Australian Government
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National Measurement Institute

Proficiency Test Final Report AQA 23-03 MDMA/Methamphetamine

October 2023

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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TABLE OF CONTENTS

SUMMARY

AQA 23-03 MDMA/Methamphetamine commenced in January 2023. Sample sets each containing two 3,4-methylenedioxymethamphetamine (MDMA) samples and two methamphetamine samples were sent to 32 laboratories, with one laboratory requesting two sets of test samples to be analysed by different analysts. Thirty-one participants returned results.

Samples were prepared at the NMI Sydney laboratory. Samples S1 and S2 were prepared from MDMA hydrochloride and Samples S3 and S4 were prepared from methamphetamine hydrochloride, all supplied by the Australian Federal Police.

The assigned values for all samples were the reference values as determined by quantitative nuclear magnetic resonance (qNMR) spectroscopy, 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 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.*

Of 114 *z*-scores, 105 (92%) returned $|z| \leq 2.0$, indicating a satisfactory performance.

Of 114 E_n-scores, 101 (89%) returned $|E_n| \leq 1.0$, indicating agreement of the participant's results with the assigned value within their respective expanded uncertainties.

Laboratories **3**, **4**, **5**, **6**, **8**, **12**, **13**, **15**, **16**, **19**, **20**, **24**, **25**, **27**, **29**, **31** and **32** returned satisfactory *z*-scores and E_n-scores for all four samples.

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

Of 114 numeric results, 104 (91%) were reported with an associated expanded measurement uncertainty. The magnitudes of uncertainties were within the range 0.9% to 127% relative.

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

Sample S1 was cut with sucrose, Sample S2 was cut with cellulose, Sample S3 was left uncut and Sample S4 was cut with dimethyl sulfone. Twenty participants (65%) reported on the identity of at least one cutting agent in the samples.

Laboratory **22** correctly identified all cutting agents in this study.

- *Produce materials that can be used in method validation and as control samples.*

The samples produced for this study are homogeneous and are well characterised. Surplus of these samples is available for purchase and can be used for quality control and for method validation purposes.

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 soil, water, fruit, vegetables and herbs;
- petroleum hydrocarbons in soil and water;
- per- and polyfluoroalkyl substances in water, soil, food and biota;
- inorganic analytes in soil, water, filters, food and pharmaceuticals;
- controlled drug assay, drugs in wipes, 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;
- test the ability of participants to identify cutting agents commonly found in controlled drug preparation; and
- produce materials that can be used in method validation and as control samples.

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

1.3 Study Conduct

The conduct of NMI PT studies is described in the NMI Study Protocol for Proficiency Testing.[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/IEC 17043 and The International Harmonized Protocol for the Proficiency Testing of Analytical Chemistry Laboratories.[1,4]

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

2 STUDY INFORMATION

2.1 Study Timetable

The timetable of the study was:

Invitations sent	24/01/2023
Samples sent	27/03/2023
Results due	28/08/2023
Interim Report	31/08/2023
Preliminary Report	5/09/2023

Due to significant sample delivery delays to some international participants, the project timeline was extended.

2.2 Participation and Laboratory Code

Thirty-two laboratories registered to participate, with one laboratory requesting two sets of samples to be analysed independently by different analysts (total of 33 participants). Each participant was assigned a confidential laboratory code number for this study. Thirty-one participants submitted results.

2.3 Test Material Specification

Four test samples were prepared in February 2023. Samples S1 and S2 contained MDMA hydrochloride, and Samples S3 and S4 contained methamphetamine hydrochloride. The starting materials were supplied by the Australian Federal Police.

Sucrose, cellulose and dimethyl sulfone purchased from Sigma-Aldrich were used as cutting agents. Sample S1 was cut with sucrose, Sample S2 was cut with cellulose, Sample S3 was left uncut, and Sample S4 was cut with dimethyl sulfone.

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 with known amounts 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 16.5% MDMA base (m/m).

Sample S2 was prepared to contain approximately 65.4% MDMA base (m/m).

Sample S3 was prepared to contain approximately 80.0% methamphetamine base (m/m).

Sample S4 was prepared to contain approximately 39.6% methamphetamine base (m/m).

2.4 Test Sample Homogeneity

The preparation of homogeneous test samples is an important part of a PT 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.

Homogeneity testing was performed for Sample S2, and is described in Appendix 1. Samples were demonstrated to be sufficiently homogeneous for this PT study with a target standard deviation (SD) (as performance coefficient of variation (PCV)) of 3%. Partial homogeneity checks for Samples S1 and S3 also indicated that samples were sufficiently homogeneous for the same target SD (as PCV). The partial homogeneity check for Sample S4 indicated there was slightly greater variability for these samples, and so a larger target SD (as PCV) of 5% was applied for this sample.

2.5 Sample Dispatch and Receipt

A set of four test samples, with each sample containing approximately 150 mg of test material, was dispatched to each participant on 27 March 2023.

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 emailed to participants.

2.6 Instructions to Participants

Participants were instructed as follows:

- Analyse each sample for the amount of drug by your routine test method. It is recommended to thoroughly mix the content of each vial before taking a test portion for analysis.
- For each sample report % m/m drug as base. Report this figure as if reporting to a client.
- For each result report an estimate of your expanded uncertainty as % m/m drug as base.
- Report the identity of cutting agents in all samples if this is within your normal scope of analysis.
- Give brief details of your:
    - basis of uncertainty estimate (e.g. uncertainty budget, repeatability precision)
    - analytical method (e.g. sample treatment, instrument type, calibration method)
    - reference standard (e.g. source, purity)

  as requested by the results sheet.
- A result spreadsheet will be emailed to you. Please complete the results spreadsheet and return by email to jenny.xu@measurement.gov.au.
- Results are to be returned by 22 May 2023.

The results due date was changed to 28 August 2023. This was to accommodate for significant sample delivery delays to some international participants caused by customs clearance and distributor delays.

2.7 Interim Report and Preliminary Report

An Interim Report was emailed to all participants on 31 August 2023.

A Preliminary Report was emailed to all participants on 5 September 2023. This report included a summary of the results reported by participants, assigned values, PCVs, *z*-scores and E_n-scores for each analyte in this study. No data from the Preliminary Report has been changed in the present Final Report.

3 PARTICIPANT LABORATORY INFORMATION

3.1 Test Methods Reported by Participants

Participants were requested to provide information about their test methods. Responses received are presented in Table 1. Some responses may be modified so that the participant cannot be identified.

Table 1 Summary of Participants' Test Methods

Lab. Code	Analyte	Extraction Solvent	Internal Standard	Calib. Points	Technique	Detector	Column
1	MDMA	ACN/MeOH/H_2O	Analog of MDMA	7	UPLC	MS/MS	C-18 column
	Methamphetamine		Analog of methamphetamine				
2	Methamphetamine	Dissolution in acetonitrile/water	Methoxyphenamine HCl	3	HPLC	DAD	Alltima C-18
3	All	D_2O	Maleic Acid		QNMR		
4	All	water	none	4	HPLC	DAD	Zorbax RX-SIL
5	All	Purified Water	Phentermine	1	UPLC	DAD	Agilent Zorbax SB-C8
6	All	MeOH	Strychnine	6	UPLC	DAD	UPLC BEH Phenyl
8	All	Methanol	2,4,6-trimethylpyridine	6	GC	FID	RTX-5-Amine
9	All	Eluent: Acetonitrile, ammonium acetate, diethylamine & water	None	4	HPLC	UV-VIS	LiChrosphere RP-18 (5 um)
10	MDMA	H_2O	nil	1	UPLC	PDA	Acquity UPLC BEH C18 1.7µm 2.1x100mm
	Methamphetamine			S3: 1 S4: 4	S3: UPLC S4: HPLC		S3: Acquity UPLC BEH C18 1.7µm 2.1x100mm (UPLC) S4: C18 µbondapak stainless steel, 10µmPS, 3.9x150mm (HPLC)
11	All	Methanol	Propylparaben	3	UPLC	PDA	ACQUITY C-18
12	All	Methanol	None	5	HPLC	DAD	Phenomenex C-18-XB
13	All	80:20(Water/ACN)	N/A	3	HPLC	DAD	Luna 2.5um C18(2)-HST 100 A (LC Column 100 x 3mm)

Lab. Code	Analyte	Extraction Solvent	Internal Standard	Calib. Points	Technique	Detector	Column
14	MDMA	buffer phosphate pH 3 / methanol (70/30)	none	3	HPLC	DAD	C18
15	All	Methanol:KOH Buffer (50:50)	Methoxyphenamine	3	UPLC	DAD	Acquity BEH C18
16	All	Ethyl Acetate	Diphenylamine	5	GC	FID	HP1
17	MDMA	acetic acid, acetonitrile, water	No IS	4	HPLC	DAD	Poroshell 120 EC-C18
	Methamphetamine						Poroshell 120 EC-C19
18	MDMA	D_2O	Maleic acid + DMS	3	NMR		
19	All	Purified Water	Phentermine	1	UPLC	DAD	Agilent Zorbax SB-C8
20	All	Methanol	N/A	6	HPLC	UV/Vis	Luna C-18
21	MDMA	hexane	C20	4	GC	FID	HP-1
	Methamphetamine	D_2O	calcium formate		NMR (proton)		-
22	MDMA	acetonitrile/water (80/20)	external standard	2	HPLC	DAD	C8
23	All	Methanol	Diazepam	6	GC	FID	J&W 128-5512
24	All	phosphate buffer pH 2.5	-	5	HPLC	DAD	Luna Omega 3um PS C18 100Å, 150 x 4.6 mm
25	All	Water	N/A	7	HPLC	DAD	Phenomenex PFP (2) Luna 3u Narrow Bore 100 mm
27	All	Methanol	Selegiline	4	UPLC	DAD	C18
28	MDMA	METHANOL	MDMA-D5	1	GC	MS	HP5MSUI
	Methamphetamine		METHMAPHETAMINE-D5				
29	All	methanol	External Standard	1	HPLC	DAD	zorbax eclipse XDB-C18 (4.6x1500 mm)

Lab. Code	Analyte	Extraction Solvent	Internal Standard	Calib. Points	Technique	Detector	Column
30	MDMA	Acetonitrile	None	4	HPLC	DAD	Interchrom C8 5UM 150x4.6MM
31	All	isooctane / NH_4OH	dodecane	3	GC	FID	HP1MS
32	All	D_2O	Maleic acid		QNMR		NA
33	MDMA	Ethanol	Propyl Paraben	8	UPLC	DAD	BEH Shield RP18
	Methamphetamine			7			

3.2 Reported Basis of Participants' Measurement Uncertainty Estimates

Participants were requested to provide information about their basis of measurement uncertainty (MU). Responses received are presented in Table 2. Some responses may be modified so that the participant cannot be identified.

Table 2 Reported Basis of Uncertainty Estimate

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation*		Guide Document for Estimating MU
		Precision	Method Bias	
1	Top Down - precision and estimates of the method and laboratory bias			
2	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
3	Under Determination. Fixed at 20% (relative)	Control samples - RM		ISO/GUM
4	Top Down - precision and estimates of the method and laboratory bias	Control samples - Sample from case	Laboratory bias from PT studies	Nordtest Report TR537
5	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Laboratory bias from PT studies Recoveries of SS	Eurachem/CITAC Guide
6	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - RM Duplicate analysis	Instrument calibration Homogeneity of sample	ISO/GUM

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation*		Guide Document for Estimating MU
		Precision	Method Bias	
			Masses and volumes Laboratory bias from PT studies	
8	Top Down - precision and estimates of the method and laboratory bias	Standard deviation from PT studies only		ISO/GUM
9	Uncertainty Budget Method	Control samples - RM Duplicate analysis	Instrument calibration Masses and volumes Standard purity	Internal SOP Document
10	Validation (k=2)			
11	Top Down - precision and estimates of the method and laboratory bias	Control samples - CRM Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes	NATA GAG Estimating and Reporting Measurement Uncertainty of Chemical Test Results
12	Standard deviation of replicate analyses multiplied by 2 or 3	Control samples - RM Duplicate analysis		
13	Top Down - precision and estimates of the method and laboratory bias	Control samples - Previously analysed sample		LGC Validation course
14		Standard deviation from PT studies only		
15	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM Duplicate analysis	Standard purity	Eurachem/CITAC Guide
16	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM	Standard purity	ISO/GUM
17	Top Down - precision and estimates of the method and laboratory bias accuracy profile - based on intermediate precision and repeatability	Control samples - CRM		
18				
19	Top Down - precision and estimates of the method and laboratory bias	Duplicate analysis	Laboratory bias from PT studies Recoveries of SS	Eurachem/CITAC Guide

Lab. Code	Approach to Estimating MU	Information Sources for MU Estimation*		Guide Document for Estimating MU
		Precision	Method Bias	
20	Top Down - precision and estimates of the method and laboratory bias	Control samples Duplicate analysis		Eurachem/CITAC Guide
21	Top Down - precision and estimates of the method and laboratory bias	Control samples - RM Duplicate analysis		Internal document based on Eurachem/CITAC, ISO/GUM
22		Control samples - RM Duplicate analysis	Instrument calibration	Eurachem/CITAC Guide
23	Top Down – Estimating Measurement Uncertainty by black box with pairs of values	Standard deviation from PT studies only		ISO/GUM
24	Reproducibility, bias, sample heterogeneity	Control samples - RM Duplicate analysis	Instrument calibration Homogeneity of sample Standard purity	ENFSI Best Practise manual, Eurachem/CITAC guide
25	Top Down - precision and estimates of the method and laboratory bias	Control samples - In House Control Duplicate analysis	Instrument calibration Homogeneity of sample Masses and volumes Standard purity	ISO/GUM
27	Top Down - precision and estimates of the method and laboratory bias	Control samples - authentic powders Duplicate analysis	Instrument calibration Homogeneity of sample Matrix effects Laboratory bias from PT studies Recoveries of SS Standard purity	EA-04/16 EA guidelines on the expression of uncertainty in quantitative testing.
28				
29		Control samples - CRM Duplicate analysis	Instrument calibration Laboratory bias from PT studies Standard purity	
30	Standard deviation of replicate analyses multiplied by 2 or 3	Control samples - RM	Laboratory bias from PT studies	
31	Bottom Up (ISO/GUM, fish bone/cause and effect diagram)	Control samples - CRM Duplicate analysis	Instrument calibration 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	
			Masses and volumes Matrix effects Recoveries of SS Standard purity	
32	Top Down - precision and estimates of the method and laboratory bias	Control samples - previously analysed real seizure samples Duplicate analysis	Homogeneity of sample Masses and volumes Matrix effects Standard purity	Eurachem/CITAC Guide
33				

* 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. Responses may be modified so that the participant cannot be identified.

