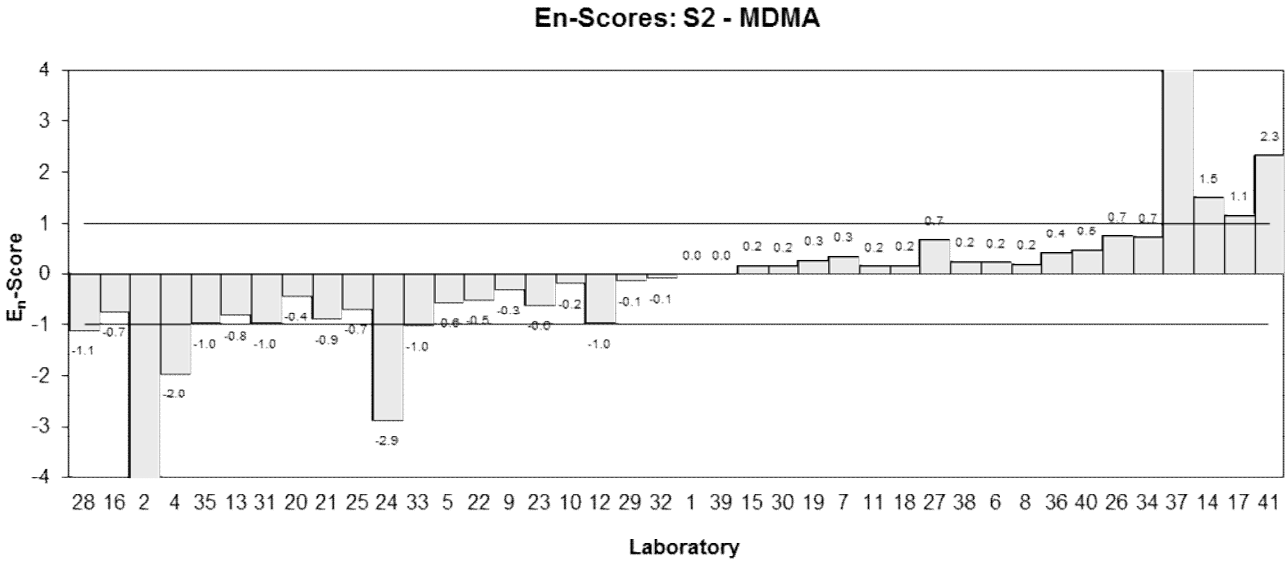

En-Scores: S2 - MDMA
En-Score
28 16 2 4 35 13 31 20 21 25 24 33 5 22 9 23 10 12 29 32 1 39 15 30 19 7 11 18 27 38 6 8 36 40 26 34 37 14 17 41
Laboratory

Figure 3

Table 7

Sample Details

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

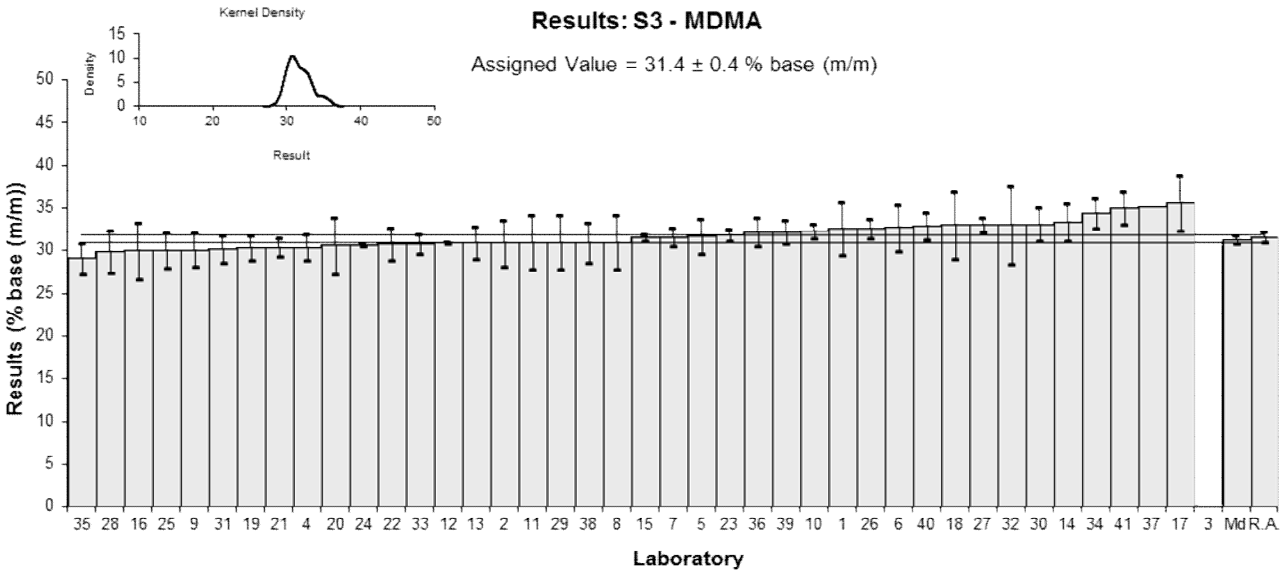
Participant Results

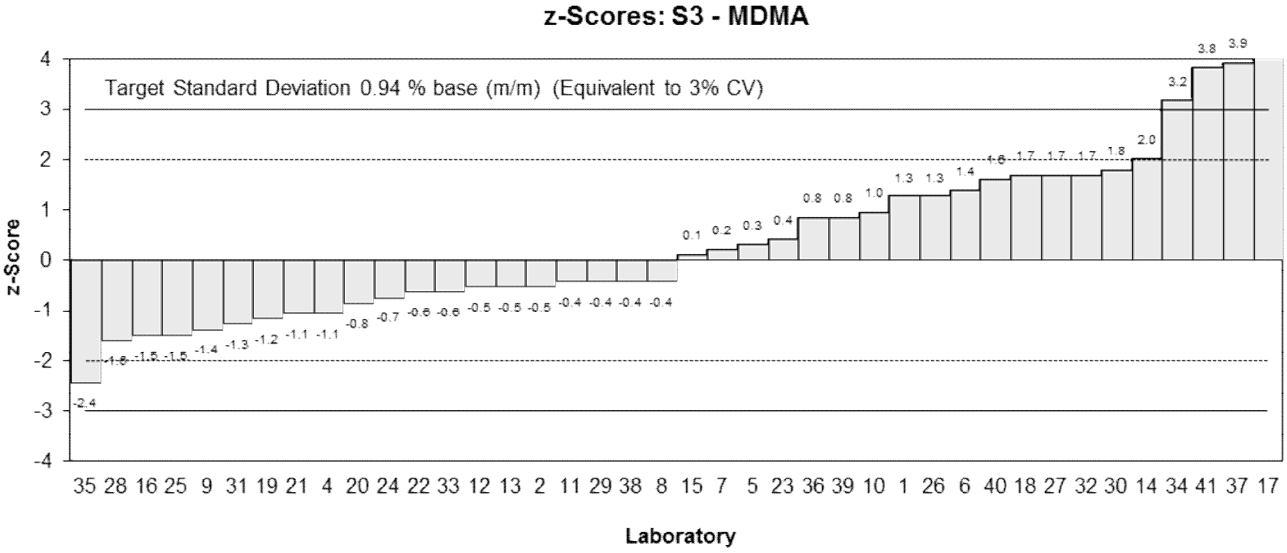
Lab. Code	Result	Uncertainty	z-Score	E_n-Score
1	32.6	3.1	1.27	0.38
2	30.9	2.7	-0.53	-0.18
3	NR	NR		
4	30.4	1.5	-1.06	-0.64
5	31.7	2	0.32	0.15
6	32.7	2.7	1.38	0.48
7	31.60	1.10	0.21	0.17
8	31	3.1	-0.42	-0.13
9	30.1	1.9	-1.38	-0.67
10	32.3	0.8	0.96	1.01
11	31	3.1	-0.42	-0.13
12	30.9	0.09	-0.53	-1.22
13	30.9	1.9	-0.53	-0.26
14	33.3	2.2	2.02	0.85
15	31.5	0.4	0.11	0.18
16	30	3.3	-1.49	-0.42
17	35.6	3.2	4.46	1.30
18	33	3.9	1.70	0.41
19	30.3	1.4	-1.17	-0.76
20	30.6	3.3	-0.85	-0.24
21	30.4	1.1	-1.06	-0.85
22	30.8	1.88	-0.64	-0.31
23	31.8	0.7	0.42	0.50
24	30.7	0.1114	-0.74	-1.69
25	30	2	-1.49	-0.69
26	32.6	1.1	1.27	1.03
27	33	0.8	1.70	1.79
28	29.9	2.5	-1.59	-0.59
29	31	3.1	-0.42	-0.13
30	33.1	2	1.80	0.83
31	30.2	1.6	-1.27	-0.73
32	33	4.6	1.70	0.35
33	30.8	1.1	-0.64	-0.51
34	34.4	1.7	3.18	1.72
35	29.1	1.8	-2.44	-1.25
36	32.2	1.6	0.85	0.49
37	35.1	NR	3.93	9.25
38	31	2.33	-0.42	-0.17
39	32.2	1.4	0.85	0.55
40	32.93	1.55	1.62	0.96
41	35.01	1.84	3.83	1.92

Statistics

Assigned Value*	31.4	0.4
Robust Average	31.6	0.6
Median	31.3	0.5
Mean	31.7	
N	40	
Max.	35.6	
Min.	29.1	
Robust SD	1.5	
Robust CV	4.6%	

* Assigned value is the robust average of the combined results of duplicate Samples S2 and S3.


