Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

CIPM MRA

NATA
ACCREDITED FOR TECHNICAL COMPETENCE

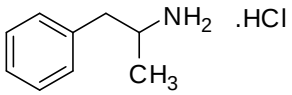
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D736c: (±)-Amphetamine hydrochloride

Report ID: D736c.2021.01 (Bottled 210511)

Chemical Formula: $C_9H_{13}N.HCl$

Molecular Weight: 171.7 g/mol (HCl), 135.2 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
11-D-22	**2706-50-5 (HCl)** **300-62-9 (base)**	**98.7% ± 0.8%**

The uncertainty has been calculated according to ISO Guide 35 and is stated at the 95% confidence limit (k = 2).

IUPAC name: *(R, S)*-1-Phenyl)-2-aminopropane hydrochloride (1:1)

Expiration of certification: The property values are valid till 17 May 2026, i.e. five years from the date of re-certification provided the **unopened** material is handled and stored in accordance with the recommendations below. The material as issued in the unopened container and stored as recommended below should be suitable for use beyond this date, subject to confirmation of batch stability from the issuing body. The expiry date/shelf life does not apply to sample bottles that have been opened. In such cases it is recommended that the end-user conduct their own in-house stability trials.

Description: White powder prepared by synthesis, and certified for identity and purity by NMIA. Packaged in amber glass bottles with a septum and crimped aluminium cap or screw top cap.

Intended use: This certified reference material is suitable for use as a primary calibrator.

Instructions for use: Equilibrate the bottled material to room temperature before opening.

Recommended storage: When not in use this material should be stored at or below 25 ºC in a closed container in a dry, dark area.

Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%. Quantitative NMR provides an independent direct measure of the mass fraction of the analyte of interest, calibrated with an internal standard certified for purity (mass fraction).

Stability: In the absence of stability data the measurement uncertainty at the 95% coverage interval has been expanded to accommodate any potential change in the property value. The stability component has been estimated from stability trials conducted on similar materials by NMI Australia over the last 10 years. The long-term stability of the compound in solution has not been examined.

Homogeneity assessment: The homogeneity of the material was assessed using purity assay by GC-FID on ten randomly selected 1-2 mg sub samples of the material. The material was judged to be sufficiently homogeneous at this level of sampling as the variation in analysis results between samples was not significantly different at a 95% confidence level from that observed on repeat analysis of the same sample.

Safety: Treat as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust.

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
21 May 2021.

This report supersedes any issued prior to 21 May 2021.

NATA logo notice: Accredited for compliance with ISO Guide 17034. Accreditation No. 198 / Corporate Site No. 20844. The results of the tests, calibrations and/or measurements included in this document are traceable to Australian/national standards.

CIPM MRA notice: This certificate is consistent with the capabilities that are included in Appendix C of the CIPM MRA drawn up by the CIPM. Under the CIPM MRA, all participating institutes recognize the validity of each other's calibration and measurement certificates for the quantities, ranges and measurement uncertainties specified in Appendix C. The "CIPM MRA Logo" and this statement attest only to the measurement(s) applied for determining the certified values on the certificate (for details see http://www.bipm.org).

Legal notice: Neither NMIA as a representative of the Commonwealth of Australia, nor any person acting on NMIA's behalf, assumes any liability with respect to the use of, or for damages resulting from the use of, this reference material or the information contained in this document.

Characterisation Report:

The certified purity value was obtained from a combination of traditional analytical techniques and quantitative nuclear magnetic resonance (qNMR). The techniques used in the mass balance approach include GC-FID, Karl Fischer analysis and ^{1}H NMR spectroscopy. The purity value is calculated as per Equation 1.

Purity = (100 % - I_{ORG}) x (100 % - I_{VOL} – I_{NVR}) Equation 1

I_{ORG} = Organic impurities of related structure, I_{VOL} = volatile impurities, I_{NVR} = non-volatile residue

The certified purity value by qNMR was obtained using a combination of the two-proton multiplet at 2.9 ppm and the one-proton multiplet at 3.6 ppm measured against a certified internal standard of potassium hydrogen maleate.