Table 3 Participant Calibration Standard

Lab. Code	MDMA		Methamphetamine	
	Reference Standard	Purity (%)	Reference Standard	Purity (%)
1		99	Sigma Aldrich	100
2	NT		NMI	99.8
3	Maleic acid origin: Sigma Aldrich Batch Number: M0375-100G Lot: SLBZ5070	> 99	Maleic acid origin: Sigma Aldrich Batch Number: M0375-100G Lot: SLBZ5070	> 99
4	Internal	100	Sigma	100
5	Lipomed	99.950 ± 0.050	Lipomed	99.950 ± 0.050
6	NMI	99.9	NMI	99.8
8	Lipomed	99.987	Lipomed	99.95
9	Lipomed	99.95	Lipomed	99.005

10	In-house synthesis	100.8	In-house synthesis	99.8
11	NMI	99.8	NMI	99.8
12	Chiron	99.4	Sigma	99.9
13	NMI	99.4	Sigma	100
14	Lipomed/Euromedex	99.95	NT	
15	NMI	99.8	NMI	99.8
16	Lipomed	99.95	Lipomed	99.987
17	Lipomed	99.95	Lipomed	99.95
18			NT	
19	Lipomed	99.950±0.050	Lipomed	99.950±0.050
20	NMI	99.4	In house	100
21	In house	100		
22	NMI	99.6	NT	
23	Lipomed	99.95	Lipomed	99.1
24	Chiron	99.4	Chiron	99.4
25	NMI	99.4	NMI	99.8
27	Lipomed	99.9985 +/- 0.0070	Lipomed	99.005 +/- 0.027
28	LGC Standards	>99.9	LIPOMED	>99.9
29				
30	Lipomed (MDM-94-HC)	83.7	NT	
31	NMI	99.8	NMI	99.8
32	NA	NA	NA	NA
33	NMI	97.5	NMI	99.8

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. Responses may be modified so that the participant cannot be identified.

Table 4 Participants' Comments

Lab. Code	Participants' Comments	Study Coordinator's Response
2	Methamphetamine Methodology: Linear regression	
10	Methamphetamine Methodology: 2 different quantification methods used	
14	it is requested to warn the laboratories before the registration, on the distribution of the type of samples included in the circuit (amphetamine, MDMA, Methamphetamine) because we only do the quantification of MDMA.	We issue an invitation letter at the start of each study, which specifies the analytes that will be included for that study. Distributors are requested to pass this information onto prospective participants. If participants are unsure of the analytes, they may contact us to confirm which analytes will be in the study before enrolling.
16	Accreditation for MDMA but not for methamphetamine	
17	Accreditation for identification only. MDMA Methodology: 5,20,60,100 Methamphetamine Methodology: 5,20,60,100	
29	Quantitative analysis is based on the use of a historical value obtained from different batches of Certified reference material	
30	the laboratory only performs the quantification of MDMA, We have no results for Methamphetamine to report	
31	For sample S2 a diluent/adulterant was present, however it was unable to be identified using our available techniques and standard processes.	
32	MDMA and Methamphetamine Methodology: No reference standard involved	
33	Precursor present in S1 and S2: PMK	

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.

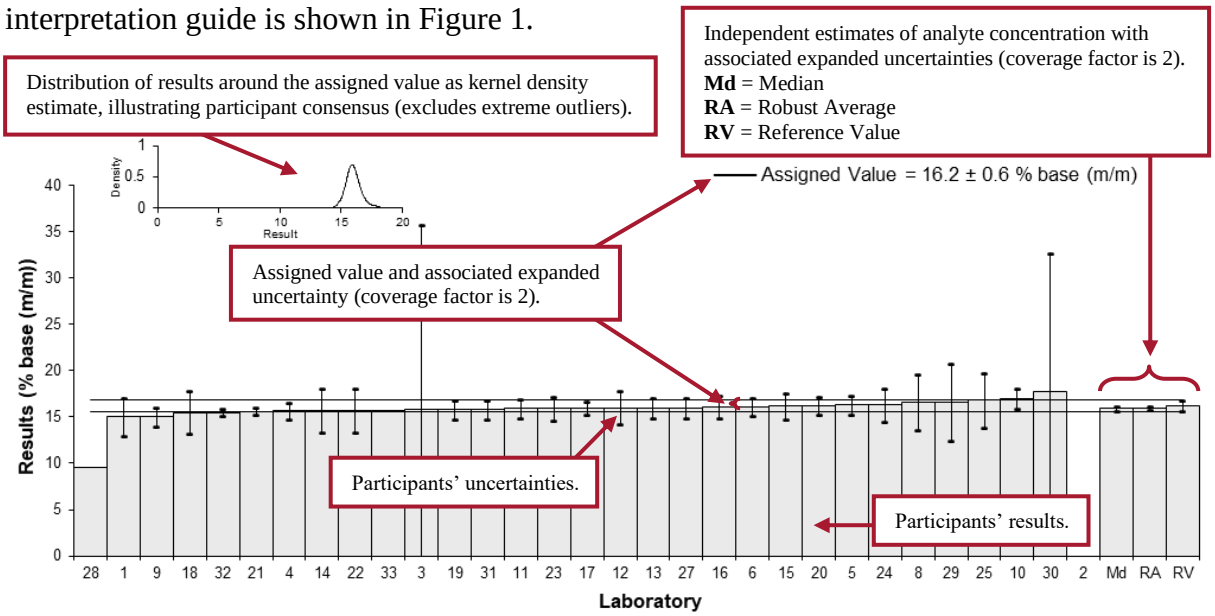


Figure 1 Guide to Presentation of Results

4.2 Outliers and Extreme Outliers

Outliers were any result less than 50% and greater than 150% of the robust average, and these were removed before the calculation of the assigned value (if by consensus).[3,4] Extreme outliers were any obvious blunders, e.g. results with incorrect units, or for a different analyte or sample, and such results were removed before the calculation of all summary statistics.[3]

4.3 Assigned Value

The assigned value is defined as the 'value attributed to a particular property of a proficiency test item'.[1] In this PT study, the property is the % MDMA or methamphetamine base (m/m) in the samples. The assigned values for all samples in this study were reference values determined by quantitative nuclear magnetic resonance (qNMR) spectroscopy (Appendix 1).

4.4 Robust Average and Robust Between-Laboratory Coefficient of Variation

Robust averages and associated expanded MUs, and robust CVs (a measure of the variability of participants' results) were calculated as described in ISO 13528.[5]

4.5 Performance Coefficient of Variation (PCV)

The PCV is a measure of the between-laboratory variation that in the judgement of the study coordinator would be expected from participants, given the analyte levels present. The PCV is set by the study coordinator, and it is not the CV of participants' results. The PCV is based on the mass fraction of the analytes and experience from previous studies, and is also supported by mathematical models such as the Thompson-Horwitz equation.[6] By setting a fixed and realistic value for the PCV, a participant's performance does not depend on other participants' performances.

4.6 Target Standard Deviation for Proficiency Assessment

The target SD for proficiency assessment (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.

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

4.7 *z*-Score

For each participant's result, a *z*-score is calculated according to Equation 2.

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

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 the absolute value of a *z*-score:

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

4.8 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.

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

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 the absolute value of an E_n-score:

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

4.9 Traceability and Measurement Uncertainty

Laboratories accredited to ISO/IEC 17025 must establish and demonstrate the traceability and measurement uncertainty associated with their test results.[7]

Guidelines for quantifying uncertainty in analytical measurement are described in the Eurachem/CITAC Guide.[8]

5 TABLES AND FIGURES

Table 5

Sample Details

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

Participant Results

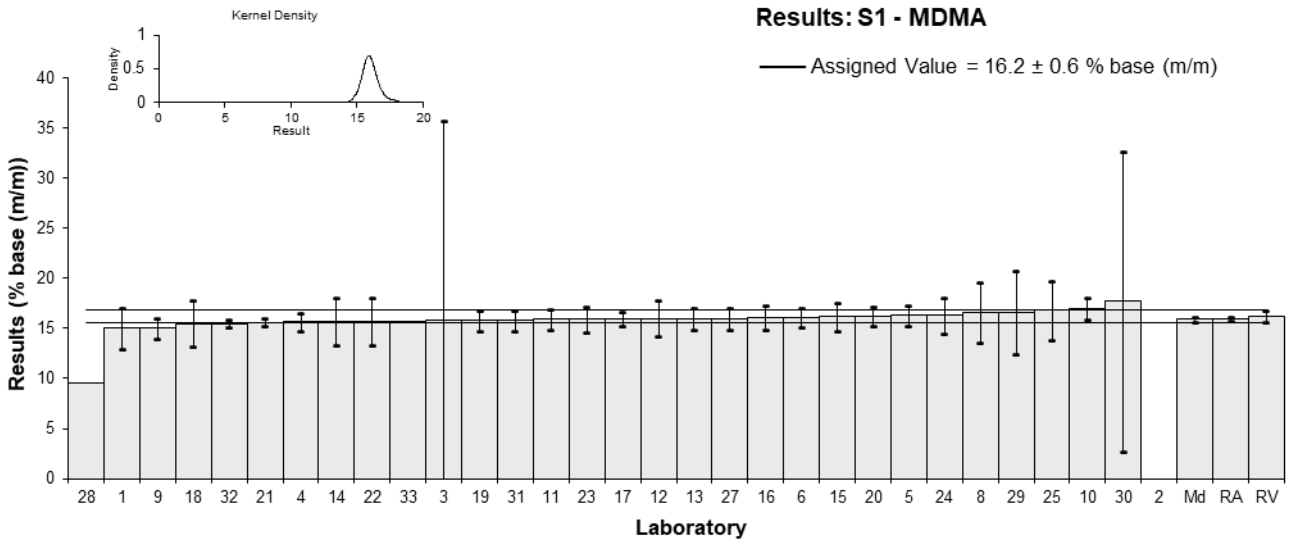
Lab. Code	Result	Uncertainty	z	E_n
1	15	2.1	-2.47	-0.55
2	NR	NR		
3	15.8	20	-0.82	-0.02
4	15.65	0.94	-1.13	-0.49
5	16.3	1.0	0.21	0.09
6	16.1	1	-0.21	-0.09
8	16.6	3	0.82	0.13
9	15	1.0	-2.47	-1.03
10	17.0	1.1	1.65	0.64
11	15.9	1	-0.62	-0.26
12	16	1.8	-0.41	-0.11
13	16	1.10	-0.41	-0.16
14	15.66	2.35	-1.11	-0.22
15	16.2	1.4	0.00	0.00
16	16.09	1.2	-0.23	-0.08
17	15.94	0.75	-0.53	-0.27
18	15.5	2.3	-1.44	-0.29
19	15.8	1	-0.82	-0.34
20	16.2	1.0	0.00	0.00
21	15.6	0.4	-1.23	-0.83
22	15.7	2.4	-1.03	-0.20
23	15.9	1.3	-0.62	-0.21
24	16.3	1.8	0.21	0.05
25	16.8	3	1.23	0.20
27	16.0	1.1	-0.41	-0.16
28**	9.5	NR	-13.79	-11.17
29	16.6	4.2	0.82	0.09
30	17.7	15	3.09	0.10
31	15.8	1.0	-0.82	-0.34
32	15.5	0.37	-1.44	-0.99
33	15.7	NR	-1.03	-0.83

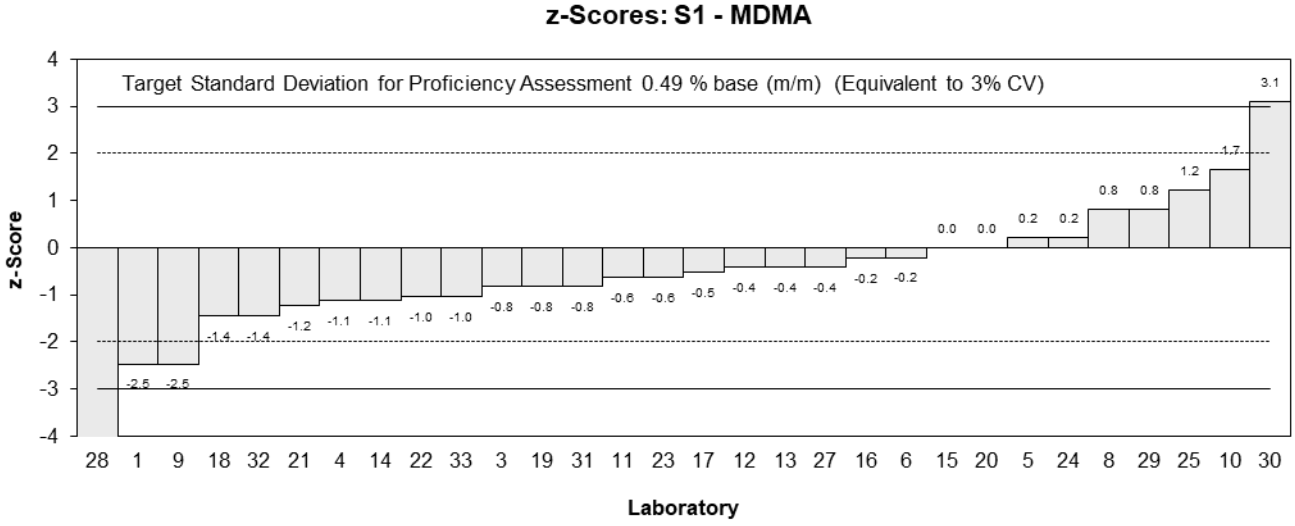
** Extreme Outlier, see Section 4.2

Statistics

Assigned Value	16.2	0.6
Reference Value	16.2	0.6
Robust Average	16.0	0.2
Median	15.9	0.2
Mean	16.0	
N	29	
Max	17.7	
Min	15	
Robust SD	0.46	
Robust CV	2.8%	

Assigned value is the reference value as determined by qNMR spectroscopy.