Kernel Density
Density
Result
Results: S3 - MDMA
Assigned Value = 31.4 ± 0.4 % base (m/m)
Results (% base (m/m))
Laboratory
35 28 16 25 9 31 19 21 4 20 24 22 33 12 13 2 11 29 38 8 15 7 5 23 36 39 10 1 26 6 40 18 27 32 30 14 34 41 37 17 3 Md R.A.


z-Scores: S3 - MDMA
Target Standard Deviation 0.94 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
35 28 16 25 9 31 19 21 4 20 24 22 33 12 13 2 11 29 38 8 15 7 5 23 36 39 10 1 26 6 40 18 27 32 30 14 34 41 37 17

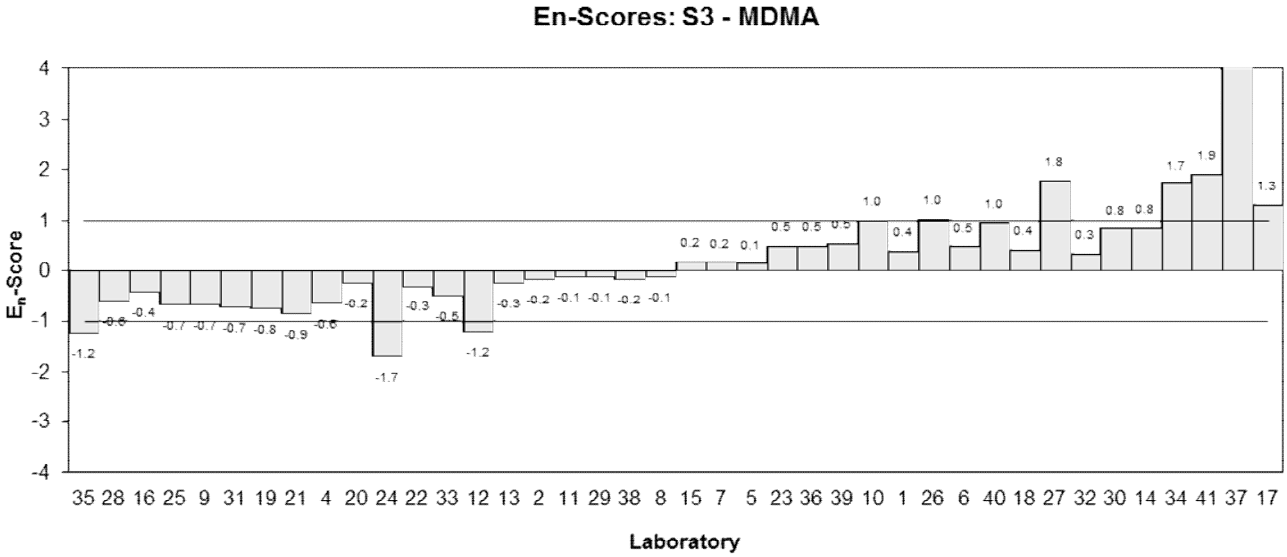

En-Scores: S3 - MDMA
En-Score
Laboratory
35 28 16 25 9 31 19 21 4 20 24 22 33 12 13 2 11 29 38 8 15 7 5 23 36 39 10 1 26 6 40 18 27 32 30 14 34 41 37 17

Figure 4

Table 8

Sample Details

Sample No.	S4
Matrix	Powder
Analyte	Methamphetamine
Units	% base (m/m)

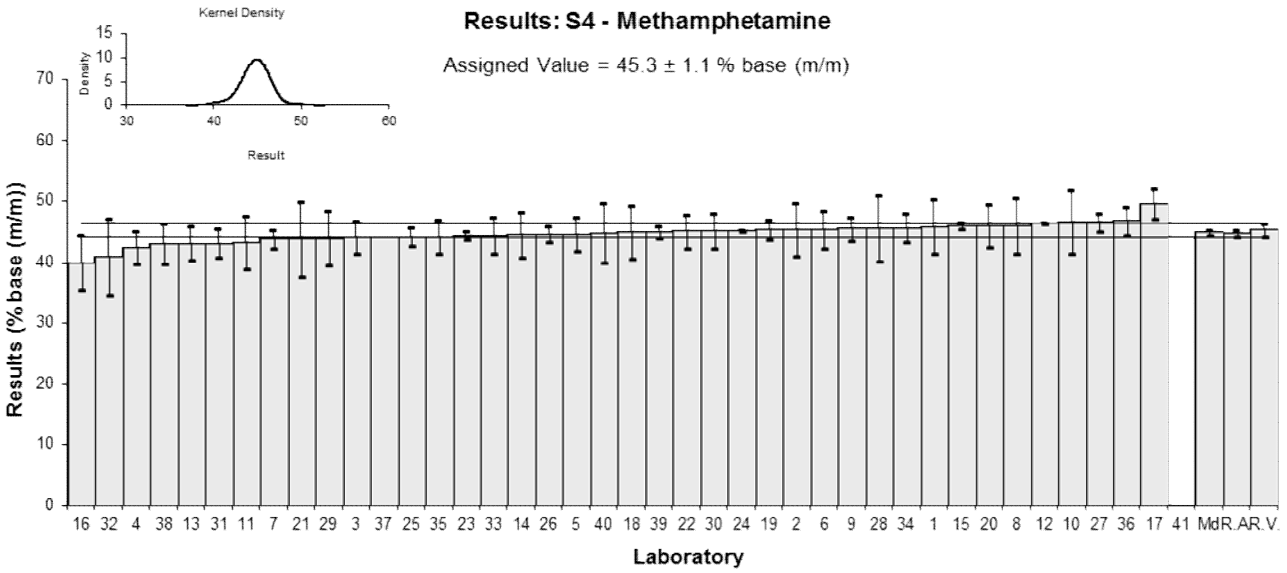
Participant Results

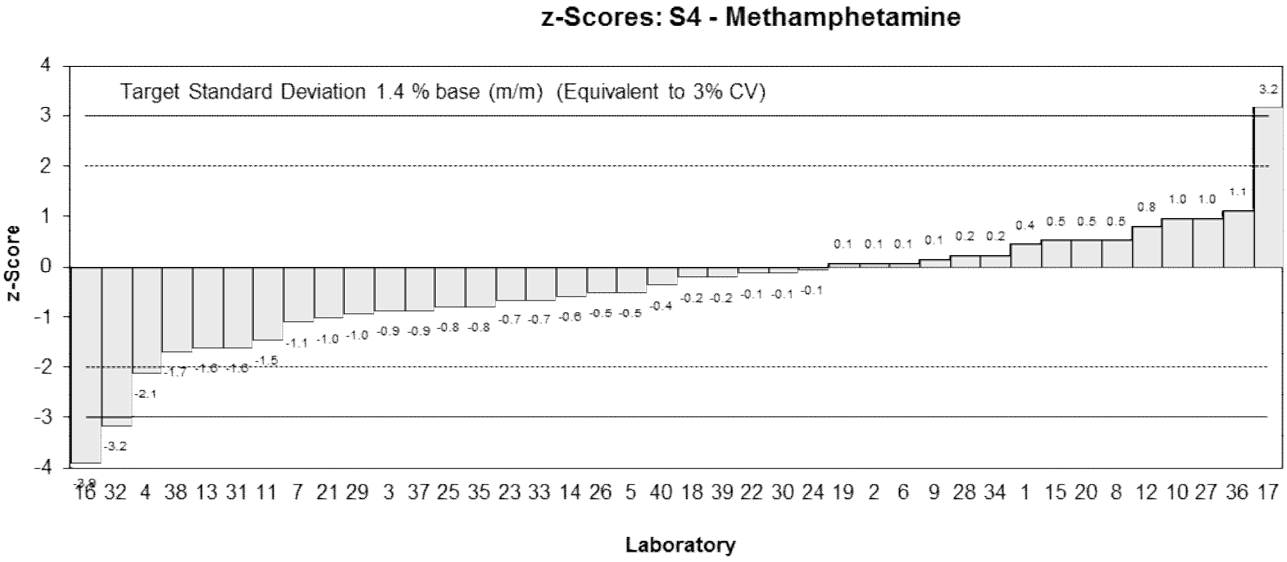
Lab. Code	Result	Uncertainty	z-Score	E_n-Score
1	45.9	4.5	0.44	0.13
2	45.4	4.3	0.07	0.02
3	44.1	2.6	-0.88	-0.43
4	42.4	2.6	-2.13	-1.03
5	44.6	2.7	-0.52	-0.24
6	45.4	3.1	0.07	0.03
7	43.80	1.40	-1.10	-0.84
8	46	4.6	0.52	0.15
9	45.5	1.9	0.15	0.09
10	46.6	5.2	0.96	0.24
11	43.3	4.3	-1.47	-0.45
12	46.4	0.09	0.81	1.00
13	43.1	2.7	-1.62	-0.75
14	44.5	3.7	-0.59	-0.21
15	46.0	0.5	0.52	0.58
16	40	4.4	-3.90	-1.17
17	49.6	2.5	3.16	1.57
18	45	4.3	-0.22	-0.07
19	45.4	1.5	0.07	0.05
20	46	3.4	0.52	0.20
21	43.9	6.1	-1.03	-0.23
22	45.1	2.76	-0.15	-0.07
23	44.4	0.7	-0.66	-0.69
24	45.2	0.092	-0.07	-0.09
25	44.2	1.5	-0.81	-0.59
26	44.6	1.3	-0.52	-0.41
27	46.6	1.5	0.96	0.70
28	45.6	5.4	0.22	0.05
29	44	4.4	-0.96	-0.29
30	45.1	2.8	-0.15	-0.07
31	43.1	2.3	-1.62	-0.86
32	41	6.2	-3.16	-0.68
33	44.4	2.9	-0.66	-0.29
34	45.6	2.3	0.22	0.12
35	44.2	2.8	-0.81	-0.37
36	46.8	2.3	1.10	0.59
37	44.1	NR	-0.88	-1.09
38	43	3.23	-1.69	-0.67
39	45	1	-0.22	-0.20
40	44.79	4.84	-0.38	-0.10
41	NR	NR		

Statistics

Assigned Value*	45.3	1.1
Reference Value	45.3	1.1
Robust Average	44.8	0.5
Median	44.9	0.4
Mean	44.7	
N	40	
Max.	49.6	
Min.	40	
Robust SD	1.3	
Robust CV	3.0%	

* Assigned value is the reference value, determined by qNMR.


