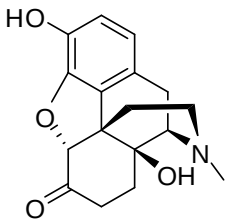
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D1038: Oxymorphone



Report ID: D1038.2023.01

Chemical Formula: $C_{17}H_{19}NO_4$

Molecular Weight: 301.3 g/mol

Certified value

Batch No.	CAS No.	Purity (mass fraction)
14-D-38	**76-41-5**	**99.4 ± 0.8%**

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

IUPAC name: (5α)-3,14-Dihydroxy-17-methyl-4,5-epoxymorphinan-6-one.

Expiration of certification: The property values are valid till 11 May 2028, 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 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. 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% 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 HPLC with UV detection 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 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.
15 May 2023

This report supersedes any issued prior to 15 May 2023.

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 quantitative nuclear magnetic resonance (qNMR). A combination of two one-proton doublets at 6.56 ppm and 6.64 ppm were measured against a certified internal standard of dimethyl terephthalate.

Supporting evidence is provided by HPLC with detection at 281 nm, Karl-Fisher analysis, thermogravimetric analysis, qualitative headspace GC-MS analysis of occluded solvent and elemental microanalysis.

HPLC:	Instrument:	Shimadzu Binary pump LC-20AB, SIL-20 A HT autosampler
	Column:	Agilent Pursuit C18, 5 μm (4.6 mm x 250 mm)
	Column oven:	40 °C
	Mobile Phase:	A = MilliQ water; B = Methanol 0-10 min 20-80% B, 10-24 min 80% B, 24-25 min 80-20% B, 25-30 min 20% B The aqueous phase contained 20mM NH_4HCO_3
	Flow rate:	1.0 mL/min
	Detector:	Shimadzu SPD-M20A PDA operating at 281 nm
	Relative mass fraction of the main component:	
	Initial analysis:	Mean = 100.00%, s = 0.01% (10 sub samples in duplicate, January 2016)
	Re-analysis:	Mean = 100.00%, s = 0.00% (5 sub samples in duplicate, January 2018)
	Re-analysis:	Mean = 100.00%, s = 0.00% (5 sub samples in duplicate, November 2020)
	Re-analysis:	Mean = 100.00%, s = 0.00% (5 sub samples in duplicate, May 2023)
Karl Fischer analysis:		Moisture content ≤ 0.1% mass fraction (November 2015, 2017, 2020 and 2023)
Thermogravimetric analysis:		Volatiles content 0.2% and non-volatile residue < 0.2% mass fraction (November 2015)
QNMR:	Instrument:	Bruker Avance-III-500
	Field strength:	500 MHz
	Solvent:	Acetone-d_6 (2.05 ppm)
	Internal standard:	Dimethyl terephthalate (100.0% mass fraction)
	Initial analysis:	Mean (6.6 ppm) = 99.4%, s = 0.3% (5 sub samples, January 2016)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	HP-1 MS, 30 m × 0.25 mm I.D. × 0.25 μm
	Program:	200 °C (1 min), 10 °C/min to 300 °C (10 min)
	Injector:	260 °C
	Split ratio:	30/1
	Transfer line temp:	280 °C
	Carrier:	Helium
	Scan range:	50-550 *m/z*
	The retention time of the parent compoundis reported with the major peaks in the mass spectra. The latter are reported as mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	Parent (8.4 min):	301 (M^+, 100), 216 (38), 203 (15), 115 (11), 70 (17) *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:	None
TLC:	Conditions:	Kieselgel 60F254. *tert*-Butyl methyl ether/diethyl amine (9/1). Single spot observed, Rf = 0.5. Visualisation with UV at 254 nm).
IR:	Instrument:	Bruker Alpha Platinum ATR
	Range:	4000-400 cm^{-1}, neat
	Peaks:	3147, 2944, 2815, 1727, 1613, 1458, 1242, 1226, 1146, 1112, 1062, 1047, 954, 943, 934, 920, 852, 762, 745, 631 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III-500
	Field strength:	500 MHz
	Solvent:	Acetone-d_6 (2.05 ppm)
	Spectral data:	δ 1.42 (1H, dd, *J* = 3.2, 12.9 Hz), 1.56 (1H, m), 1.81 (1H, ddd, *J* = 3.0, 5.0, 13.4 Hz), 2.06-2.15 (2H, m), 2.40 (3H, s), 2.39-2.49 (2H, m), 2.56 (1H, dd, *J* = 5.6, 18.2 Hz), 2.88 (1H, d, *J* = 5.8 Hz), 2.97 (1H, ddd, *J* = 5.0, 14.0, 14.0 Hz), 3.16 (1H, d, *J* = 18.5 Hz), 4.67 (1H, s), 6.56 (1H, d, *J* = 8.1 Hz), 6.64 (1H, d, *J* = 8.1 Hz) ppm
	Methanol estimated at < 0.1% mass fraction was observed in the ^{1}H NMR	
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	126 MHz
	Solvent:	Acetone-d_6 (29.84 ppm)
	Spectral data:	δ 22.4, 31.4, 32.2, 36.6, 42.9, 46.0, 51.0, 65.4, 71.0, 90.9, 118.4, 120.1, 124.9, 130.5, 140.4, 144.8, 208.7 ppm
Melting point:		249-253 °C
Microanalysis:	Found:	C = 67.9%; H = 6.3%; N = 4.6% (November 2015)
	Calculated:	C = 67.8%; H = 6.4%; N = 4.6% (Calculated for $C_{17}H_{19}NO_4$)