Kernel Density
Density
Result
Results: S1 - MDMA
Assigned Value = 16.2 ± 0.6 % base (m/m)
Results (% base (m/m))
Laboratory
28 1 9 18 32 21 4 14 22 33 3 19 31 11 23 17 12 13 27 16 6 15 20 5 24 8 29 25 10 30 2 Md RA RV


z-Scores: S1 - MDMA
Target Standard Deviation for Proficiency Assessment 0.49 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
28 1 9 18 32 21 4 14 22 33 3 19 31 11 23 17 12 13 27 16 6 15 20 5 24 8 29 25 10 30

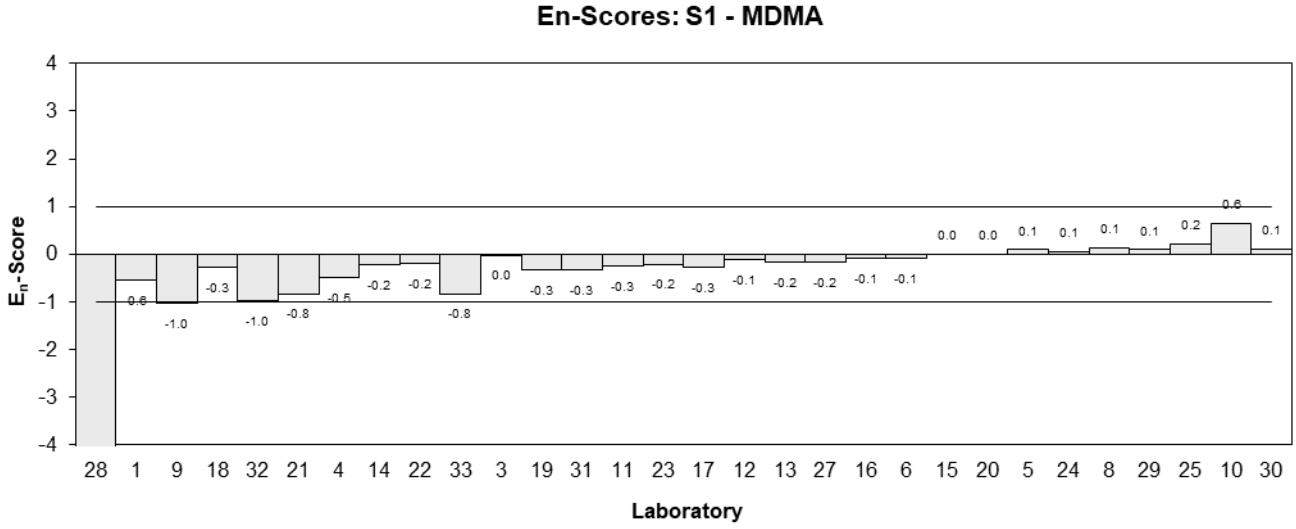

En-Scores: S1 - MDMA
En-Score
Laboratory
28 1 9 18 32 21 4 14 22 33 3 19 31 11 23 17 12 13 27 16 6 15 20 5 24 8 29 25 10 30

Figure 2

Table 6

Sample Details

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

Participant Results

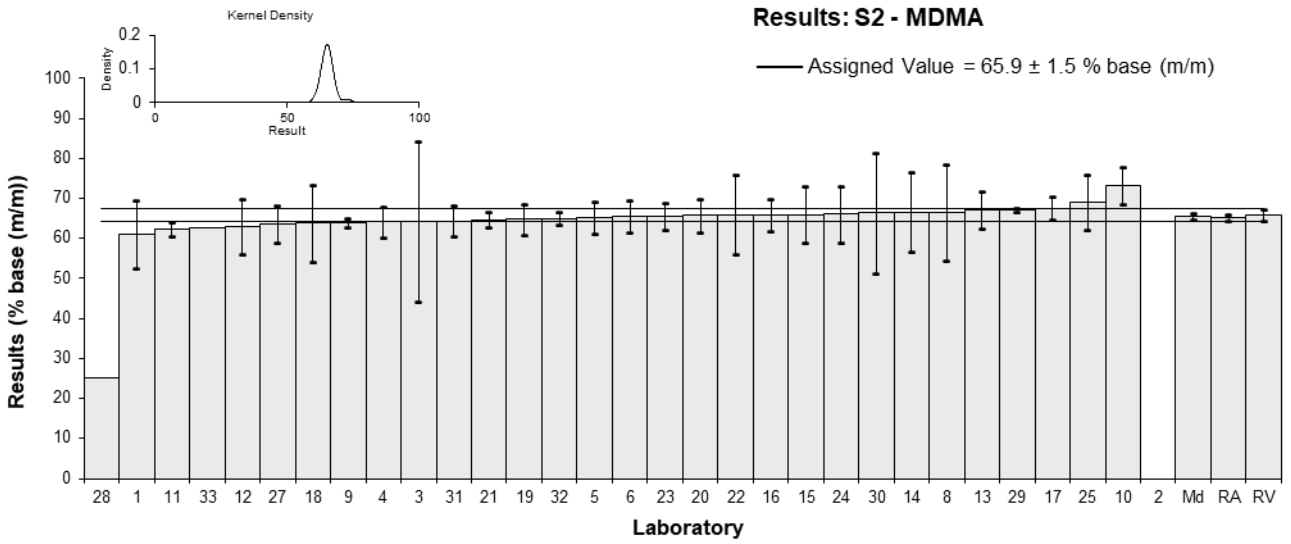
Lab. Code	Result	Uncertainty	z	E_n
1	61	8.5	-2.48	-0.57
2	NR	NR		
3	64.3	20	-0.81	-0.08
4	64.14	3.85	-0.89	-0.43
5	65.1	4.0	-0.40	-0.19
6	65.5	4.1	-0.20	-0.09
8	66.6	12	0.35	0.06
9	64	1.1	-0.96	-1.02
10	73.2	4.6	3.69	1.51
11	62.2	1.8	-1.87	-1.58
12	63	6.9	-1.47	-0.41
13	67	4.62	0.56	0.23
14	66.58	9.99	0.34	0.07
15	66.0	7.0	0.05	0.01
16	65.93	4	0.02	0.01
17	67.58	2.84	0.85	0.52
18	63.9	9.6	-1.01	-0.21
19	64.8	3.9	-0.56	-0.26
20	65.7	4.2	-0.10	-0.04
21	64.7	1.8	-0.61	-0.51
22	65.9	9.9	0.00	0.00
23	65.5	3.3	-0.20	-0.11
24	66.1	7.1	0.10	0.03
25	69.1	6.91	1.62	0.45
27	63.6	4.5	-1.16	-0.48
28**	25.1	NR	-20.64	-27.20
29	67.1	0.6	0.61	0.74
30	66.4	15	0.25	0.03
31	64.4	3.9	-0.76	-0.36
32	65.0	1.56	-0.46	-0.42
33	62.8	NR	-1.57	-2.07

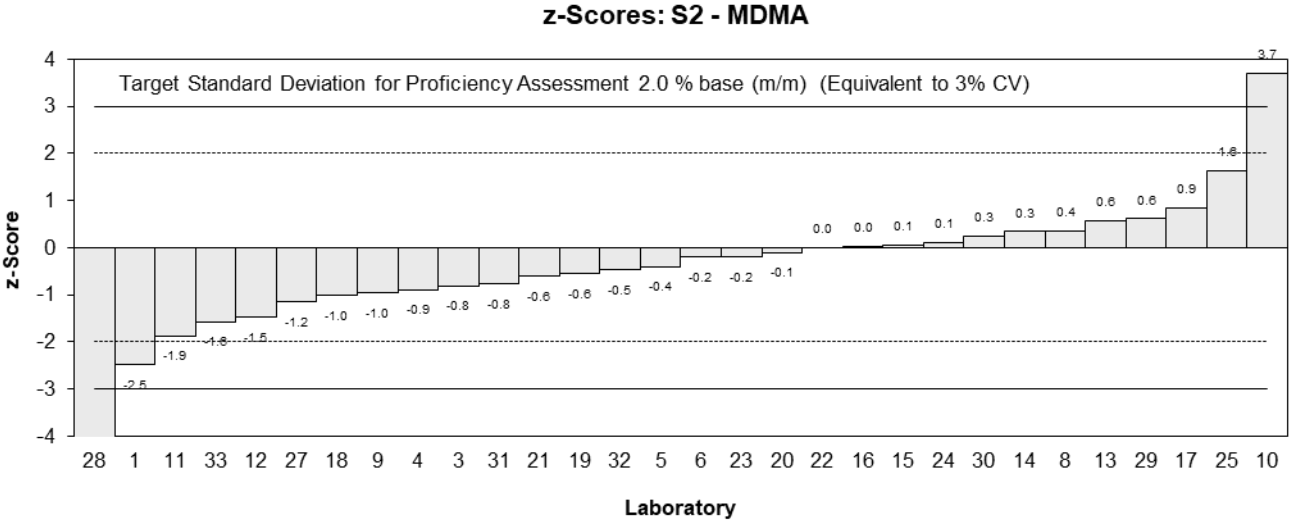
** Extreme Outlier, see Section 4.2

Statistics

Assigned Value	65.9	1.5
Reference Value	65.9	1.5
Robust Average	65.3	0.8
Median	65.5	0.8
Mean	65.4	
N	29	
Max	73.2	
Min	61	
Robust SD	1.8	
Robust CV	2.7%	

Assigned value is the reference value as determined by qNMR spectroscopy.


Results: S2 - MDMA
Assigned Value = 65.9 ± 1.5 % base (m/m)
Kernel Density
Density
Result
Results (% base (m/m))
Laboratory
28 1 11 33 12 27 18 9 4 3 31 21 19 32 5 6 23 20 22 16 15 24 30 14 8 13 29 17 25 10 2 Md RA RV


z-Scores: S2 - MDMA
Target Standard Deviation for Proficiency Assessment 2.0 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
28 1 11 33 12 27 18 9 4 3 31 21 19 32 5 6 23 20 22 16 15 24 30 14 8 13 29 17 25 10

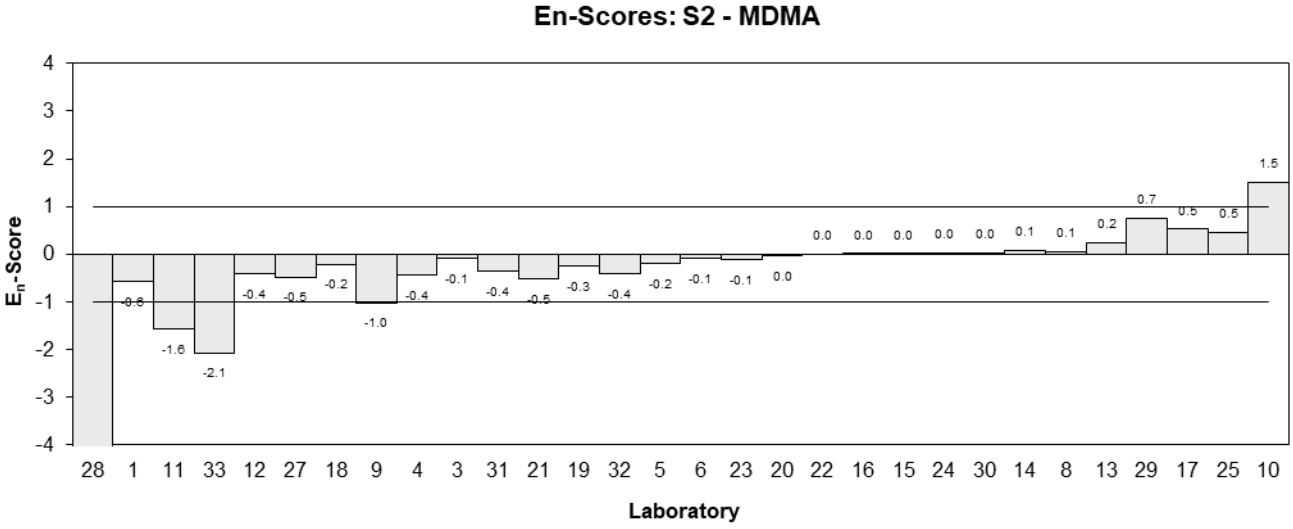

En-Scores: S2 - MDMA
En-Score
Laboratory
28 1 11 33 12 27 18 9 4 3 31 21 19 32 5 6 23 20 22 16 15 24 30 14 8 13 29 17 25 10

Figure 3

Table 7

Sample Details

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

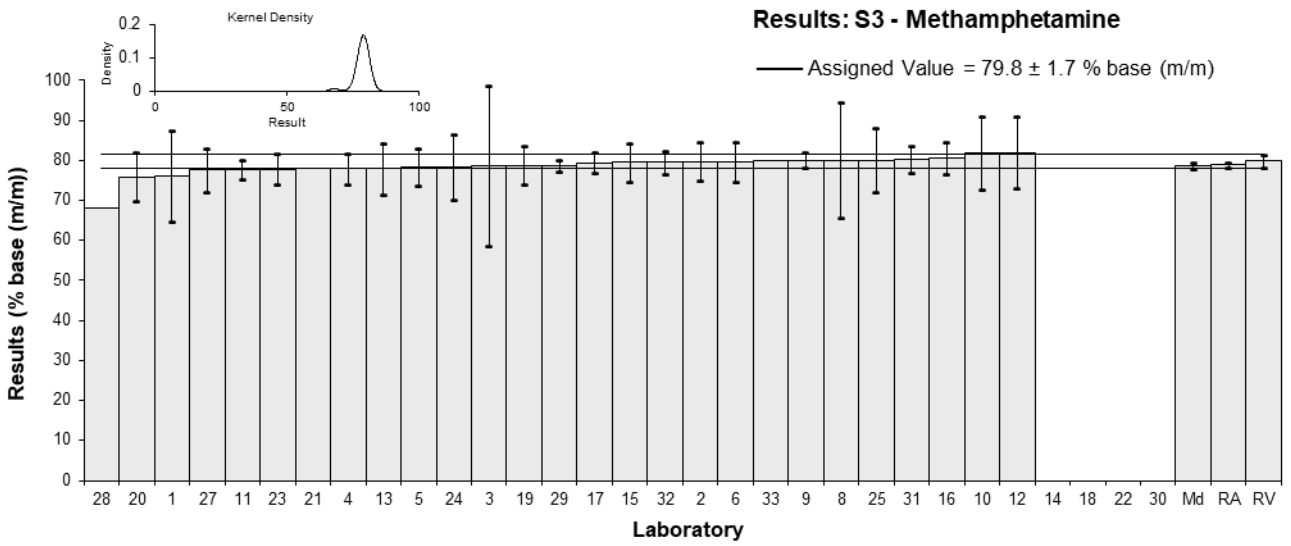
Participant Results

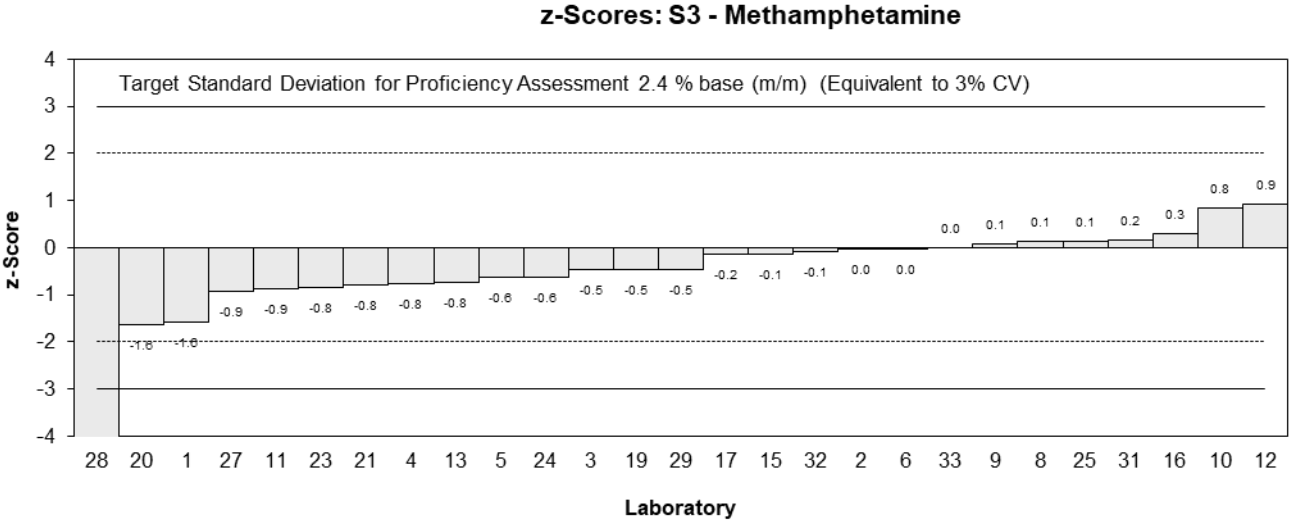
Lab. Code	Result	Uncertainty	z	E_n
1	76	11.4	-1.59	-0.33
2	79.7	4.8	-0.04	-0.02
3	78.7	20	-0.46	-0.05
4	77.96	3.9	-0.77	-0.43
5	78.3	4.7	-0.63	-0.30
6	79.7	5	-0.04	-0.02
8	80.1	14.4	0.13	0.02
9	80	1.9	0.08	0.08
10	81.8	9.2	0.84	0.21
11	77.7	2.5	-0.88	-0.69
12	82	9	0.92	0.24
13	78	6.40	-0.75	-0.27
14	NR	NR		
15	79.5	4.9	-0.13	-0.06
16	80.53	4	0.30	0.17
17	79.44	2.62	-0.15	-0.12
18	NR	NR		
19	78.7	4.8	-0.46	-0.22
20	75.9	6.1	-1.63	-0.62
21	77.9	NR	-0.79	-1.12
22	NR	NR		
23	77.8	3.9	-0.84	-0.47
24	78.3	8.1	-0.63	-0.18
25	80.1	8.01	0.13	0.04
27	77.6	5.4	-0.92	-0.39
28	68	NR	-4.93	-6.94
29	78.7	1.5	-0.46	-0.49
30	NR	NR		
31	80.2	3.3	0.17	0.11
32	79.6	2.87	-0.08	-0.06
33	79.8	NR	0.00	0.00