Kernel Density
Density
Result
Results: S4 - Methamphetamine
Assigned Value = 45.3 ± 1.1 % base (m/m)
Results (% base (m/m))
Laboratory
16 32 4 38 13 31 11 7 21 29 3 37 25 35 23 33 14 26 5 40 18 39 22 30 24 19 2 6 9 28 34 1 15 20 8 12 10 27 36 17 41 MdR AR V


z-Scores: S4 - Methamphetamine
Target Standard Deviation 1.4 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
16 32 4 38 13 31 11 7 21 29 3 37 25 35 23 33 14 26 5 40 18 39 22 30 24 19 2 6 9 28 34 1 15 20 8 12 10 27 36 17

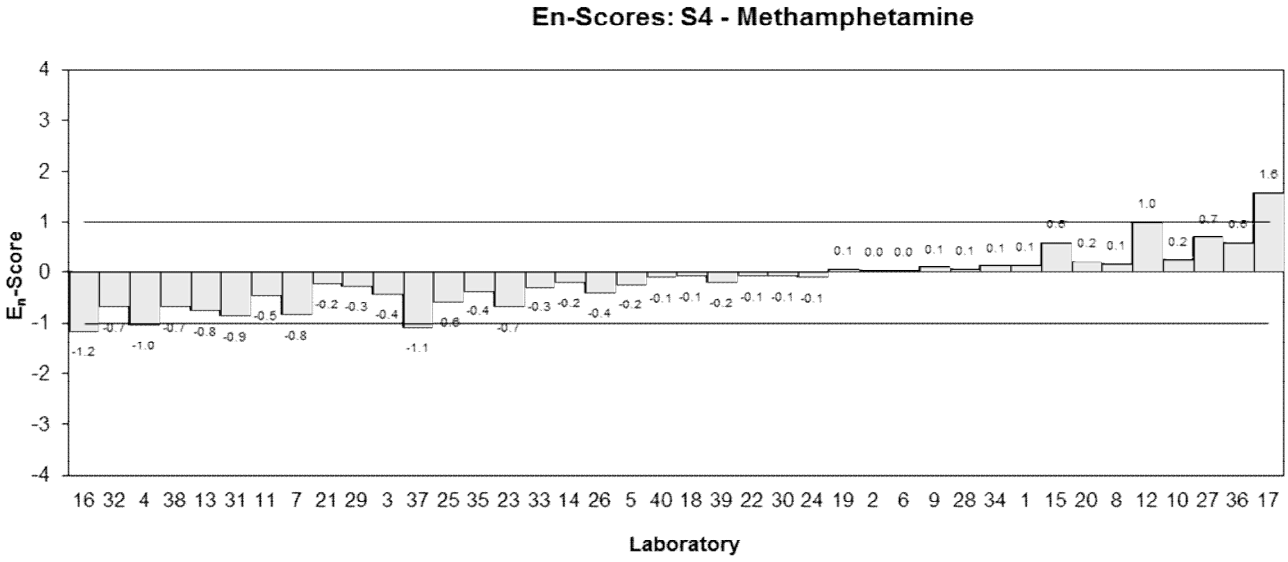

En-Scores: S4 - Methamphetamine
En-Score
Laboratory
16 32 4 38 13 31 11 7 21 29 3 37 25 35 23 33 14 26 5 40 18 39 22 30 24 19 2 6 9 28 34 1 15 20 8 12 10 27 36 17

Figure 5

Table 9 Participants' Identification of Cutting Agents

Lab. Code	Cutting Agents			
	S1	S2	S3	S4
Preparation	Cellulose	Caffeine, Glucodin	Caffeine, Glucodin	Procaine hydrochloride
1	-	Caffeine	Caffeine	Procaine
2	NONE DETECTED	CAFFEINE	CAFFEINE	PROCAINE
3	NT			Procaine
4	none	caffeine	caffeine	none
5	-	Caffeine	Caffeine	Procaine
6		Caffeine	Caffeine	Procaine
7		Caffeine	Caffeine	Procaine
8	Cellulose	Caffeine , Glucose	Caffeine. Glucose	Procaine
9	Cellulose indicated	Caffeine; Glucose	Caffeine; Glucose	Procaine
10	not determined	caffeine	caffeine	procaine
11	-	Caffeine	Caffeine	Procaine
12	Nil	Caffeine	Caffeine	Procaine
13		Caffeine	Caffeine	Procaine
14				
15	Insoluble material not identified	Caffeine 39.1% , glucose 19.1%	Caffeine 40.5%, glucose 17.6%	Procaine 36.6% (as base)
16	None	Caffeine	Caffeine	Procaine
17		Caffeine	Caffeine	Procaine
18		caffeine	caffeine	procaine
19	Not Detected	Caffeine	Caffeine	Procaine
20	None	Caffeine	Caffeine	none
21	Not Detected	Caffeine	Caffeine	Procaine
22	(-)	caffeine	caffeine	procaine
23		caffeine	caffeine	procaine
24	-	Caffeine	Caffeine	Procaine
25	Not Detected	Caffeine	Caffeine	Procaine
26	cellulose	caffeine	caffeine	procaine
27		caffeine	caffeine	procaine
28		Caffeine	Caffeine	Procaine
29	Cellulose	Caffeine	Caffeine	Procaine
30	-	Caffeine	Caffeine	Procaine
31	not detected	caffeine	caffeine	procaine
32	none	Caffeine	Caffeine	Procaine
33	Not Detected	Caffeine	Caffeine	Procaine
34		Caffeine	Caffeine	Procaine
35		caffeine 31.4%	caffeine 33.2%	procaine
36		Caffeine	Caffeine	Procaine
37		caffeine	caffeine	procaine
38	none detected	caffeine	caffeine	Procaine
39	(micro)cellulose	caffeine	caffeine	procaine
40				
41	N/A	Caffeine	Caffeine	Procaine

6 DISCUSSION OF RESULTS

6.1 Assigned Value

Reference values obtained using the qNMR measurement method described in Appendix 1 were used as the assigned values for Samples S1 and S4. Maleic acid (NMI CRM QNMR010) was used as the 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[8] 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, an estimate of potential interference bias made by comparing the results from different NMR signals, and the between-batch variation.

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 CRM (QNMR010, Batch No.: 10-Q-02).

Assigned values for duplicate Samples S2 and S3 were the robust average of the combined results reported by participants for these samples. The robust average and associated expanded uncertainties were calculated using the procedure described in ISO 13528:2015.[5] Results that were less than 50% and greater than 150% of the robust average were removed before the calculation of the assigned value.[3,4] The calculation procedure for the expanded uncertainty for robust averages is presented in Appendix 2, with Sample S3 as an example.

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 ISO/IEC 17025 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.[6] From 1 July 2012 this is also a requirement of ASCLD/LAB accreditation program.

Of 160 reported results, 156 (98%) were reported with an associated expanded uncertainty. Laboratory **37** did not report any uncertainties; this laboratory was not accredited.

Laboratories **12** and **24** reported identical uncertainties for samples which were of significantly different concentrations. Laboratories **2** and **10** reported similar results for duplicate Samples S2 and S3, but significantly different uncertainties.

The magnitudes of reported uncertainties were within the range 0.1% to 15% relative. Of 156 expanded measurement uncertainties, 108 (69%) were between 3% and 10% relative to the reported 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 64.01 ± 3.37%, the recommended reporting format is 64.0 ± 3.4%).[7]

6.3 z-Score

A target SD equivalent to 3% PCV was used to calculate z-scores. The CVs predicted by the Thompson-Horwitz equation,[9] target SDs, and between-laboratory CVs obtained in this study are presented in Table 10.

Table 10 Comparison of Target SDs, Thompson-Horwitz CVs and Between Laboratories CVs

Sample	Analyte	Assigned Value (% base (m/m))	Thompson-Horwitz CV (%)	Target SD (as PCV) (%)	Between-Laboratories CV (%)
S1	MDMA	63.0	1.3	3	3.5
S2	MDMA	31.4	1.8	3	4.4
S3					4.6
S4	Methamphetamine	45.3	1.5	3	3.0

Of 160 results for which z-scores were calculated, 138 (86%) returned a satisfactory z-score of $|z| \leq 2.0$.

Twenty-nine participants: **1**, **3** (only 1 result submitted), **5**, **6**, **7**, **8**, **9**, **10**, **11**, **12**, **13**, **15**, **18**, **19**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27**, **29**, **30**, **31**, **33**, **36**, **39** and **40** returned satisfactory z-scores for all samples. Twelve participants returned at least one questionable or unsatisfactory z-score. The dispersal of participants' z-scores is presented graphically in Figure 6.