Supporting evidence is provided by headspace GC-MS analysis of occluded solvent and elemental microanalysis.

GC-FID:	Instrument:	Varian CP-3800 or Agilent 7890A
	Column:	HP-5 or HP-1, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	60 °C (1 min), 10 °C/min to 100 °C (3 min), 30 °C/min to 300 °C (3 min)
	Injector:	180 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative mass fraction of the main component as the free base:	
	Initial analysis:	Mean = 99.7%, s = 0.01% (10 sub samples in duplicate, July 2014)
	Re-analysis:	Mean = 99.8%, s = 0.04% (5 sub samples in duplicate, July 2015)
	Re-analysis:	Mean = 99.7%, s = 0.01% (5 sub samples in duplicate, August 2018)
	Re-analysis:	Mean = 99.7%, s = 0.03% (5 sub samples in duplicate, May 2021)
Karl Fischer analysis:		Moisture content 0.4% mass fraction (July 2014) Moisture content 0.6% mass fraction (July 2015) Moisture content 1.0% mass fraction (June 2018) Moisture content 0.9% mass fraction (May 2021)
QNMR:	Instrument:	Bruker Avance-III-500
	Field strength:	500 MHz
	Solvent:	D_2O (4.79 ppm)
	Internal standard:	Potassium hydrogen maleate (100% mass fraction)
	Initial analysis:	Mean (3.6 ppm) = 99.4%, s = 0.06% (5 sub samples, July 2014)
	Initial analysis:	Mean (2.9 ppm) = 99.4%, s = 0.04% (5 sub samples, July 2014)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	TG-1MS, 30 m x 0.25 mm I.D. x 0.25 μm
	Program:	60 °C (1 min), 10 °C/min to 300 °C (3 min)
	Injector:	250 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	30/1
	The retention time of the free base compound is reported along with the major peaks in the mass spectrum. The latter are reported as mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	7.1 min:	134 (M^+-1, 2), 120 (9), 103 (4), 91 (35), 77 (6), 65 (16), 44 (100) *m/z*
ESI-MS:	Instrument:	Micromass Quatro LC Micro
	Operation:	Positive ion mode, direct infusion at 10 μL/min
	Ionisation:	ESI spray voltage at 3.5 kV positive ion
	EM voltage:	650 V
	Cone voltage:	5 V
	Peak:	136.1 (M^+H^+) *m/z*
HS-GC-MS:	Instrument:	Agilent 6890/5973/G1888
	Column:	DB-624, 30 m x 0.25 mm I.D. x 1.4 μm
	Program:	50 °C (5 min), 7 °C/min to 120 °C, 15 °C/min to 220 °C (8.3 min)
	Injector:	150 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.2 mL/min
	Split ratio:	50/1
	Solvents detected:	No solvents detected
IR:	Instrument:	FT-IR, Biorad FTS 3000MX
	Range:	4000-400 cm^{-1}, KBr
	Peaks:	3430, 3300-2700 (broad), 2579, 2501, 1950, 1573, 1498, 1455, 1389, 1202, 1096, 740, 700 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance 500
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.26 (3H, d, *J* = 6.6 Hz), 2.81 (1H, dd, *J* = 8.4, 13.5 Hz), 3.01 (1H, dd, *J* = 6.1, 13.5 Hz), 3.52 (1H, m), 7.26-7.30 (3H, m), 7.34-7.37 (2H, m) ppm
^{13}C NMR:	Instrument:	Bruker DPX-300
	Field strength:	75 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 18.3, 41.8, 50.3, 128.4, 130.0, 130.4, 137.4 ppm
Melting point:		151-152 °C
Microanalysis:	Found:	C = 62.9%; H = 8.4%; N = 8.2%; Cl = 20.6% (July 2014)
	Calculated:	C = 63.0%; H = 8.2%; N = 8.2%; Cl = 20.7% (Calculated for $C_9H_{14}ClN$)