Statistics

Assigned Value	79.8	1.7
Reference Value	79.8	1.7
Robust Average	78.9	0.7
Median	78.7	0.7
Mean	78.6	
N	27	
Max	82	
Min	68	
Robust SD	1.5	
Robust CV	1.9%	

Assigned value is the reference value as determined by qNMR spectroscopy.


Results: S3 - Methamphetamine
Assigned Value = 79.8 ± 1.7 % base (m/m)
Kernel Density
Density
Result
Results (% base (m/m))
Laboratory
28 20 1 27 11 23 21 4 13 5 24 3 19 29 17 15 32 2 6 33 9 8 25 31 16 10 12 14 18 22 30 Md RA RV


z-Scores: S3 - Methamphetamine
Target Standard Deviation for Proficiency Assessment 2.4 % base (m/m) (Equivalent to 3% CV)
z-Score
Laboratory
28 20 1 27 11 23 21 4 13 5 24 3 19 29 17 15 32 2 6 33 9 8 25 31 16 10 12

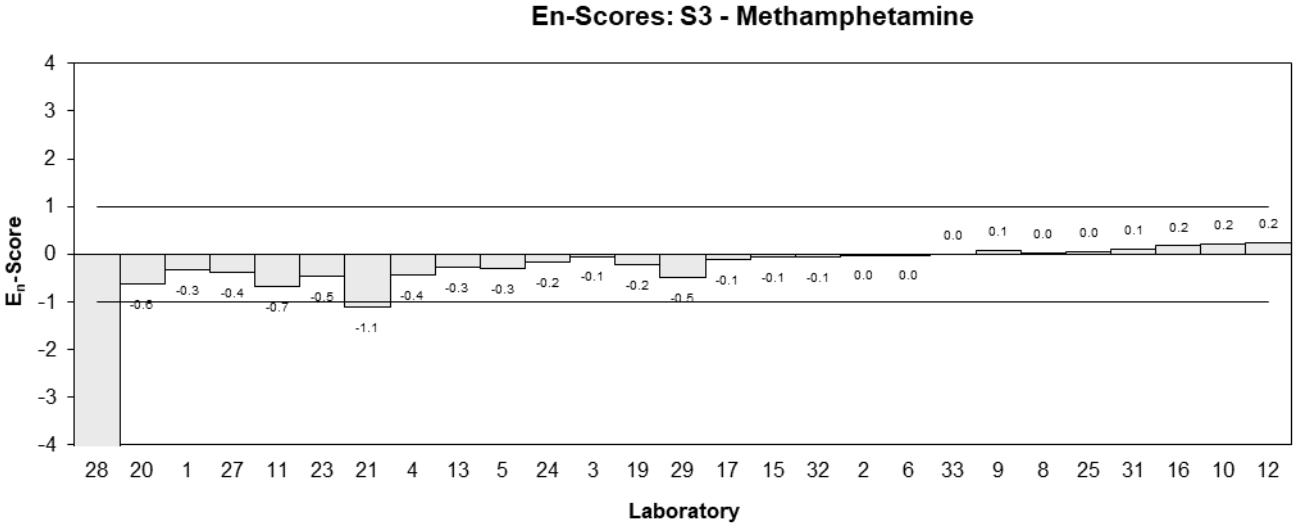

En-Scores: S3 - Methamphetamine
En-Score
Laboratory
28 20 1 27 11 23 21 4 13 5 24 3 19 29 17 15 32 2 6 33 9 8 25 31 16 10 12

Figure 4

Table 8

Sample Details

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

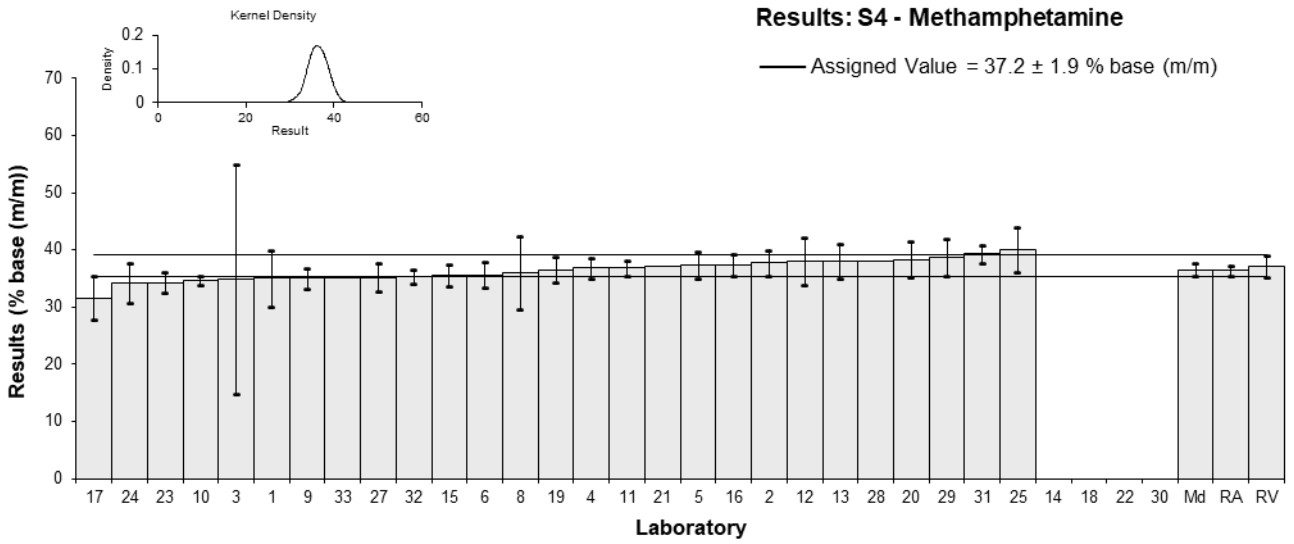
Participant Results

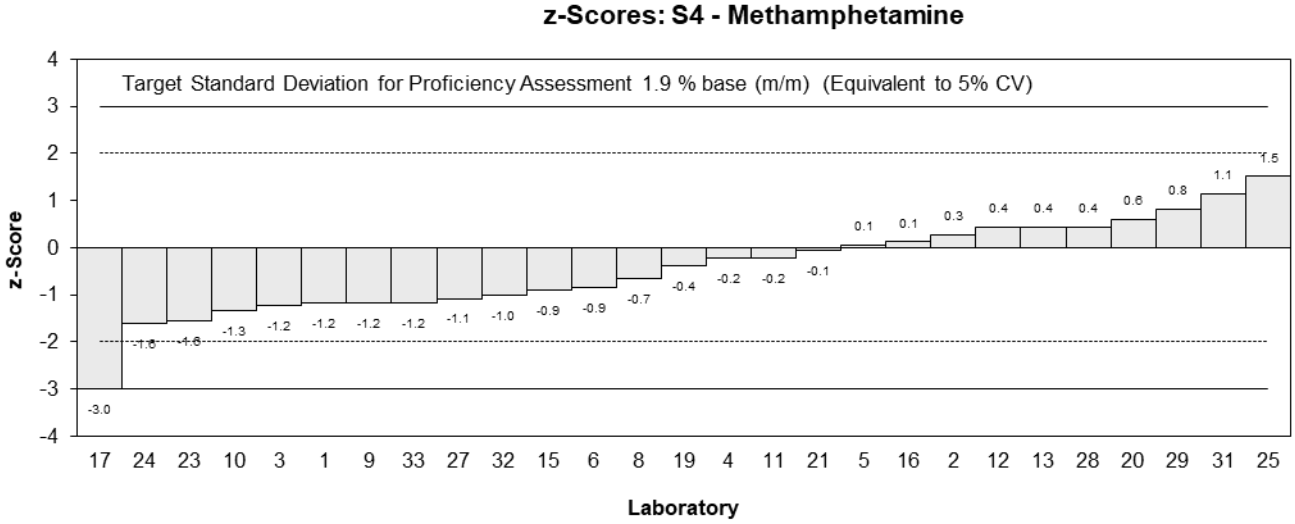
Lab. Code	Result	Uncertainty	z	E_n
1	35	4.9	-1.18	-0.42
2	37.7	2.3	0.27	0.17
3	34.9	20	-1.24	-0.11
4	36.8	1.84	-0.22	-0.15
5	37.3	2.3	0.05	0.03
6	35.6	2.2	-0.86	-0.55
8	36	6.5	-0.65	-0.18
9	35	1.7	-1.18	-0.86
10	34.7	0.8	-1.34	-1.21
11	36.8	1.4	-0.22	-0.17
12	38	4.1	0.43	0.18
13	38	3.10	0.43	0.22
14	NR	NR		
15	35.5	1.9	-0.91	-0.63
16	37.42	1.9	0.12	0.08
17	31.62	3.89	-3.00	-1.29
18	NR	NR		
19	36.5	2.2	-0.38	-0.24
20	38.3	3.1	0.59	0.30
21	37.1	NR	-0.05	-0.05
22	NR	NR		
23	34.3	1.7	-1.56	-1.14
24	34.2	3.5	-1.61	-0.75
25	40.0	4.0	1.51	0.63
27	35.2	2.5	-1.08	-0.64
28	38	NR	0.43	0.42
29	38.7	3.2	0.81	0.40
30	NR	NR		
31	39.3	1.6	1.13	0.85
32	35.3	1.27	-1.02	-0.83
33	35.0	NR	-1.18	-1.16

Statistics

Assigned Value	37.2	1.9
Reference Value	37.2	1.9
Robust Average	36.4	0.9
Median	36.5	1.1
Mean	36.4	
N	27	
Max	40	
Min	31.62	
Robust SD	1.8	
Robust CV	5.1%	

Assigned value is the reference value as determined by qNMR spectroscopy.


Kernel Density
Density
Result
Results: S4 - Methamphetamine
Assigned Value = 37.2 ± 1.9 % base (m/m)
Results (% base (m/m))
Laboratory
17 24 23 10 3 1 9 33 27 32 15 6 8 19 4 11 21 5 16 2 12 13 28 20 29 31 25 14 18 22 30 Md RA RV


z-Scores: S4 - Methamphetamine
Target Standard Deviation for Proficiency Assessment 1.9 % base (m/m) (Equivalent to 5% CV)
z-Score
Laboratory
17 24 23 10 3 1 9 33 27 32 15 6 8 19 4 11 21 5 16 2 12 13 28 20 29 31 25

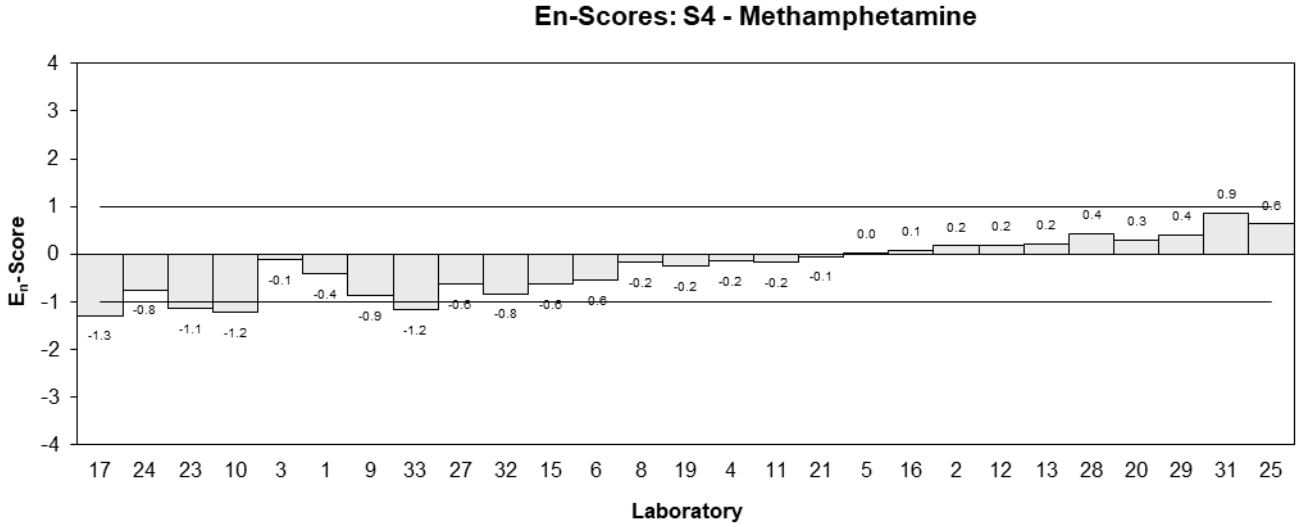

En-Scores: S4 - Methamphetamine
En-Score
Laboratory
17 24 23 10 3 1 9 33 27 32 15 6 8 19 4 11 21 5 16 2 12 13 28 20 29 31 25

Figure 5

Table 9 Participants' Identification of Cutting Agents*

Lab. Code	Cutting Agents			
	S1	S2	S3	S4
Preparation	Sucrose	Cellulose	N/A	Dimethyl sulfone
1	none	none	none	none
2				Dimethyl sulfone
3	Saccharose			Dimethylsulfone
4				
5	Nil	Nil	Nil	Dimethyl sulfone
6	Sucrose			Dimethylsulfone
8	Sucrose			Dimethylsulfone
9				Dimethylsulfone (not confirmed)
10	sucrose			MSM
11				Dimethylsulfone
12	None found	None found	None found	None found
13	Sucrose			Dimethylsulfone
14	saccharose			
15				MSM
16				dimethylsulfone
17	saccharose			
18				
19	Nil	Nil	Nil	Dimethyl sulfone
20	Not determined	Not determined	Not determined	Not determined
21	sucrose			dimethylsulfone
22	sucrose	Cellulose		Dimethylsulfone
23				
24				
25	Sucrose			Dimethyl sulfone
27				
28				
29				
30				
31	sucrose	none identifiable	none detected	dimethyl sulfone
32				dimethylsulfone
33			Dimethyl sulfone	Dimethyl sulfone

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

6 DISCUSSION OF RESULTS

6.1 Assigned Value

The reference values obtained using qNMR spectroscopy were used as the assigned values for all samples. Maleic acid (NMI CRM QNMR010) was used as the internal standard. The uncertainty of the reference value was estimated in accordance with the ISO GUM.[9] Additional details are given in Appendix 1.