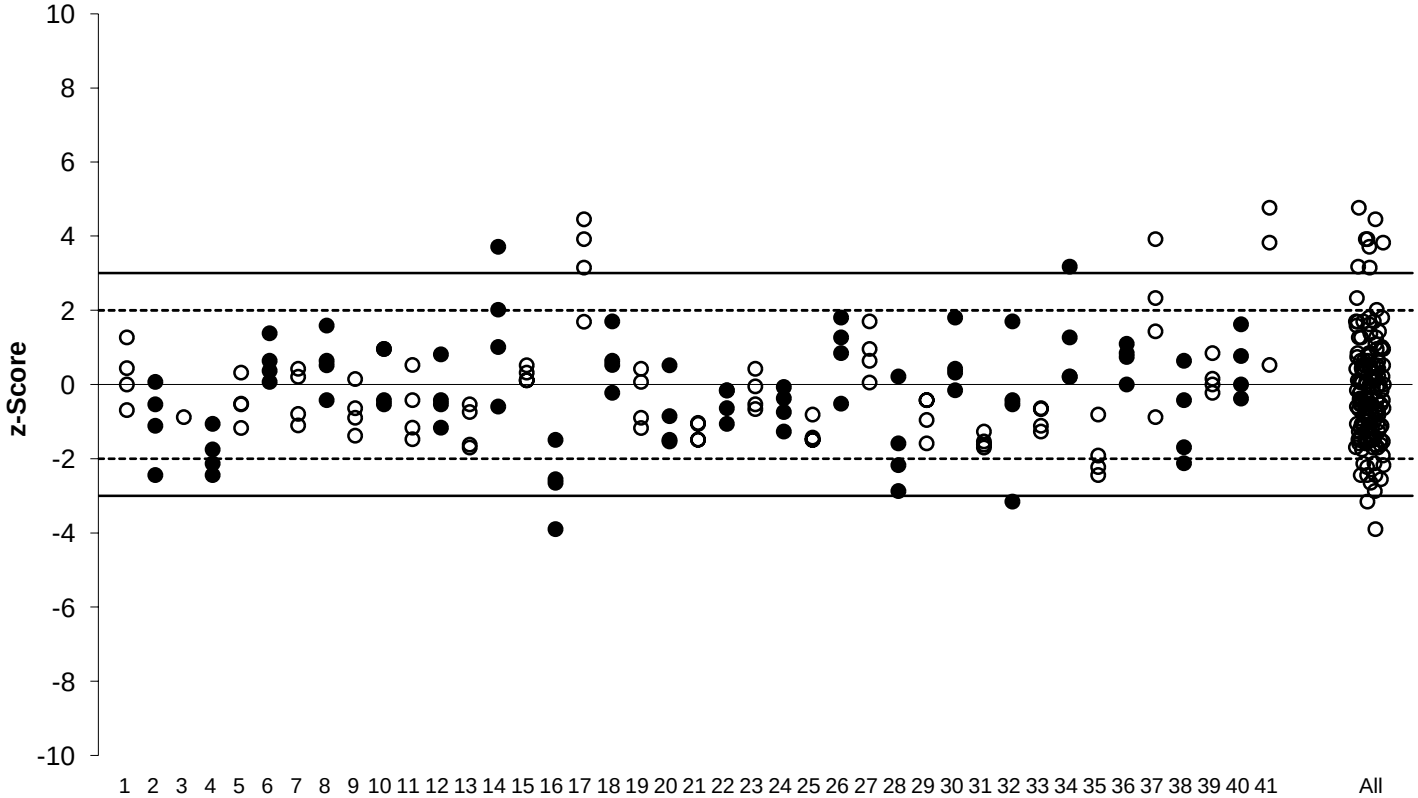
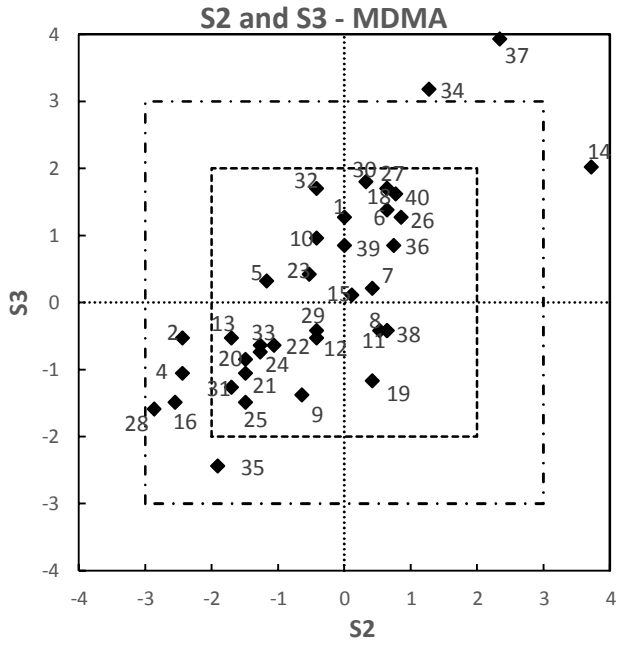


Figure 6 z-Score Dispersal by Laboratory

A scatter plot of z-scores for blind duplicate MDMA Samples S2 and S3 is presented in Figure 7. Scores are predominantly in the upper right or lower left quadrants, indicating that laboratory bias is the major contributor to the variability of results. Points close to the diagonal axis demonstrate excellent repeatability while points close to zero demonstrate excellent repeatability and accuracy.



Laboratories 17 and 41 are off scale.

Figure 7 z-Score Scatter Plot – MDMA in Samples S2 and S3

6.4 E_n-Score

If a participant did not report an expanded uncertainty with a result, an expanded uncertainty of zero (0) was used to calculate the E_n-score.

Of 160 results for which E_n-scores were calculated, 131 (82%) returned a satisfactory E_n-score of $|E_n| \leq 1.0$.

Twenty-four participants: **1**, **3** (only 1 result submitted), **5**, **6**, **7**, **8**, **9**, **11**, **13**, **15**, **18**, **19**, **20**, **22**, **23**, **25**, **29**, **30**, **31**, **32**, **36**, **38**, **39** and **40** returned satisfactory E_n-scores for all samples. Seventeen participants returned at least one unsatisfactory E_n-score. Laboratory **37** returned unsatisfactory E_n-scores for all samples. The dispersal of participants' E_n-scores is presented graphically in Figure 8.

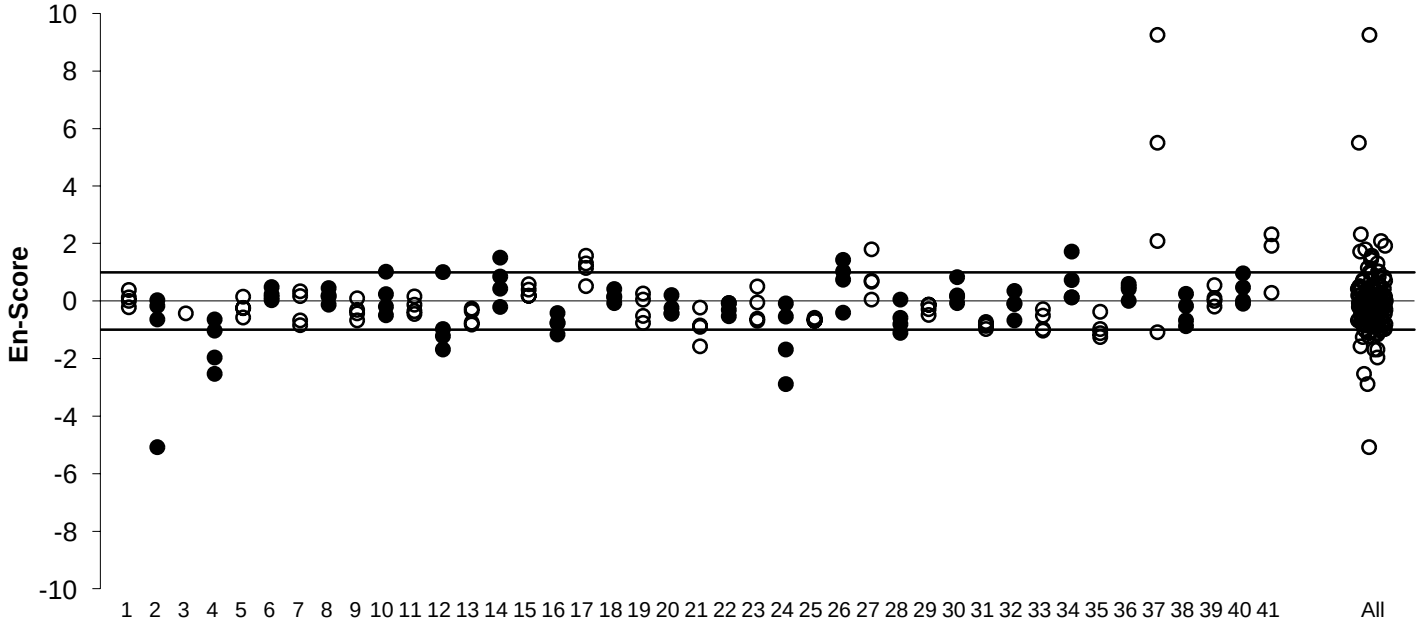


Figure 8 E_n-Score Dispersal by Laboratory

6.5 Identification of Cutting Agents

Sample S1 was prepared by adding cellulose to MDMA hydrochloride. Duplicate Samples S2 and S3 were prepared by adding caffeine and glucodin to MDMA hydrochloride. Sample S4 was prepared by adding procaine hydrochloride to methamphetamine hydrochloride.

Thirty-nine participants (95%) reported on the identity of at least one cutting agent in the samples. Results reported by participants are presented in Table 9.

Laboratories **8** and **9** correctly identified all cutting agents added to the samples in this study.

For Sample S1, five participants reported on the identity of the cutting agent, with all reported results correctly identifying cellulose. Most participants in this study were unable to or did not identify this insoluble cutting agent. The identification rate has improved when compared to the last NMI controlled drug PT study with cellulose as a cutting agent (AQA 11-19 MDMA),[10] where only one participant (out of thirty-nine participants) correctly identified cellulose.

For Sample S2 and S3, three participants correctly reported that both caffeine and glucodin had been added to the sample. An additional thirty-five participants only reported caffeine as the cutting agent.

For Sample S4, thirty-seven participants correctly identified procaine as the cutting agent.

