Australian Government
Department of Industry, Science and Resources

National Measurement Institute

CIPM MRA

NATA
WORLD RECOGNISED ACCREDITATION

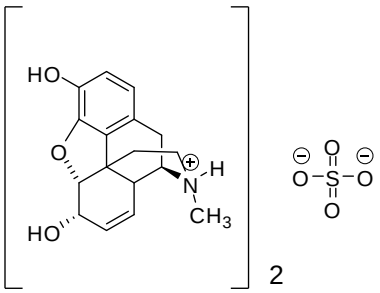
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D925: Morphine sulfate

Report ID: D925.2020.03 (Bottled 190814)

Chemical Formula: $(C_{17}H_{19}NO_3)_2.H_2SO_4$

Molecular Weight: 668.8 g/mol



Certified value

Batch No.	CAS No.	Purity (mass fraction)
08-D-04	64-31-3	87.7 ± 1.2%

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

IUPAC name: Bis[(6β,9α,13α,14α)-3,6-dihydroxy-17-methyl-7,8-didehydro-4,5-epoxymorphinan-17-ium] sulfate

Expiration of certification: The property values are valid till 27 March 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: Off-white powder 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.

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: This material has demonstrated stability over a minimum period of five years. The measurement uncertainty at the 95% coverage interval includes a stability component which has been estimated from long term 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 qNMR on five randomly selected 20-30 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 a 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.
19 September 2022

This report supersedes any issued prior to 19 September 2022.

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

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

Characterisation Report:

The purity value was obtained by quantitative nuclear magnetic resonance (qNMR). The two-proton multiplet at 6.7 ppm was measured against a certified internal standard of potassium hydrogen maleate.

Supporting evidence is provided by Karl Fischer analysis and elemental microanalysis.

QNMR:	Instrument:	Bruker Avance-III-500
	Field strength:	500 MHz Solvent: D_2O (3.31 ppm)
	Internal standard:	Potassium hydrogen maleate (99.8% mass fraction)
	Initial analysis:	Mean (2.4 ppm) = 87.8%, s = 0.1% (5 sub samples, May 2017)
Karl Fischer analysis:		Moisture content ca 12% mass fraction (February 2008, July 2011) Moisture content ca 11.6% mass fraction (May 2014) Moisture content ca 12.3% mass fraction (April 2017) Moisture content ca 12.3% mass fraction (March 2020)

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Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	ZB-5, 30 m × 0.25 mm I.D. × 0.25 μm
	Program:	200 °C (1 min), 4 °C/min to 260 °C, 20 °C/min to 300 °C (3 min)
	Injector:	250°C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	20/1
	The retention time of the parent 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.	
	9.4 min:	286 (M+H, 17), 285 (M^+, 100), 284 (22), 268 (15), 215 (26), 126 (31) *m/z*
ESI-MS:	Instrument:	Micromass Quatro LC Micro
	Operation:	Positive ion mode, direct infusion at 5 μL/min
	Ionisation:	ESI spray voltage at 3.2 kV positive ion
	EM voltage:	500 V
	Cone voltage:	30 V
	Peak:	286 ($M+H^+$) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. MeOH/NH_3 (100/1.5) Single spot observed, R_f = 0.4. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400 cm^{-1}, KBr pellet
	Peaks:	3392, 3165, 2634, 2497, 1649, 1500, 1360, 1312, 1124, 1073, 961, 841, 791, 627 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX500
	Field strength:	500 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	δ 1.94 (1H, m), 2.20 (1H, m), 2.74-3.24 (5H, m), 2.84 (3H, s), 4.05 (1H, s), 4.22 (1H, d, *J* = 2.9 Hz), 4.90 (1H, d, *J* = 6.3 Hz), 5.22 (1H, d, *J* = 9.1 Hz), 5.57 (1H, d, *J* = 9.8 Hz), 6.52 (1H, d, *J* = 8.2 Hz), 6.61 (1H, d, *J* = 8.2 Hz) ppm
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	126 MHz
	Solvent:	D_2O
	Spectral data:	δ 20.8, 32.4, 38.2, 40.8, 41.4, 47.0, 60.4, 65.5, 90.2, 117.5, 120.2, 123.2, 125.5, 129.2, 133.0, 137.8, 145.4 ppm
Melting point:		229-231 °C
Microanalysis:	Found:	C = 53.9 %; H = 6.9 %; N = 3.6 %; S = 4.2 % (February 2008)
	Calculated:	C = 53.8 %; H = 6.6 %; N = 3.7 %; S = 4.2 % (Calculated for $(C_{17}H_{19}NO_3)_2.H_2SO_4.5H_2O$)