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).

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). One participant reported using the NATA GAG Estimating and Reporting MU as their guide; NATA no longer publishes this document.[10]

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.[7]

Of 114 numeric results, 104 (91%) were reported with an associated expanded uncertainty. Laboratories **28** and **33** did not report any uncertainties; these participants were not accredited to ISO/IEC 17025. Laboratory **21** did not report uncertainties for Samples S3 and S4; they reported that they were not accredited for the method of analysis used for these samples.

For this PT study, participants were instructed to report uncertainties as % drug as base (m/m). Laboratory **3** reported all their uncertainties as '20' and Laboratory **30** reported all their uncertainties as '15'; these participants may have reported relative uncertainties instead.

The magnitudes of reported uncertainties were within the range 0.9% to 127% relative to the reported result. In general, an expanded uncertainty of less than 3% relative may be unrealistically small for a routine measurement, while an expanded uncertainty of over 10% relative may be too large and not fit for purpose. Of the 104 expanded MUs reported, ten were less than 3% relative, while 33 were greater than 10% relative.

Uncertainties associated with results returning a satisfactory *z*-score but an unsatisfactory E_n-score may have been underestimated.

In some cases, results were reported with an inappropriate number of significant figures. Including too many significant figures may inaccurately reflect the precision of measurements. 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 31.62 ± 3.89%, it is recommended to report 31.6 ± 3.9%.[8]

6.3 *z*-Score

Target SDs equivalent to 3% PCV were used to calculate *z*-scores for Samples S1, S2 and S3. A partial homogeneity test for Sample S4 indicated there was slightly greater variability in these samples, and therefore a target SD equivalent to 5% PCV was used to calculate *z*-scores for Sample S4. The CVs predicted by the Thompson-Horwitz equation,[6] between-laboratory CVs (as robust CV) and target SDs (as PCV) obtained in this study are presented for comparison in Table 10.

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

Sample	Analyte	Assigned Value (% base (m/m))	Thompson-Horwitz CV (%)	Between-Laboratory CV* (%)	Target SD (as PCV) (%)
S1	MDMA	16.2	2.5	2.8	3
S2	MDMA	65.9	1.2	2.7	3
S3	Methamphetamine	79.8	1.1	1.9	3
S4	Methamphetamine	37.2	1.6	5.1	5

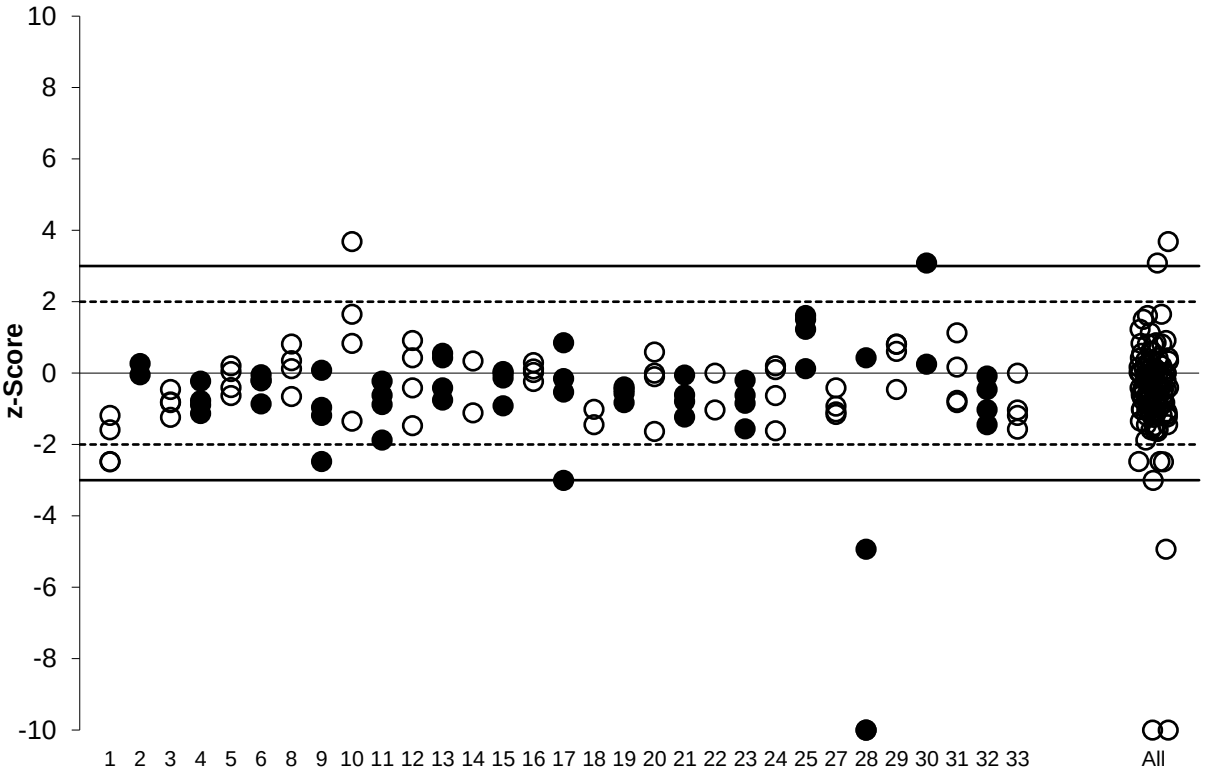
* Robust between-laboratory CV with outliers removed, if applicable.

Of 114 results for which *z*-scores were calculated, 105 (92%) returned a *z*-score of $|z| \leq 2.0$, indicating a satisfactory performance.

Twenty-five participants: **2** (methamphetamine only), **3**, **4**, **5**, **6**, **8**, **11**, **12**, **13**, **14** (MDMA only), **15**, **16**, **18** (MDMA only), **19**, **20**, **21**, **22** (MDMA only), **23**, **24**, **25**, **27**, **29**, **31**, **32** and **33** returned satisfactory *z*-scores for all reported numeric results.

Six participants returned at least one questionable or unsatisfactory *z*-score. The MDMA results from Laboratory **28** were extremely low (59% and 38% of the assigned value for Samples S1 and S2 respectively).

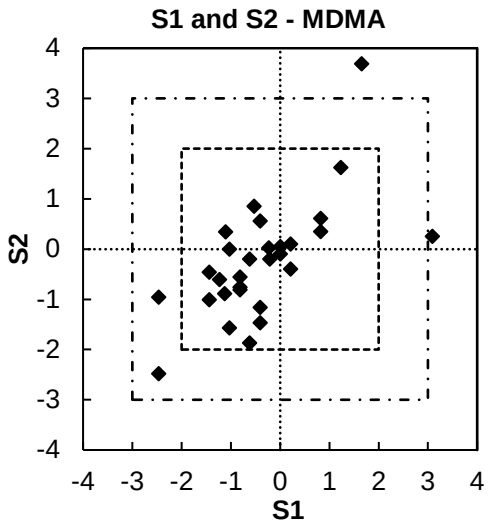
The dispersal of participants' *z*-scores is presented graphically in Figure 6.



z-Scores less than -10.0 have been plotted at -10.0.

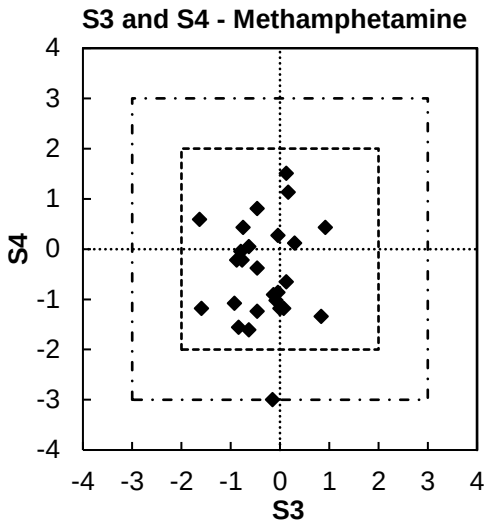
Figure 6 *z*-Score Dispersal by Laboratory

Scatter plots of *z*-scores for MDMA in Samples S1 and S2, and methamphetamine in Samples S3 and S4, are presented in Figures 7 and 8 respectively. Scores are predominantly in the upper right and 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 the zero demonstrate excellent repeatability and accuracy.



Laboratory 28 is off-scale.

Figure 7 *z*-Score Scatter Plot – MDMA



Laboratories 28 is off-scale.

Figure 8 *z*-Score Scatter Plot – Methamphetamine

6.4 E_n-Score

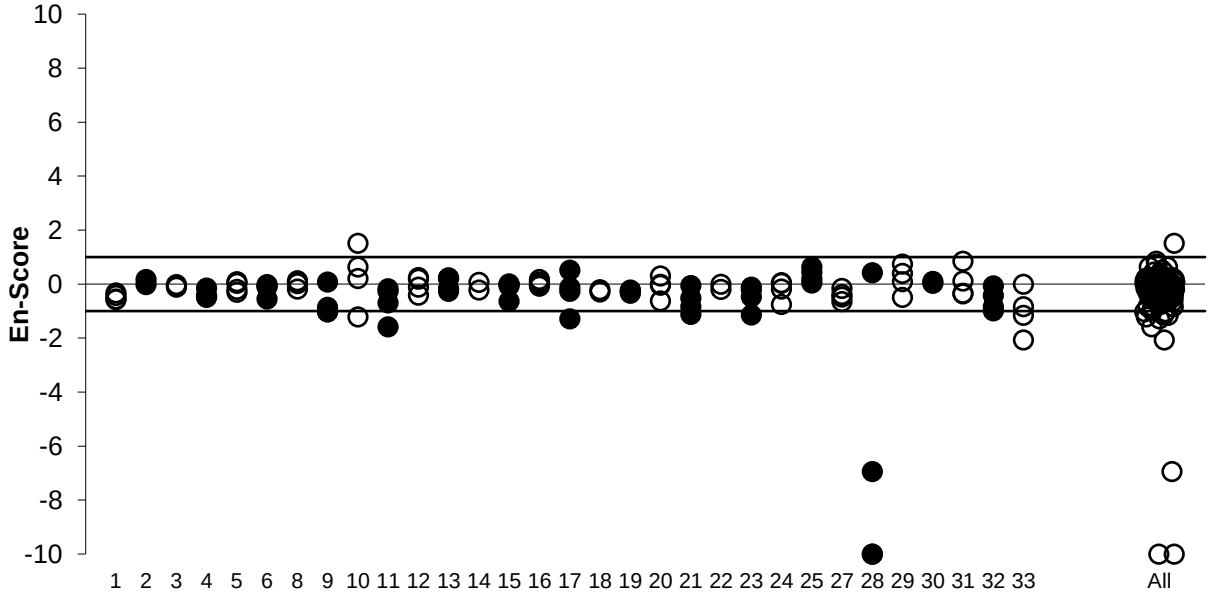
E_n-scores can be interpreted in conjunction with *z*-scores, as an unsatisfactory E_n-score can either be caused by issues with measurement, or uncertainty, or both. Where a participant did not report an expanded uncertainty with a result, an expanded uncertainty of zero (0) was used to calculate the E_n-score.

Of 114 results for which E_n-scores were calculated, 101 (89%) returned an E_n-score of $|E_n| \leq 1.0$, indicating agreement of the participant's result with the assigned value within their respective uncertainties.

Twenty-three participants: **1**, **2** (methamphetamine only), **3**, **4**, **5**, **6**, **8**, **12**, **13**, **14** (MDMA only), **15**, **16**, **18** (MDMA only), **19**, **20**, **22** (MDMA only), **24**, **25**, **27**, **29**, **30** (MDMA only), **31** and **32** returned satisfactory E_n-scores for all reported numeric results.

Eight participants returned at least one unsatisfactory E_n-score.

The dispersal of participants' E_n-scores is presented graphically in Figure 9.



E_n-scores less than -10.0 have been plotted at -10.0.

Figure 9 E_n-Score Dispersal by Laboratory

6.5 Identification of Cutting Agents

Samples S1 and S2 were prepared by adding sucrose and cellulose respectively to MDMA hydrochloride. Sample S3 was prepared from methamphetamine hydrochloride, and no cutting agents were added. Sample S4 was prepared by adding dimethyl sulfone to methamphetamine hydrochloride.

Participants were requested to identify the cutting agents in the samples if part of their routine analysis, and the results reported are presented in Table 9.

Twenty participants (65%) reported on the identity of at least one cutting agent in the samples.

Laboratory **22** correctly identified all cutting agents in this study.

For Sample S1, 11 participants correctly identified sucrose as the cutting agent (Laboratories **3**, **6**, **8**, **10**, **13**, **14**, **17**, **21**, **22**, **25**, and **31**).

For Sample S2, only one participant correctly identified cellulose as the cutting agent (Laboratory **22**). As with previous PTs, generally fewer participants correctly identify insoluble cutting agents such as cellulose.

For Sample S3, one participant (Laboratory **33**) reported dimethyl sulfone as a cutting agent. This may have been a small impurity in the original methylamphetamine matrix.

For Sample S4, 18 participants correctly identified dimethyl sulfone as the cutting agent (Laboratories **2**, **3**, **5**, **6**, **8**, **9**, **10**, **11**, **13**, **15**, **16**, **19**, **21**, **22**, **25**, **31**, **32** and **33**).