6.6 Duplicate Samples S2 and S3

Samples S2 and S3 were blind duplicate MDMA samples. The results for these are presented in Figure 9. The majority of participants' results for these samples were in agreement with each other within their reported expanded uncertainties.

Results for Samples S2 and S3 for Laboratories **24** and **37** were not in agreement within respective expanded uncertainties. Laboratory **24** reported very small uncertainties relative to the result (approximately 0.4% relative for both results), while laboratory **37** did not report any uncertainties with their results.

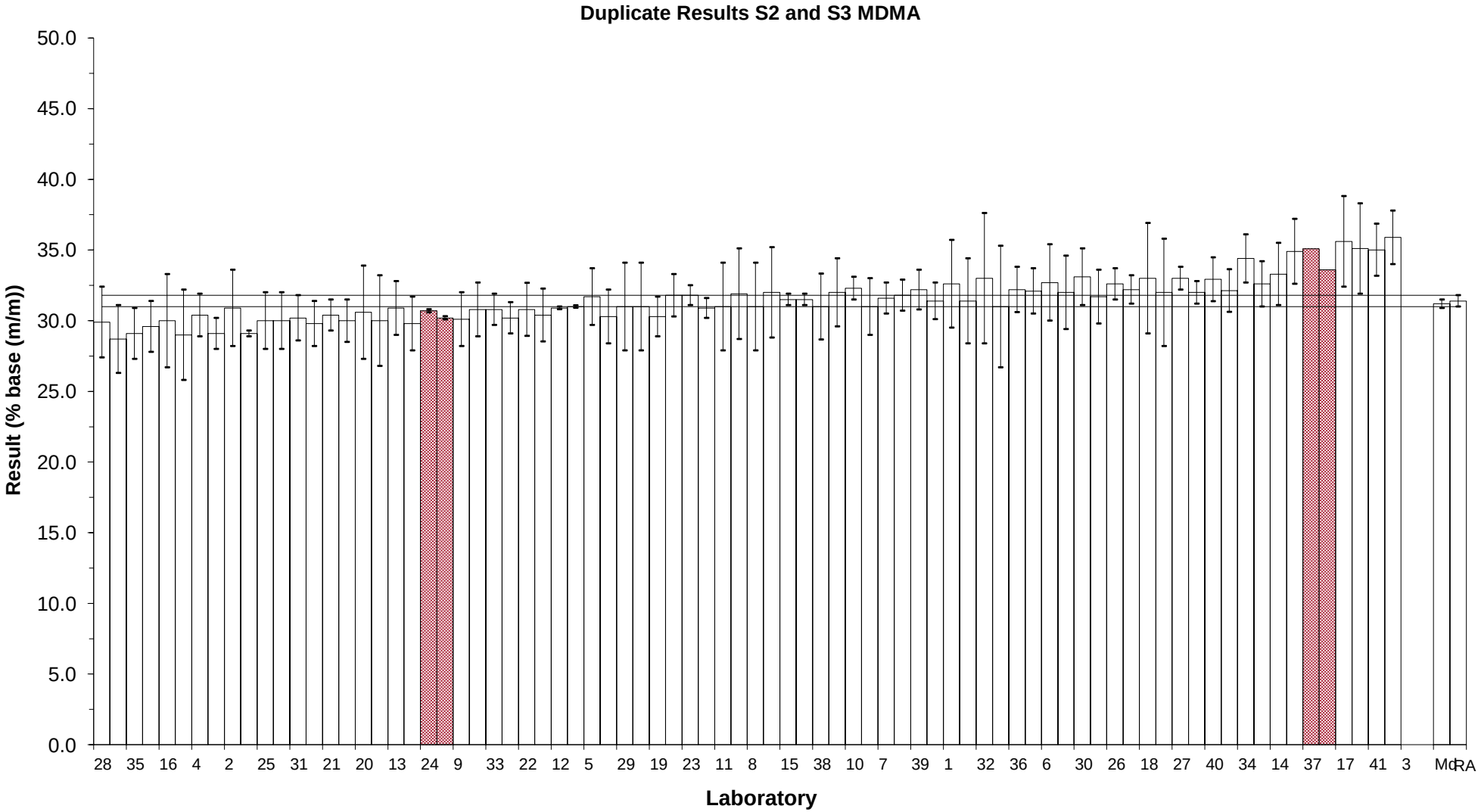


Figure 9 Results for Blind Duplicate Samples S2 and S3 MDMA. Horizontal lines are the upper and lower 95% confidence interval of the assigned value. Participants' results which are not in agreement with each other within reported uncertainties are shaded.

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 sources is presented in Table 11.

Table 11 Summary of Participants' Analytical Methods

		Lab. Code
Accreditation	Yes to ISO/IEC 17025	3 (methamphetamine), 6, 7, 8, 9, 10, 11, 13, 14, 17, 18, 23, 27, 29, 32, 33, 34 (methamphetamine only), 35 (MDMA only), 36, 38, 39, 41 (MDMA)
	Yes to ANAB and ASCLD/LAB	1, 2, 4, 5, 11, 12, 19, 20, 21, 22, 23, 24, 25, 28, 30, 31
	Not accredited / Not reported	15, 16, 26, 34 (unaccredited for MDMA), 35 (unaccredited for methamphetamine), 37, 40
Average Sample Mass Used (mg)	5 – 10	27, 36
	11 – 30	1, 2, 3 (methamphetamine), 4, 5, 6, 7, 8, 9, 11, 12, 14, 15, 16, 19, 20, 21, 22, 24, 25, 28, 29, 30, 31, 33, 34, 35, 38, 40, 41 (MDMA)
	31 – 50	13, 17, 18, 23, 26, 32, 37, 39
	51 – 100	
	101 – 150	10
Conversion to Base?	Yes	1, 2, 4, 6, 9, 10, 11, 12, 13, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 31, 33, 34, 35, 36, 37, 39 (MDMA only), 40, 41 (MDMA)
	No	3 (methamphetamine), 5, 8, 14, 15, 16, 29, 30, 38, 39 (methamphetamine only)
Instrument Used for Quantification	HPLC-DAD	3 (methamphetamine), 10 (MDMA only), 16, 17, 18, 23, 26, 34, 37, 38, 40
	HPLC-UV	14
	UPLC-DAD	6, 7, 8, 10, 13, 29
	UPLC-MS/MS	32
	LC-DAD	5, 30
	GC-FID	1, 2, 4, 9, 11, 12, 19, 20, 21, 22, 24, 25, 28, 31, 33, 35, 36, 39 (MDMA only), 41 (MDMA)
	GC-MS	9
	qNMR	15, 27, 39 (methamphetamine only)
Solvent	Chloroform	1, 2, 4, 11, 12, 19, 20, 21, 22, 24, 25, 28, 31, 33
	Water	5, 8, 10, 18 (methamphetamine only), 29, 30, 34, 38
	Methanol	7, 13, 14, 16, 17, 26, 36, 37, 41 (MDMA)
	Other / Not reported	3 (methamphetamine), 6, 9, 15, 18 (MDMA only), 23, 27, 32, 35, 39, 40

		Lab. Code
Sources of Calibration Standard (MDMA)	NMI Australia	6, 7, 8, 9, 13, 14, 23, 26, 29
	Toronto Research Chemicals (TRC)	1, 2, 4, 11, 12, 19, 20, 21, 22, 24, 25, 28, 31, 33
	Lipomed	5, 17, 18, 30, 35, 36, 40
	Merck / Sigma Aldrich	15, 38
	LGC	16, 41
	Other	10, 32, 34, 39
	Not reported	27, 37
Sources of Calibration Standard (Methamphetamine)	NMI Australia	6, 7, 8, 9, 13, 23, 26, 29
	Lipomed	5, 17, 18, 30, 35, 36, 40
	Merck / Sigma Aldrich	15, 16, 32, 34, 38
	Other	1, 2, 3, 4, 10, 11, 12, 14, 19, 20, 21, 22, 24, 25, 28, 31, 33
	Not reported	27, 37, 39

Plots of the z-score versus the sample mass used per analysis, solvent, measurement instrument, and source of calibration standard are presented in Figures 10 to 14. A variety of methodologies were used by participants in this study. No trends were identified.

