Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

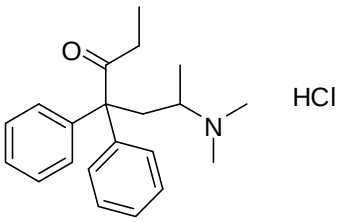
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D425b: Methadone hydrochloride

Report ID: D425b.2020.03 (Bottled 200402)

Chemical Formula: $C_{21}H_{27}NO.HCl$

Molecular Weight: 345.9 g/mol (HCl), 309.5 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
07-D-10	**1095-90-5**	**99.7 ± 0.5%**

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

Synonyms: Methadoni hydrochloridum
Phenadone

Expiration of certification: The property values are valid till 8 December 2025, 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 solid sourced from an external supplier, 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%.

Stability: This material has demonstrated stability over a minimum period of five years. The measurement uncertainty at the 95% confidence interval includes a stability component which has been estimated from annual stability trials. 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 gas chromatography with flame ionisation detection on five randomly selected 1-2 mg sub samples of the material. The material was judged to be 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. Refer to the provided safety data sheet.

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
14 September 2022

This report supersedes any issued prior to 14 September 2022.

NATA Accreditation No. 198 / Corporate Site No. 14214.

Legal notice: Terms and Conditions associated with the provision of this reference material can be found on the NMIA website.

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value was obtained by mass balance from a combination of traditional analytical techniques, including GC-FID, thermogravimetric analysis, 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

Supporting evidence is provided by elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890N, Agilent 7890 and Varian CP3800
	Column:	HP-1, HP-1MS or VF-1 30 m x 0.32 mm I.D. x 0.25 μm
	Program:	60°C (1min), 10°C/min to 100°C, 15°C/min to 250°C, 30°C/min to 300°C
	Injector:	250 °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 = 0.03 (8 sub samples in duplicate, July 2007)
	Re-analysis:	Mean = 99.6%, s = 0.04 (5 sub samples in duplicate, July 2009)
	Re-analysis:	Mean = 99.9%, s = 0.02% (5 sub samples in duplicate, June 2010)
	Re-analysis:	Mean = 99.6%, s = 0.03% (5 sub samples in duplicate, April 2013)
	Re-analysis:	Mean = 99.6%, s = 0.03% (5 sub samples in duplicate, February 2016)
	Re-analysis:	Mean = 99.8%, s = 0.04% (5 sub samples in duplicate, December 2020)
Thermogravimetric analysis:		Volatile content < 0.1% and non-volatile residue < 0.2% mass fraction (October 2007)
Karl Fischer analysis:		Moisture content < 0.4% mass fraction (September 2007, June 2010, April 2013, February 2016 and November 2020)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	ZB-5MS, 28 m × 0.25 mm I.D. × 0.25 μm
	Program:	120 °C (1 min), 20 °C/min to 300 °C (6 min)
	Injector:	250 °C
	Detector Temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	20/1
	The retention time of the free base is reported along with the major peaks in the mass spectrum. The latter are reported in as mass to charge ratios and (in brackets) as a percentage relative to the base peak.	
	Free base (9.7 min):	288 (69), 273 (10), 246 (51), 228 (18), 203 (31), 147 (39), 124 (100), 105 (28), 91 (36) 79 (30), 55 (17) *m/z*
ESI-MS:	Instrument:	Micromass Quattro Micro
	Operation:	Positive ion mode, direct infusion at 5 μL/min
	Ionisation:	ESI capillary voltage at 3.2 KV positive ion
	EM voltage:	600 V
	Cone voltage:	29 V
	M/z:	310.2 (MH^+, 100%)
TLC:	Conditions:	Kieselgel 60F_{254}. Hexane / diethyl ether / trimethylamine (33/58/8) Single spot observed, R_f = 0.54. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400cm^{-1}, KBr powder
	Peaks:	3029, 2965, 2410, 1705, 1485, 1133, 1103, 1002, 937, 764, 707 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX-500
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 0.58 (3H, d, *J* = 7.1 Hz), 0.87 (3H, t, *J* = 7.2 Hz), 2.08-2.17 (2H, m), 2.57 (1H, dq, *J* = 7.1, 17.0 Hz), 2.84 (6H, s), 3.07-3.16 (2H, m), 7.20-7.24 (2H, m), 7.34-7.51 (8H, m) ppm
	Diethyl ether at 0.3% mass fraction was observed in the ^{1}H NMR (July 2010).	
^{13}C NMR:	Instrument:	Bruker DMX-500
	Field strength:	125 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 9.4, 14.7, 34.7, 42.5, 62.0, 67.1, 129.2, 129.2, 129.9, 130.2, 130.2, 130.6, 141.2, 142.1, 215.0 ppm.
Melting point:		232-233 °C
Microanalysis:	Found:	C = 72.8%; H = 8.1%; N = 4.0% (August 2007)
	Calculated:	C = 72.9%; H = 8.2%; N = 4.1% (Calculated for $C_{21}H_{27}NO.HCl$)