6.6 Participants' Analytical Methods

Participants were requested to analyse the samples using their routine 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	1, 2, 4 (methamphetamine), 5, 6, 9, 10, 11, 13, 15, 16 (MDMA), 17 (identification only), 19, 20, 21 (MDMA), 23, 24, 25, 27, 30, 31, 32
	Not accredited / NR	3, 4 (MDMA), 8, 12, 14, 16 (methamphetamine), 18, 21 (methamphetamine), 22, 28, 29, 33
Average Sample Mass Used (mg)	< 20	2 (methamphetamine), 8, 13, 14 (MDMA), 15, 20, 21 (methamphetamine), 23, 28, 31, 32
	20 – 30	4 (MDMA), 5 (methamphetamine), 11, 12, 16, 17, 18 (MDMA), 21 (MDMA), 22 (MDMA), 24, 25, 30 (MDMA)
	31 – 50	1, 3, 4 (methamphetamine), 5 (MDMA), 9, 19, 27, 29, 33
	51 – 100	6
	> 100	10

		Lab. Code
Conversion to Base?	Yes	3, 4, 8, 9, 10, 15, 16, 18 (MDMA), 21 (MDMA), 23, 25, 27, 28, 29, 31, 32, 33
	No	2 (Methamphetamine), 5, 6, 11, 12, 13, 14 (MDMA), 17, 19, 20, 21 (Methamphetamine), 24
	NR	1, 22 (MDMA), 30 (MDMA)
Instrument Used for Quantification	HPLC-DAD	2 (methamphetamine), 4, 10 (S4 methamphetamine), 12, 13, 14 (MDMA), 17, 22 (MDMA), 24, 25, 29, 30 (MDMA)
	HPLC-UV/Vis	9, 20
	UPLC-DAD	5, 6, 10 (MDMA, S3 methamphetamine), 11, 15, 19, 27, 33
	UPLC-MS/MS	1
	GC-FID	8, 16, 21 (MDMA), 23, 31
	GC-MS	28
	QNMR	3, 18 (MDMA), 21 (methamphetamine), 32
Solvent	Acetonitrile/Water(/Other)	1, 2 (methamphetamine), 13, 17, 22 (MDMA)
	Methanol	6, 8, 11, 12, 20, 23, 27, 28, 29
	Water	4, 5, 10, 19, 25
	Other	3, 9, 14 (MDMA), 15, 16, 18 (MDMA), 21, 24, 30 (MDMA), 31, 32, 33
Sources of Calibration Standard (MDMA)	NMI Australia	6, 11, 13, 15, 20, 22, 25, 31, 33
	Lipomed	5, 8, 9, 14, 16, 17, 19, 23, 27, 30
	Other	4, 10, 12, 21, 24, 28
	NR	1, 3, 18, 29, 32
Sources of Calibration Standard (methamphetamine)	NMI Australia	2, 6, 11, 15, 25, 31, 33
	Lipomed	5, 8, 9, 16, 17, 19, 23, 27, 28
	Sigma Aldrich	1, 4, 12, 13
	Other	10, 20, 24
	NR	3, 29, 21, 32

Plots of the *z*-scores versus various parameters are presented in Figures 10 to 14 (extreme outliers have been removed). A variety of methodologies were used by participants in this study, and no significant trends were observed.

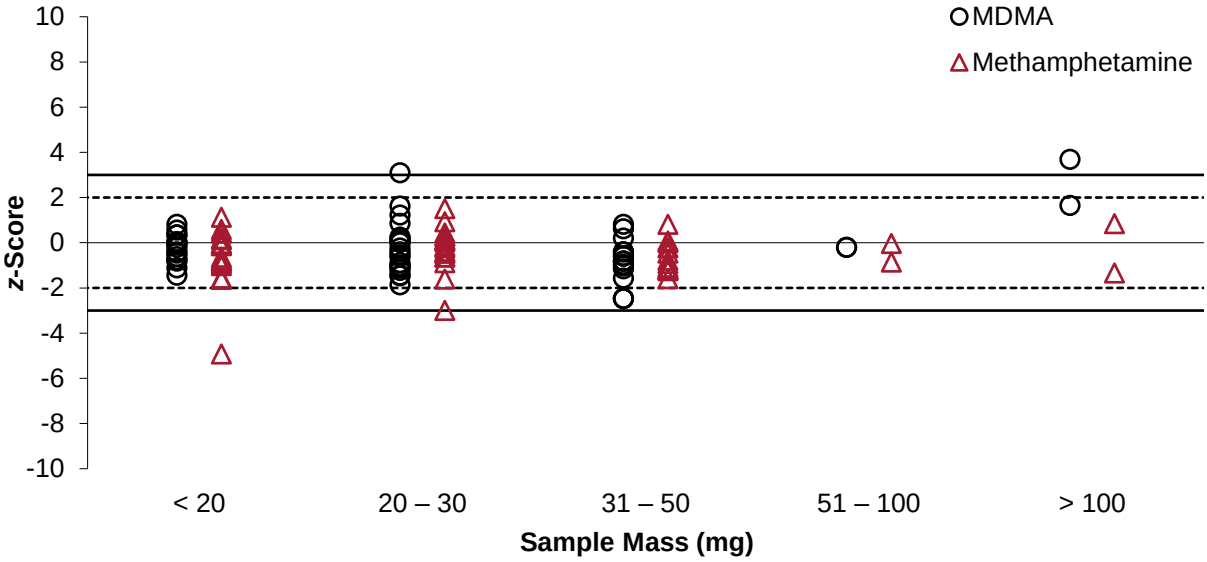


Figure 10 *z*-Score vs Sample Mass Used for Analysis

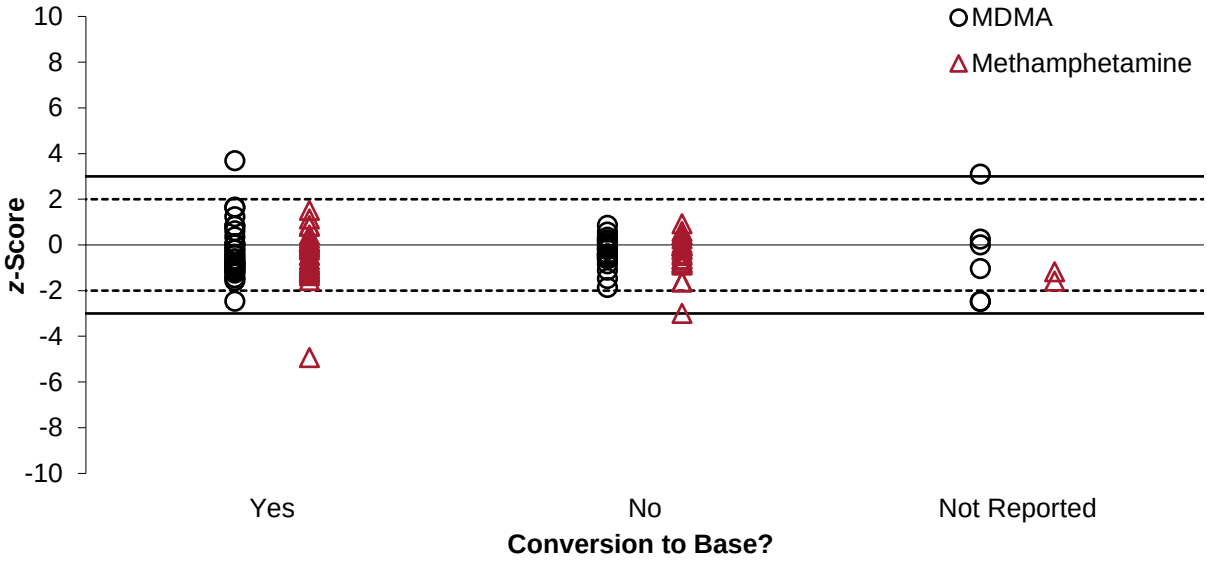


Figure 11 *z*-Score vs Sample Processing

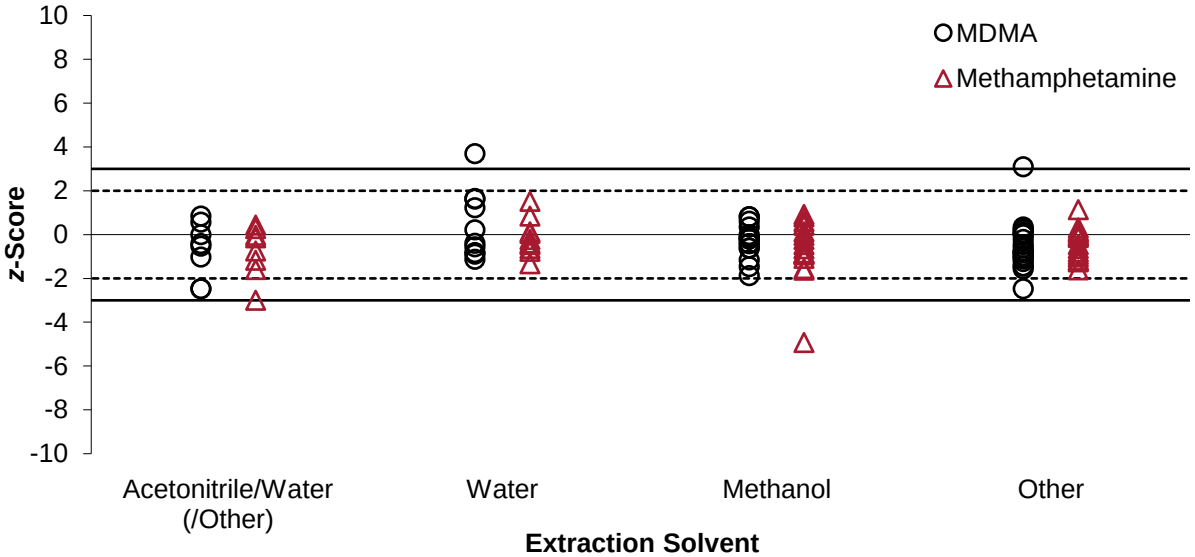


Figure 12 *z*-Score vs Extraction Solvent

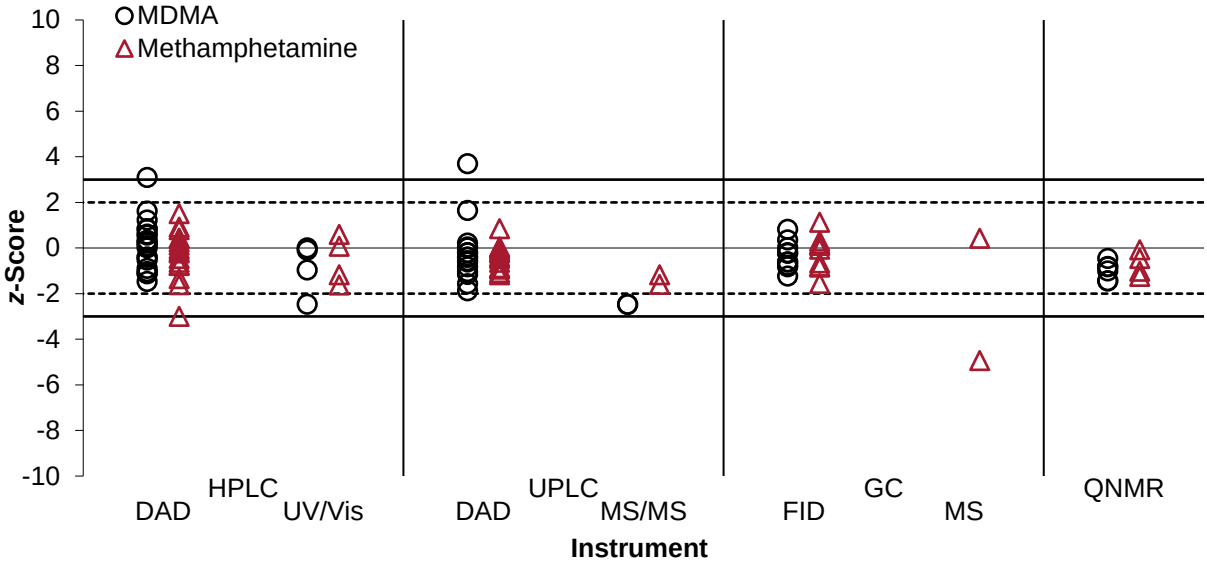


Figure 13 *z*-Score vs Measurement Instrument

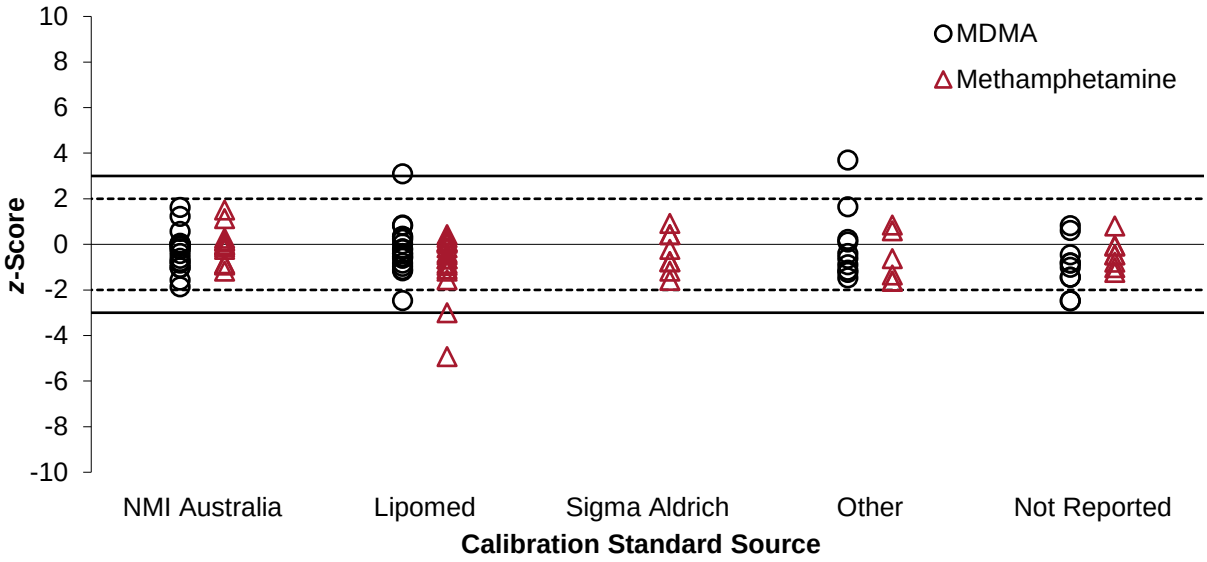


Figure 14 *z*-Score vs Calibration Standard Source

6.7 Comparison of Results and Date of Analysis

As there were delays with sample delivery to some participants, the samples were analysed by participants over approximately 3.5 months. No trend was found between when the samples were analysed and the results obtained (Figure 15; extreme outliers have been removed).