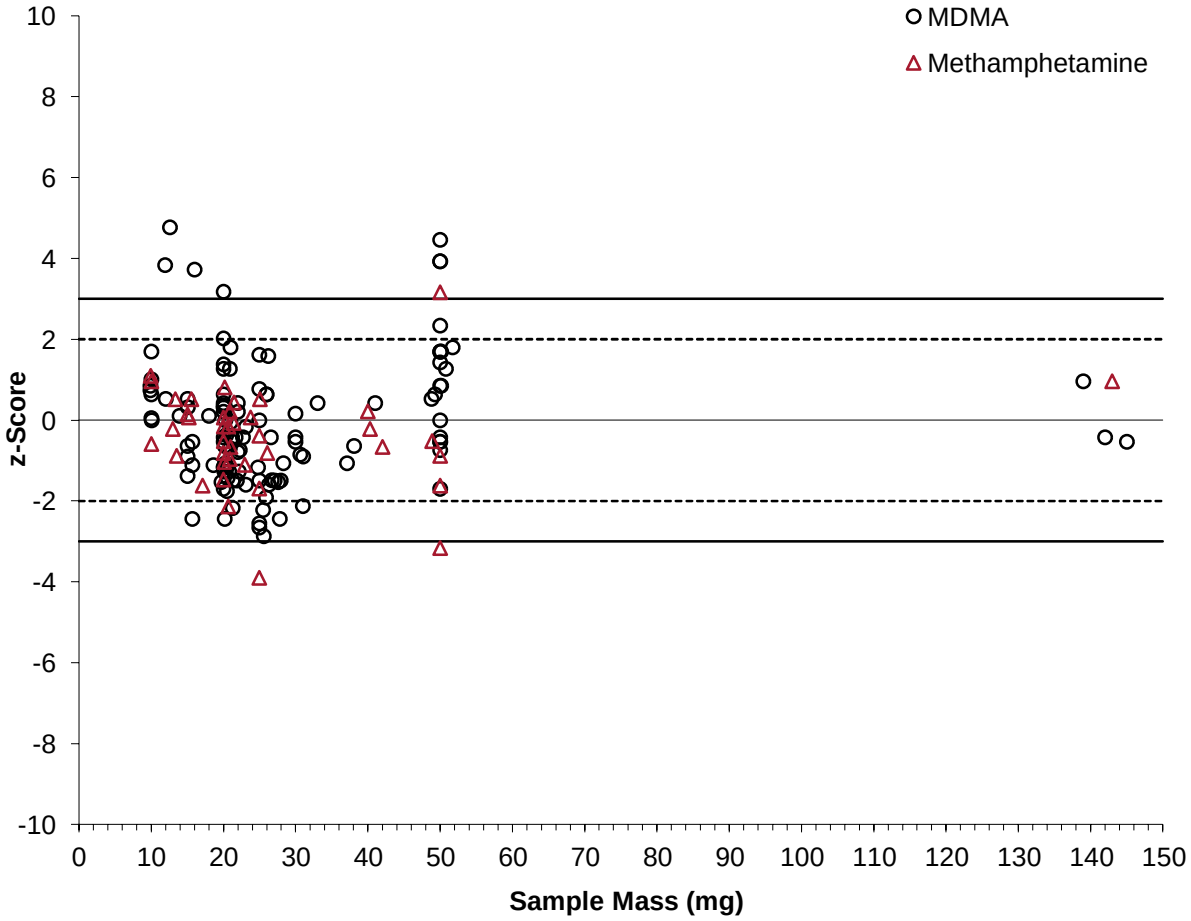


Figure 10 z-Score vs Sample Mass Used

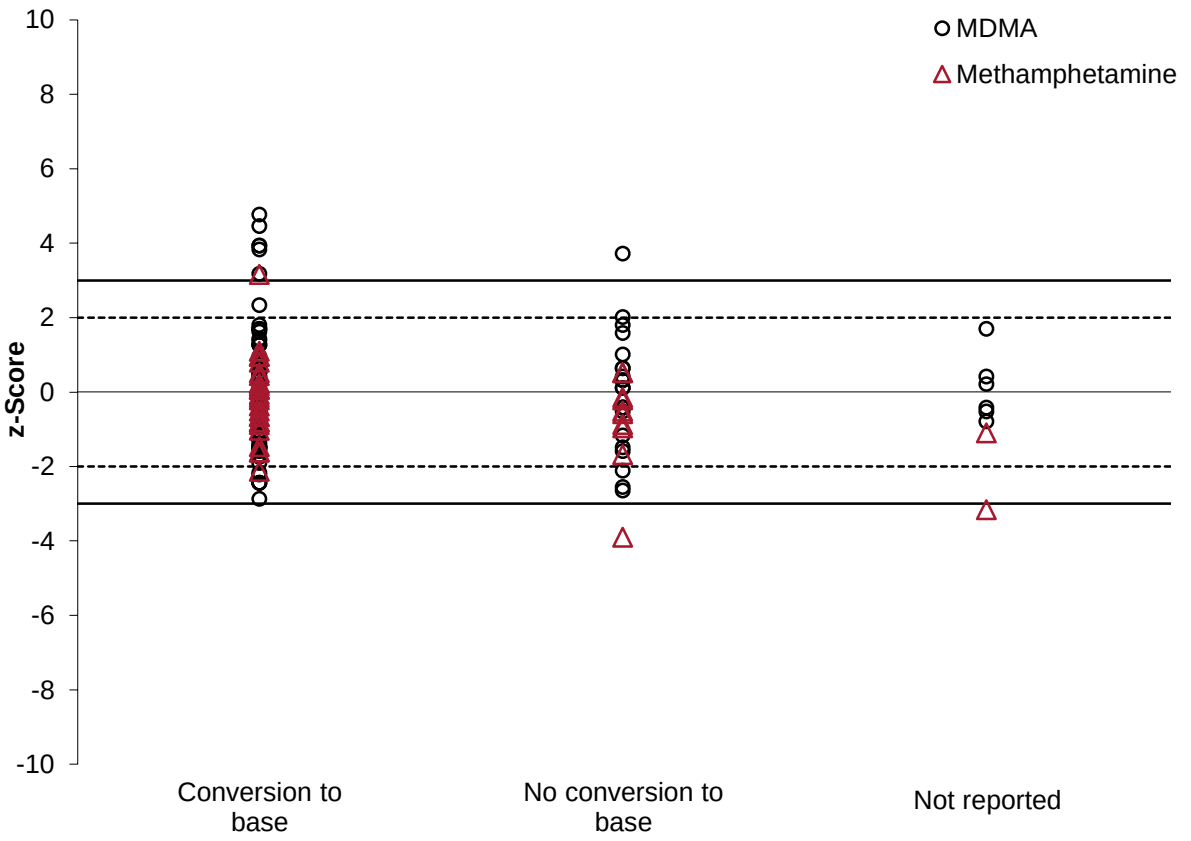


Figure 11 z-Score vs Sample Processing

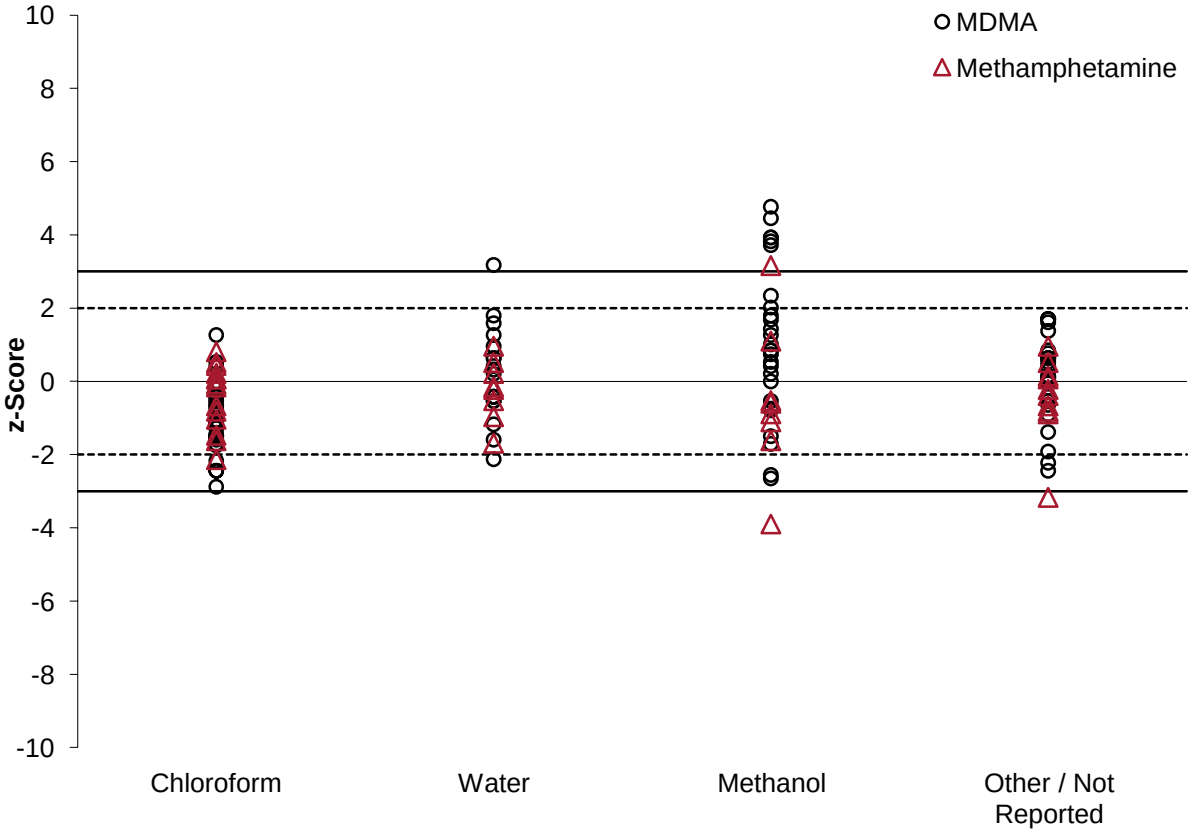


Figure 12 z-Score vs Solvent

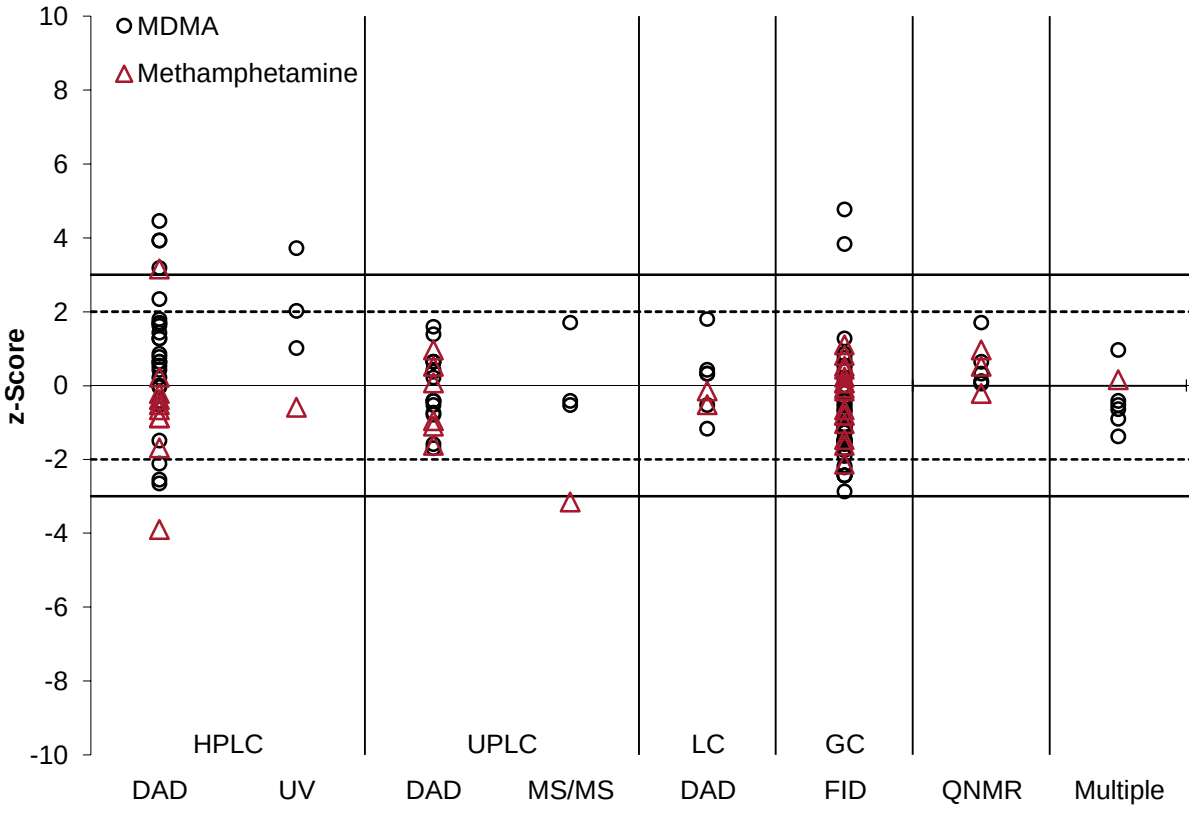


Figure 13 z-Score vs Measurement Instrument

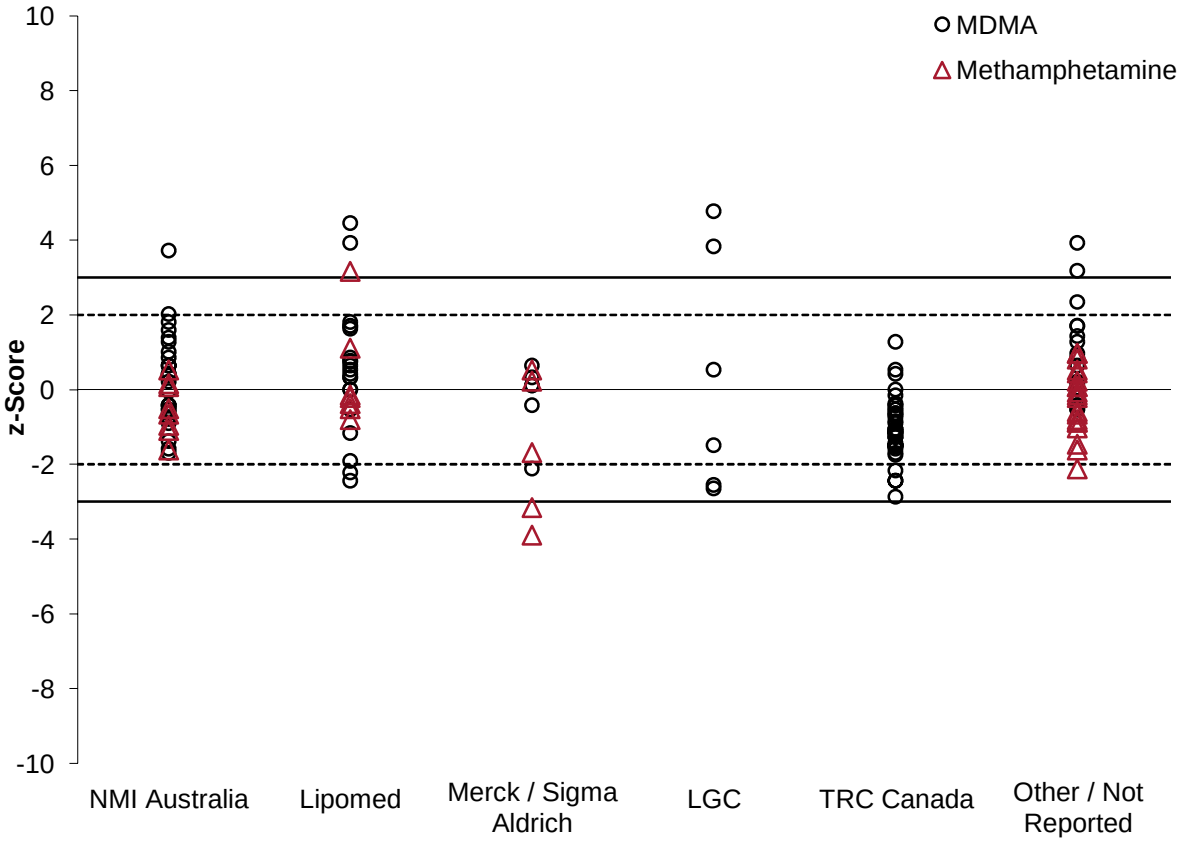


Figure 14 z-Score vs Calibration Standard Source

6.8 Comparison with Previous MDMA and Methamphetamine PT Studies

To enable direct comparison with previous MDMA and Methamphetamine PT studies, the target SD used to calculate z-scores has been kept constant at 3% PCV.

A summary of the satisfactory performance, presented as a percentage of the total number of scores, obtained by PT study participants for MDMA from 2001 – 2020 (last 8 studies with MDMA) are presented in Figure 15. The average proportion of satisfactory z-scores and E_n-scores over this period is 75% and 62% respectively. While each PT study has a different group of participants, taken as a group, the performance over this period has improved.

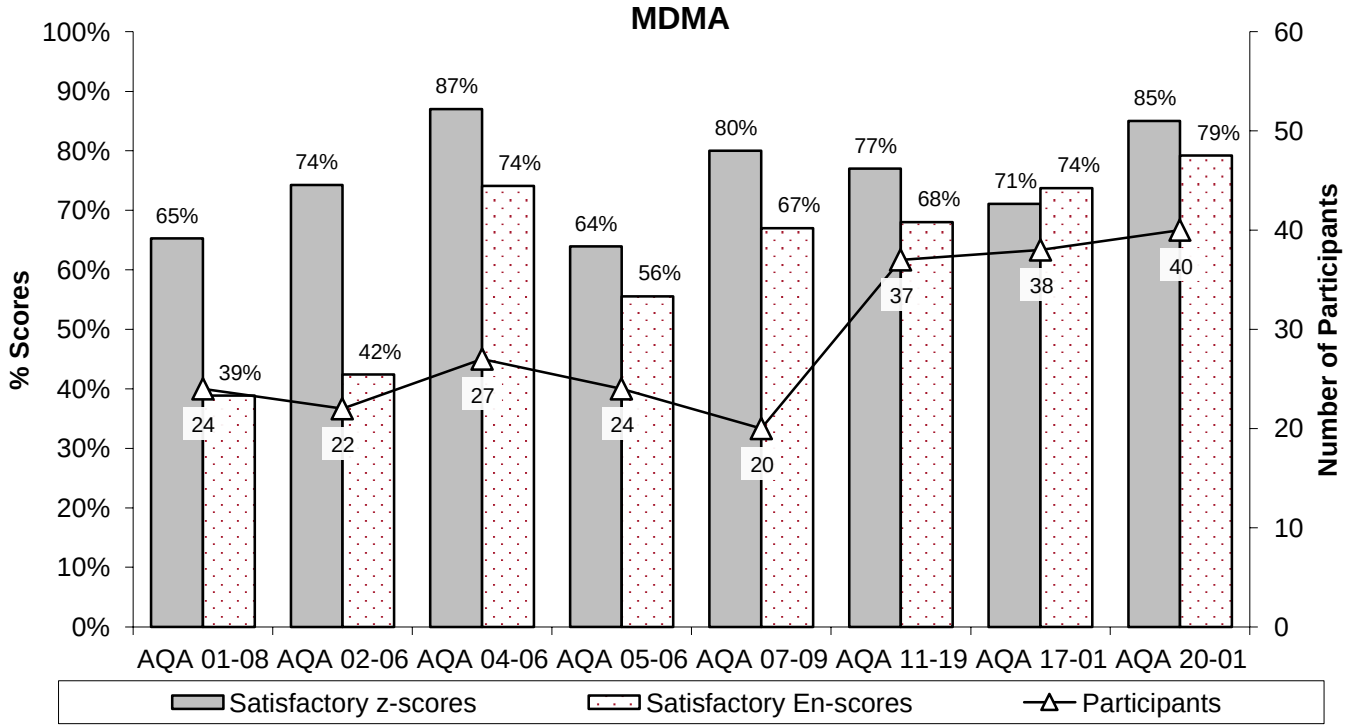


Figure 15 Summary of Participants' Performance in MDMA PT Studies

A summary of the satisfactory performance, presented as a percentage of the total number of scores, obtained by PT study participants for methamphetamine from 2009 – 2020 (last 10 studies with methamphetamine) are presented in Figure 16. The average proportion of satisfactory z-scores and E_n-scores over this period is 83% and 78% respectively. While each PT study has a different group of participants, taken as a group, the performance over this period has improved.