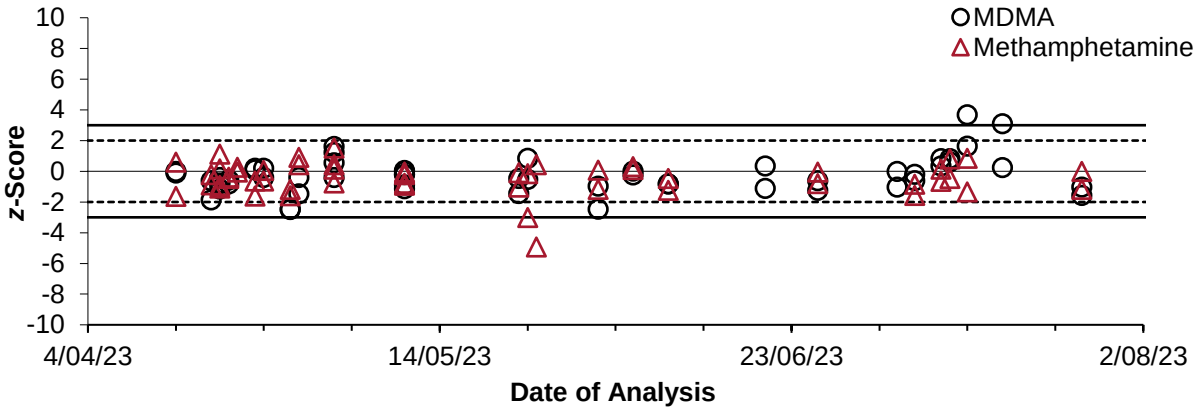


Figure 15 *z*-Score vs Sample Analysis Date

6.8 Comparison with Previous PT Studies

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 – 2023 (last ten studies with MDMA) is presented in Figure 16. The average proportion of satisfactory *z*-scores and E_n-scores over this period is 76% and 67% respectively. While each PT study contains a different group of participants, in general, participants' performance has improved over this period.

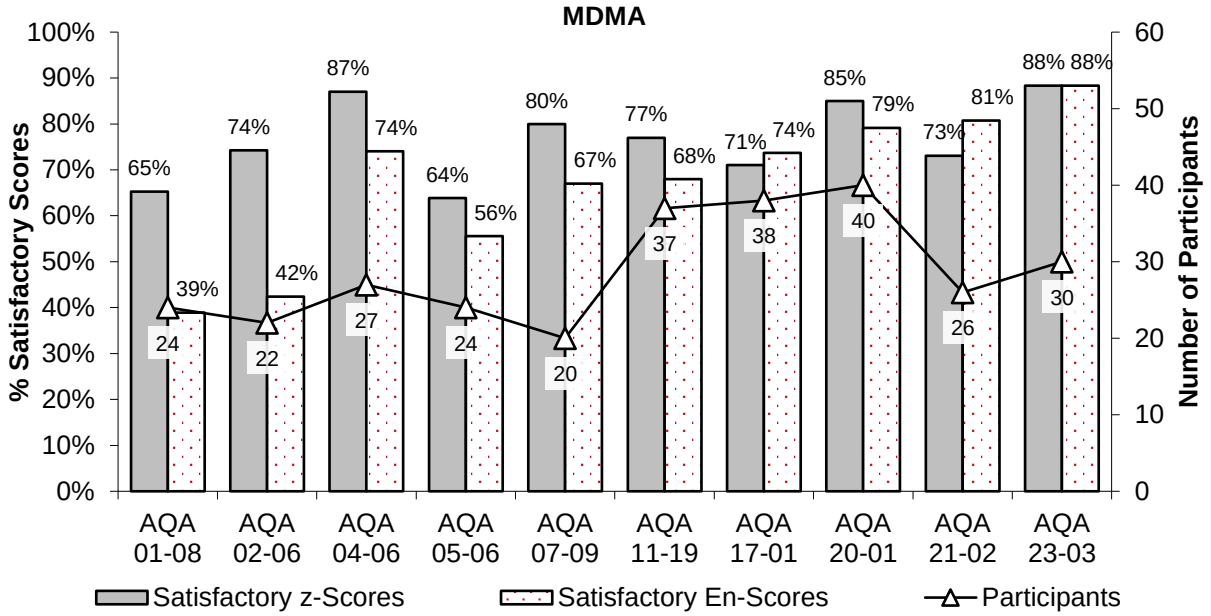


Figure 16 Summary of Participants' Performance in NMI MDMA PT Studies

A summary of the satisfactory performance, presented as a percentage of the total number of scores, obtained by PT study participants for methamphetamine from 2014 – 2023 (last ten studies with methamphetamine) is presented in Figure 17. The average proportion of satisfactory *z*-scores and E_n-scores over this period is 86% and 81% respectively. Overall, participants' performance with methamphetamine quantitation has been better than for MDMA.

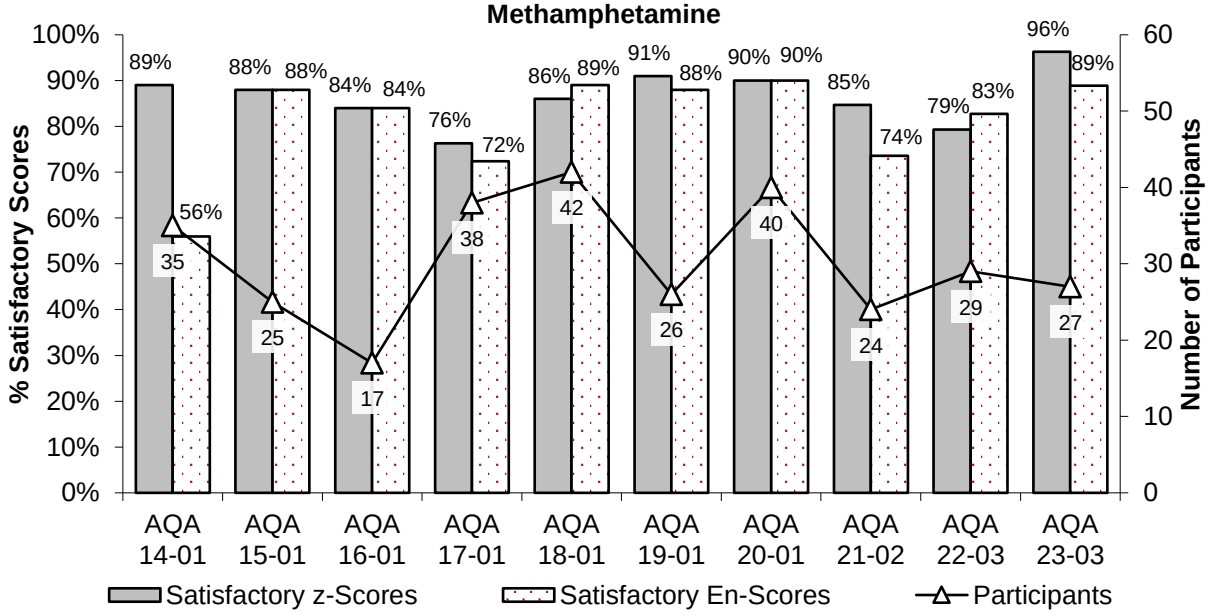


Figure 17 Summary of Participants' Performance in NMI Methamphetamine PT Studies

A number of participants have consistently participated in NMI MDMA and methamphetamine PT studies, and individual performance history reports are emailed to each participant at the end of every PT 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.

A summary of individual laboratory's performances over the last five NMI MDMA PT studies is presented in Figures 18 and 19 for Australian and international laboratories respectively. Three Australian and two international laboratories have achieved satisfactory *z*-scores across all MDMA samples in PT studies participated in over this period.

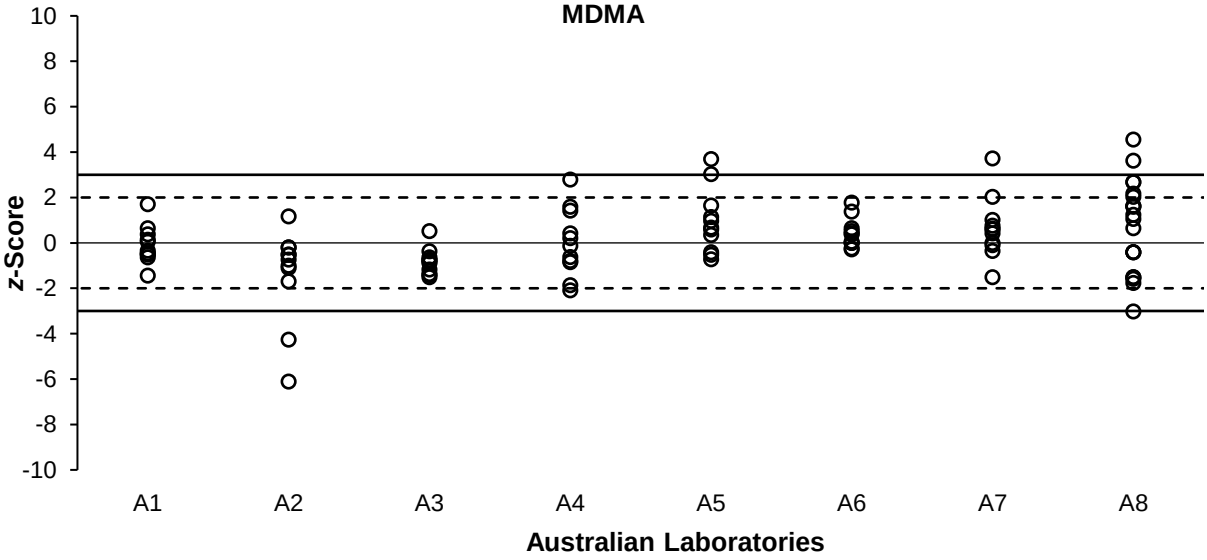
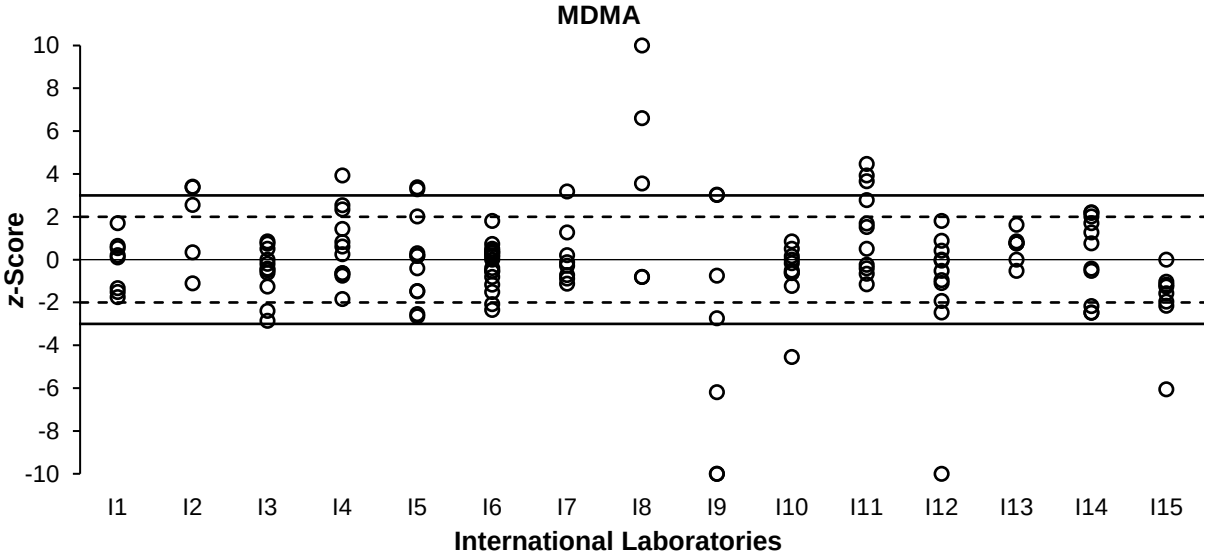


Figure 18 Summary of Australian Participants' *z*-Scores in NMI MDMA PT Studies



z-Scores greater than 10.0 or less than -10.0 have been plotted at 10.0 or -10.0 respectively.

Figure 19 Summary of International Participants' *z*-Scores in NMI MDMA PT Studies

A comparison of all results from Australian and international laboratories in NMI MDMA PT studies over the last five studies is presented in Figure 20. Overall, Australian laboratories have achieved a higher proportion of satisfactory *z*-scores over this period.

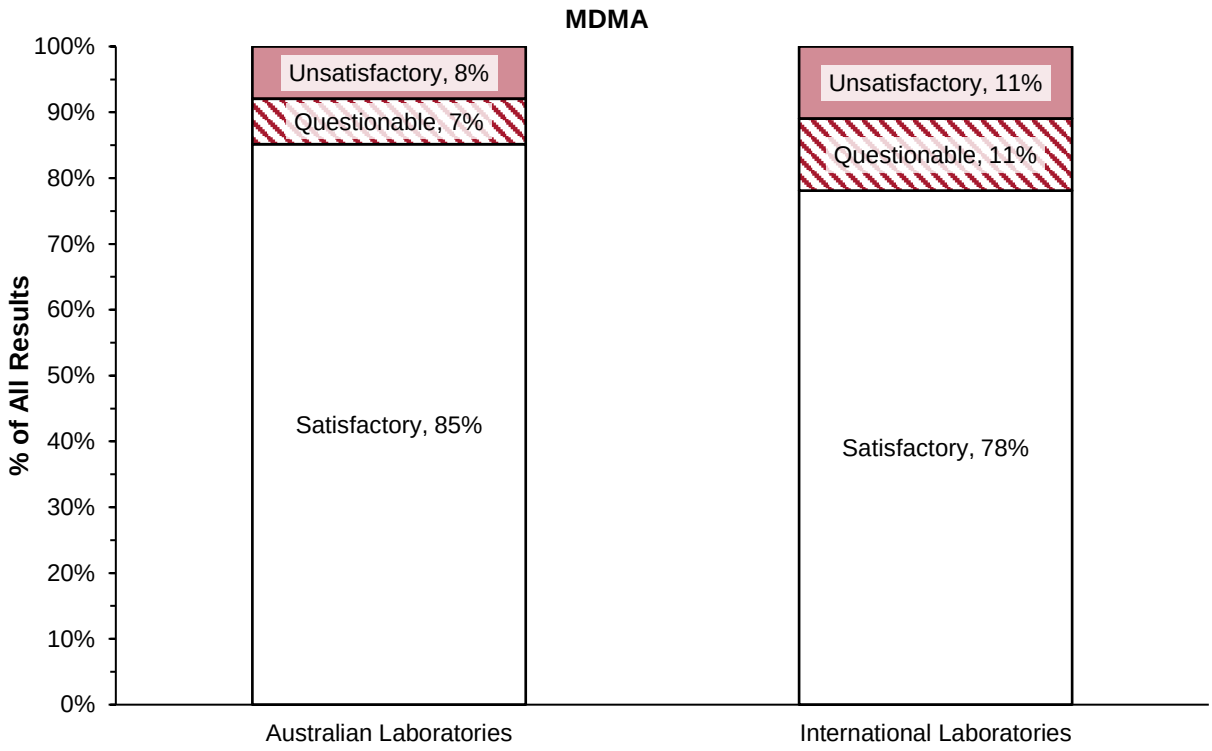


Figure 20 Comparison of Australian and International Laboratories in NMI MDMA PT Studies

A summary of individual laboratory's performances over the last ten NMI methamphetamine PT studies is presented in Figures 21 and 22 for Australian and international laboratories respectively (laboratory identifiers are not the same as for Figures 18 and 19). Five Australian and two international laboratories have achieved satisfactory *z*-scores across all methamphetamine samples in PT studies participated in over this period.