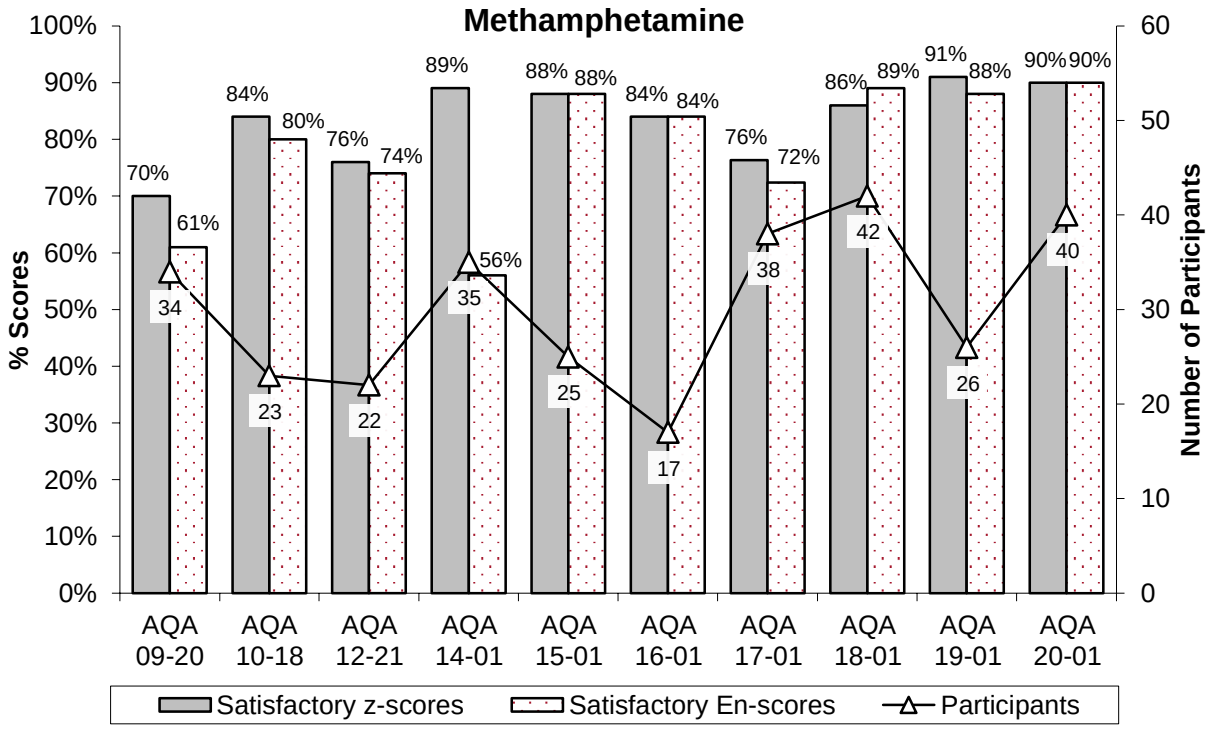


Figure 16 Summary of Participants' Performance in Methamphetamine PT Studies

Individual performance history reports are emailed to each participant at the end of the study; the consideration of z-scores for an analyte over time provides much more useful information than a single z-score. Over time, laboratories should expect at least 95% of their scores to lie within the range $|z| \leq 2.0$. Scores in the range $2.0 < |z| < 3.0$ can occasionally occur, however, these should be interpreted in conjunction with the other scores obtained by that laboratory. For example, a trend of z-scores on one side of the zero line is an indication of method or laboratory bias.

7 REFERENCES

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

[2] NMI, 2019, *Study Protocol for Proficiency Testing*, viewed January 2020, <https://www.industry.gov.au/sites/default/files/2019-07/cpt_study_protocol.pdf>.

[3] NMI, 2019, *Chemical Proficiency Testing Statistical Manual*, viewed January 2020, <https://www.industry.gov.au/sites/default/files/2019-07/cpt_statistical_manual.pdf>.

[4] Thompson, M., Ellison, S.L.R. and Wood, R., 2006, 'The International Harmonized Protocol for the Proficiency Testing of Analytical Chemistry Laboratories', *Pure Appl. Chem.*, vol 78, pp 145-196.

[5] ISO 13528:2015, *Statistical methods for use in proficiency testing by interlaboratory comparisons*.

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

[7] Eurachem/CITAC Guide CG 4, QUAM:2012.P1, *Quantifying Uncertainty in Analytical Measurement*, 3rd edition, viewed January 2020, <http://www.eurachem.org/images/stories/Guides/pdf/QUAM2012_P1.pdf>.

[8] ISO/IEC Guide 98-3:2008, *Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995).*

[9] Thompson, M., 2000, 'Recent trends in inter-laboratory precision at ppb and sub-ppb concentrations in relation to fitness for purpose criteria in proficiency testing', *Analyst*, vol 125, pp 385-386.

[10] NMI, 2011, *Proficiency Study AQA 11-19 MDMA.*

APPENDIX 1 – REFERENCE VALUES

Three sample vials from each of Samples S1 and S4 were analysed in duplicate for the purpose of assigning reference values. Measurements were made using qNMR with maleic acid as the internal standard. A CRM of maleic acid was obtained from Chemical Reference Materials, NMI. The purity data supplied with the material is shown in Table 12 and is traceable to the SI unit for mass, the kilogram (kg). Internal standard solutions were prepared gravimetrically in D_2O.

Table 12 Maleic Acid CRM Details

Supplier	Catalogue No.	Batch No.	Purity (95% confidence)
Chemical Reference Materials, NMI	QNMR010	10-Q-02	98.8 ± 0.12 %

Samples were prepared gravimetrically by accurately weighing approximately 20 mg of sample, dissolving in 900 µL of internal standard solution, 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. For Sample S1, the mass fraction of MDMA was determined from the NMR response at 1.26 ppm. For Sample S4, the mass fraction of methamphetamine was determined from the average of NMR responses at 2.68 ppm, 2.88 ppm and 3.05 ppm due to cutting agent interferences with the NMR response at 1.25 ppm.

The averages of the mass fractions determined for the different vials of Samples S1 and S4 (Tables 13 and 14 respectively) were used as the reference values and the assigned values for this PT study. The standard uncertainties on the mass fraction reference values were estimated in accordance with the ISO GUM[8] 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, an estimate of potential interference bias made by comparing the results from different NMR signals, and the between-batch variation.

The measured reference value for both Samples S1 and S4 were in agreement with the gravimetric preparation value and the robust average of participants' results, within their respective associated uncertainties.

Table 13 Reference Value for Sample S1

Vial No.	MDMA (% base (m/m))	
	Replicate 1	Replicate 2
138	63.2	63.1
144	63.2	62.6
148	63.0	62.8
Mean	63.0	
CV	0.4%	

Sample S1 Reference Value: 63.0 ± 1.3% MDMA 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 equation (k = 2.06).[8]

Table 14 Reference Value for Sample S4

Vial No.	Methamphetamine (% base (m/m))	
	Replicate 1	Replicate 2
405	45.0	45.1
412	45.4	45.1
440	45.4	45.6
Mean	45.3	
CV	0.5%	

Sample S4 Reference Value: 45.3 ± 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 equation (k = 2.09).[8]

APPENDIX 2 – ROBUST AVERAGE AND ASSOCIATED UNCERTAINTY, Z-SCORE AND E_N-SCORE CALCULATIONS

A2.1 Robust Average and Associated Uncertainty

The robust average is calculated using the procedure described in ISO 13528:2015 'Statistical methods for use in proficiency testing by interlaboratory comparisons – Annex C'.[5] The uncertainty is estimated as:

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

where:

$u_{rob\ average}$	is the standard uncertainty of the robust average
$S_{rob\ average}$	is the standard deviation of the robust average
p	is the 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 15.

Table 15 Uncertainty of Robust Average of MDMA in Sample S3

No. results (p)	40
Robust Average	31.6% base (m/m)
$S_{rob\ average}$	1.5% base (m/m)
$u_{rob\ average}$	0.3% base (m/m)
k	2
$U_{rob\ average}$	0.6% base (m/m)

Therefore, the robust average for Sample S3 is 31.6 ± 0.6% base (m/m).

A2.2 z-Score and E_n-Score Calculations

For each participant's result, a z-score and E_n-score are calculated according to Equations 2 and 3 respectively.

A worked example is set out below in Table 16.

Table 16 z-Score and E_n-Score for Sample S1 MDMA Result Reported by Laboratory 1

Participant Result (% base (m/m))	Assigned Value (% base (m/m))	Target Standard Deviation	z-Score	E_n-Score
61.7 ± 5.9	63.0 ± 1.3	3% as PCV, or: 0.03 × 63.0 = 1.89% base (m/m)	z-Score = $\frac{61.7-63.0}{1.89}$ = -0.69	E_n-Score = $\frac{61.7-63.0}{\sqrt{5.9^2+1.3^2}}$ = -0.22

APPENDIX 3 – ACRONYMS AND ABBREVIATIONS

AFP	Australian Federal Police
ANAB	ANSI (American National Standards Institute) National Accreditation Board
ASCLD/LAB	American Society of Crime Laboratory Directors/Laboratory Accreditation Board
CITAC	Cooperation on International Traceability in Analytical Chemistry
CRM	Certified Reference Material
CV	Coefficient of Variation
DAD	Diode Array Detector
FID	Flame Ionisation Detector
GC	Gas Chromatography
GUM	Guide to the expression of Uncertainty in Measurement
HPLC	High Performance Liquid Chromatography
IEC	International Electrotechnical Commission
ISO	International Standards Organisation
LC	Liquid Chromatography
Max.	Maximum value in a set of results
Md	Median value in a set of results
MDMA	3,4-Methylenedioxymethamphetamine
Min.	Minimum value in a set of results
MS	Mass Spectrometry
MS/MS	Tandem Mass Spectrometry
MU	Measurement Uncertainty
NATA	National Association of Testing Authorities, Australia
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
R.A.	Robust Average
R.V.	Reference Value
RM	Reference Material
SD	Standard Deviation
SI	International System of Units
SS	Spiked Samples
UPLC	Ultra Performance Liquid Chromatography
UV	Ultraviolet

END OF REPORT