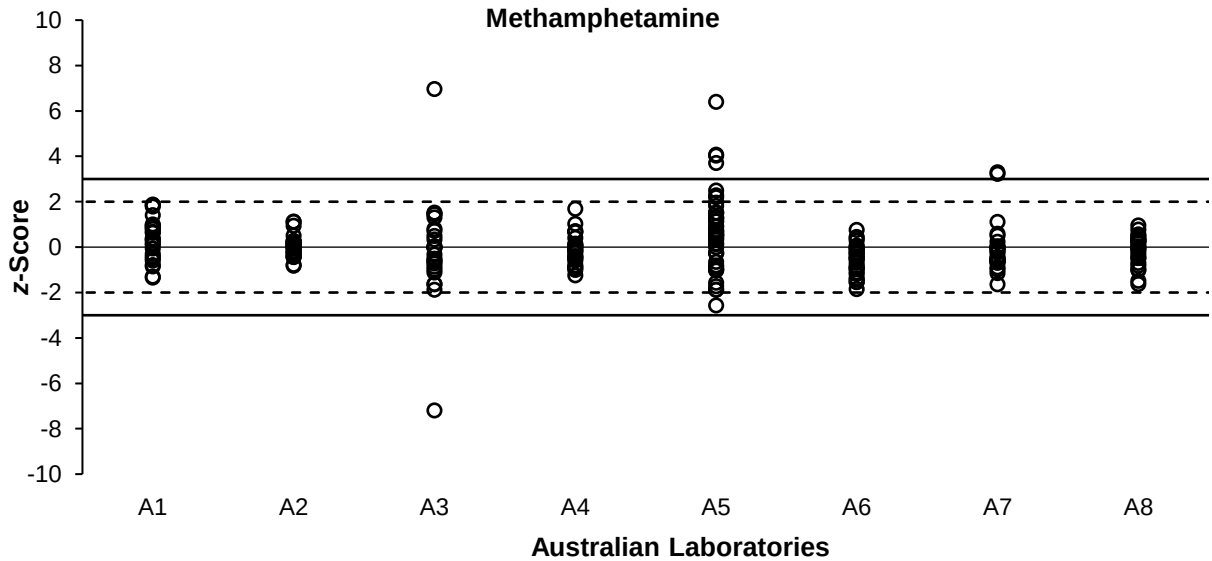


Figure 21 Summary of Australian Participants' *z*-Scores in NMI Methamphetamine PT Studies

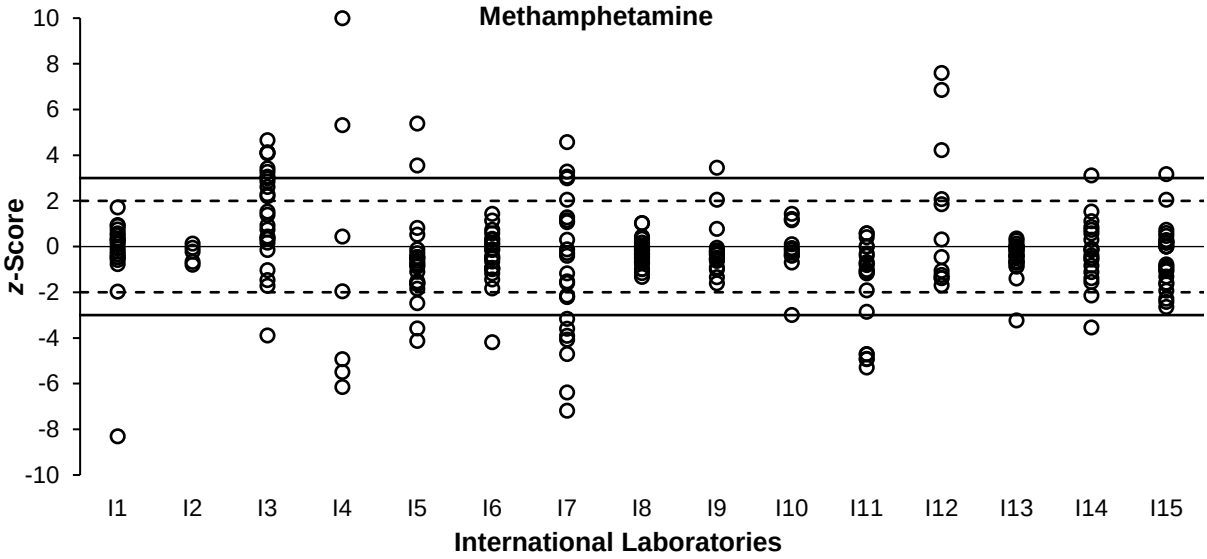


Figure 22 Summary of International Participants' *z*-Scores in NMI Methamphetamine PT Studies

A comparison of all results from Australian and international laboratories in NMI methamphetamine PT studies over the last ten studies is presented in Figure 23. Overall, Australian participants have performed well, and also have had a higher proportion of satisfactory *z*-scores over this period.

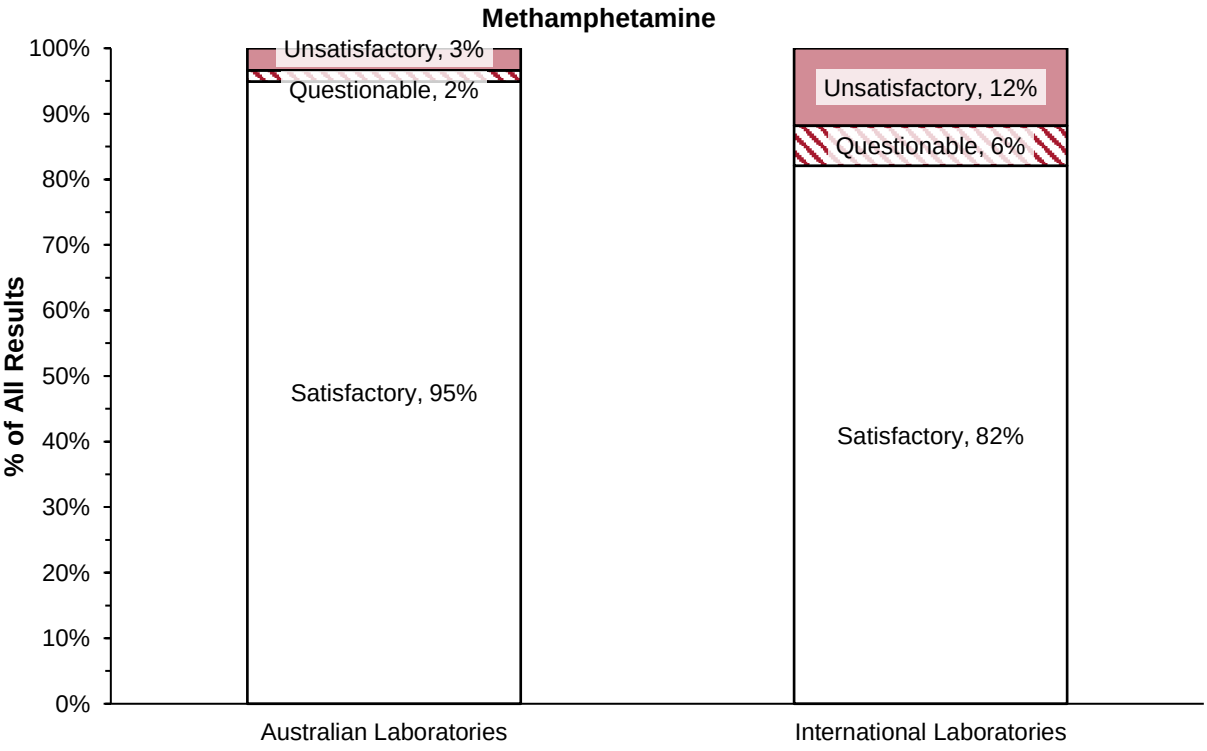


Figure 23 Comparison of Australian and International Laboratories in NMI Methamphetamine PT Studies

7 REFERENCES

Please note that for all undated references, the latest edition of the referenced document (including any amendments) applies.

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

[2] NMI, 2023, *Study Protocol for Proficiency Testing*, viewed September 2023, <https://www.industry.gov.au/sites/default/files/2020-10/cpt_study_protocol.pdf>.

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[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.

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[6] 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.

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

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

[10] NATA, 2020, *Update to Measurement Uncertainty resources*, viewed September 2023, <https://nata.com.au/news/update-to-measurement-uncertainty-resources/>

[11] Fearn, T. and Thompson, M., 2001, 'A new test for 'sufficient homogeneity'', *Analyst*, vol. 126, pp. 1414-1417.

APPENDIX 1 REFERENCE VALUES AND HOMOGENEITY TESTING

Three sample vials from each of Samples S1, S3 and S4, and five sample vials from Sample S2, were analysed in duplicate for the purpose of assigning reference values. Measurements were made using qNMR spectroscopy with maleic acid as the internal standard. A maleic acid CRM was obtained from NMI, Chemical Reference Materials. 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)
NMI, Chemical Reference Materials	QNMR010	10-Q-02	98.8 ± 0.12%

Samples were prepared gravimetrically, by accurately weighing approximately 20 mg of sample and dissolving this in 900 µL of internal standard solution which was also accurately weighed. Samples were analysed on a Bruker Ascend 500 MHz NMR spectrometer, using a qNMR relaxation time of 25 s. The mass fraction of MDMA and methamphetamine was determined from the NMR response at around 1.25 ppm.

The averages of the mass fractions determined for the different vials of each sample (Tables 13 to 16) were used as the reference values and the assigned values. The standard uncertainty on the mass fraction reference value was estimated in accordance with the ISO GUM,[9] 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 values for all samples were in agreement with the robust averages of participants' results, within their respective associated uncertainties.

For Sample S2, homogeneity checks were performed based on that described by Thompson and Fearn,[11] which is also the procedure described in the International Protocol.[4] Samples were found to be sufficiently homogeneous for use in this PT study with a target SD (as PCV) of 3%.

Table 13 Reference Value for Sample S1

Vial No.	MDMA (% base (m/m))	
	Replicate 1	Replicate 2
103	16.3	15.9
119	16.3	16.2
139	16.0	16.3
Average	16.2	
CV	1.2%	

Sample S1 Reference Value: 16.2 ± 0.6% MDMA base (m/m)

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 = 2.2).[9]

Table 14 Reference Value for Sample S2

Vial No.	MDMA (% base (m/m))	
	Replicate 1	Replicate 2
209	65.4	66.2
210	66.4	66.4
213	65.7	66.1
229	65.1	66.1
233	66.1	65.9
Average	65.9	
CV	0.64%	

Thompson and Fearn Homogeneity Tests[11]

Test	Value	Critical	Result
Cochran	0.568	0.841	**Pass**
s_{an}/σ	0.222	0.500	**Pass**
s^2_{sam}	0.000	1.239	**Pass**

Sample S2 Reference Value: 65.9 ± 1.5% MDMA base (m/m)

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 = 2.1).[9]

Table 15 Reference Value for Sample S3

Vial No.	Methamphetamine (% base (m/m))	
	Replicate 1	Replicate 2
302	79.8	79.7
325	79.5	79.8
338	80.1	79.9
Average	79.8	
CV	0.22%	

Sample S3 Reference Value: 79.8 ± 1.7% methamphetamine base (m/m)

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 = 2.2).[9]

Table 16 Reference Value for Sample S4

Vial No.	Methamphetamine (% base (m/m))	
	Replicate 1	Replicate 2
408	37.0	37.3
425	38.0	37.8
443	35.8	37.2
Average	37.2	
CV	2.0%	

Sample S4 Reference Value: 37.2 ± 1.9% methamphetamine base (m/m)

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 = 2.8).[9]

APPENDIX 2 ROBUST AVERAGE AND ASSOCIATED UNCERTAINTY, *z*-SCORE AND E_n-SCORE CALCULATIONS

A2.1 Robust Average and Associated Uncertainty

Robust averages were calculated using the procedure described in ISO 13528.[5] The associated uncertainties were estimated as according to Equation 4.

$$u_{rob\ av} = \frac{1.25 \times S_{rob\ av}}{\sqrt{p}} \quad \textit{Equation 4}$$

where:

$u_{rob\ av}$ is the standard uncertainty of the robust average

$S_{rob\ av}$ 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 two at approximately 95% confidence level.

A worked example is set out below in Table 17.

Table 17 Uncertainty of Robust Average of MDMA in Sample S2

No. results (p)	29
Robust Average	65.3% base (m/m)
$S_{rob\ average}$	1.8% base (m/m)
$u_{rob\ average}$	0.4% base (m/m)
k	2
$U_{rob\ average}$	0.8% base (m/m)

Therefore, the robust average for Sample S2 MDMA is 65.3 ± 0.8% 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 (Section 4).

A worked example is set out below in Table 18.

Table 18 *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
15 ± 2.1	16.2 ± 0.6	3% as PCV, or: 0.03 × 16.2 = 0.486% base (m/m)	$z = \frac{15 - 16.2}{0.486} = -2.47$	$E_n = \frac{15 - 16.2}{\sqrt{2.1^2 + 0.6^2}} = -0.55$

APPENDIX 3 ACRONYMS AND ABBREVIATIONS

CITAC	Cooperation on International Traceability in Analytical Chemistry
CRM	Certified Reference Material
CV	Coefficient of Variation
DAD	Diode Array Detection
EA	European Accreditation
FID	Flame Ionisation Detection
GAG	General Accreditation Guidance (NATA)
GC	Gas Chromatography
GUM	Guide to the expression of Uncertainty in Measurement
HPLC	High Performance Liquid Chromatography
IEC	International Electrotechnical Commission
ISO	International Organization for Standardization
Max	Maximum value
Md	Median value
MDMA	3,4-Methylenedioxymethamphetamine
Min	Minimum value
MS	Mass Spectrometry
MS/MS	Tandem Mass Spectrometry
MU	Measurement Uncertainty
N	Number of numeric results
NATA	National Association of Testing Authorities, Australia
NMI	National Measurement Institute, Australia
NMR	Nuclear Magnetic Resonance
NR	Not Reported
NT	Not Tested
PCV	Performance Coefficient of Variation
PDA	Photodiode Array
PT	Proficiency Testing
qNMR	Quantitative NMR
RA	Robust Average
RM	Reference Material
RV	Reference Value
SD	Standard Deviation
SI	International System of Units
SS	Spiked Samples
UPLC	Ultra Performance Liquid Chromatography
UV/Vis	Ultraviolet/Visible spectroscopy

END OF REPORT