



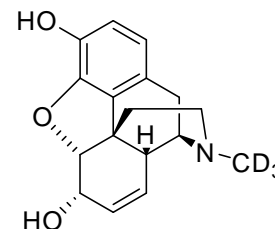
DEUTERATED INTERNAL STANDARD PRODUCT INFORMATION SHEET

NMIA D709b: d₃-Morphine

Report ID: D709b.2023.01 (Ampouled 230703)

Chemical Formula: C₁₇H₁₆D₃NO₃

Molecular Weight: 288.4 g/mol



Property value

Batch No.	CAS No.	Mass per ampoule
22-D-01	67293-88-3	930 ± 43 µg

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

IUPAC name: (5 α ,6 α)-17-(²H₃) Methyl-7,8-didehydro-4,5-epoxymorphinan-3,6-diol.

Expiration of certification: The property values are valid till 07 July 2026, three years from the date of 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 shelf life does not apply to ampoules that have been opened. In such cases it is recommended that the end-user conduct their own in-house stability trials. The material will be re-tested on an annual basis to ensure that the property values are still valid. In the event a product fails the stability trial, notification will be sent to all impacted customers.

Description: The compound is supplied as a dried aliquot in a sealed ampoule under an atmosphere of argon. The deuterated internal standard is intended for a single use to prepare a standard solution containing D709b. The material was prepared by synthesis and certified for identity and purity by NMIA. The main component of this material is d₃-morphine. d₂-, d₁- and d₀-Morphine are also present. The stated mass of the analyte per ampoule represents the approximate combined masses of deuterated (d₃, d₂ and d₁) and d₀-morphine in the material.

Intended use: The isotopic purity of this material is an estimate only. This material should be considered for use as an internal standard only and is not intended for use as a calibrator. The material does not have certified reference material status as metrological traceability of the stated purity value to the SI unit for mass (kg) has not been established.

Instructions for use: Open the ampoule and carefully rinse the interior at least three times with a suitable organic solvent (e.g. methanol). This will transfer 930 ± 43 µg of anhydrous morphine (d₃, d₂, d₁ and d₀). The mass of analyte in each ampoule is calculated from the assigned purity of the bulk and the concentration of bulk material in a stock solution used to prepare the ampoules.

Recommended storage: When not in use, this material should be stored at or below 4 °C in a closed container in a dry, dark area.

Stability: In the absence of long term 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 ten 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 six randomly selected ampoules 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.
4 August 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:

GC-FID: Instrument: Varian CP-3800
 Column: DP-17, 30 m × 0.32 mm I.D. × 0.25 μm
 Program: 220 °C (2 min), 10 °C/min to 240 °C (10 min), 30 °C/min to 280 °C (5 min)
 Injector: 250 °C
 Detector Temp: 320 °C
 Carrier: Helium
 Split ratio: 20/1
 Relative peak area of the main component:
 Initial analysis: Mean = 99.5%, s = 0.01% (6 ampoules in duplicate, July 2023)

The following analytical data was obtained on the bulk material subsequently used in the preparation of the ampoules.

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The purity value was obtained by mass balance from a combination of traditional analytical techniques, including GC-FID, thermogravimetric analysis, Karl Fischer analysis, and ¹H NMR spectroscopy. The purity value is calculated as per Equation 1.

$$\text{Purity} = (100\% - I_{\text{ORG}}) \times (100\% - I_{\text{VOL}} - I_{\text{NVR}}) \quad \text{Equation 1}$$

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

Supporting evidence is provided by elemental microanalysis.

The main component of this material is d₃-morphine. d₂-, d₁- and d₀-Morphine are also present. The stated chemical purity of the analyte represents the combined mass fractions of deuterated (d₃, d₂ and d₁) and d₀-morphine in the material.

The isotopic purity of this material is an estimate only. This material should be considered for use as an internal standard only.

Isotopic Purity: $d_3 \approx 99.0\% [= d_3 / (d_3 + d_2 + d_1 + d_0) \times 100]$
 $d_0 < 0\% [= d_0 / (d_3 + d_2 + d_1 + d_0) \times 100]$

GC-FID: Instrument: Agilent 8890
 Column: HP-5, 30 m × 0.32 mm I.D. × 0.25 μm
 Program: 220 °C (2 min), 10 °C/min to 240 °C (10 min), 30 °C/min to 300 °C (5 min)
 Injector: 250 °C
 Detector Temp: 320 °C
 Carrier: Helium
 Split ratio: 20/1
 Relative peak area of the main component:
 Initial analysis: Mean = 99.6%, s = 0.02% (10 sub samples in duplicate, February 2023)

Karl Fischer analysis: Moisture content 5.8% mass fraction (February 2022)
 Moisture content 5.4% mass fraction (February 2023)

Thermogravimetric analysis: Volatiles content 5.6% and non-volatile residue 0.5% mass fraction (February 2022)

Spectroscopic and other characterisation data

GC-MS:	Instrument: Agilent 6890/5973 Column: HP-5MS, 30 m x 0.25 mm I.D. x 0.25 μ m Program: 55 °C (1 min), 30 °C/min to 300 °C, 20 °C/min to 320 °C (3 min) Injector: 240 °C Split ratio: N/A Transfer line temp: 300 °C Carrier: Helium, 1.0 mL/min Scan range: 50-550 <i>m/z</i>
	The retention time of d ₃ -morphine is 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 (11.5 min): 288 (M ⁺ , 100), 271 (14), 218 (39), 174 (27), 165 (77), 152 (21), 127 (42), 115 (39), 45 (42) <i>m/z</i>
TLC:	Conditions: Kieselgel 60F ₂₅₄ . Methanol/concentrated ammonia (100:1.5) Single spot observed, R _f = 0.4. Visualisation with UV at 254 nm.
IR:	Instrument: Bruker Alpha Platinum ATR Range: 4000-400 cm ⁻¹ , neat Peaks: 3174, 2938, 2916, 2856, 2823, 1603, 1461, 1440, 1239, 1032, 956, 897, 799, 745, 650, 510 cm ⁻¹
¹ H NMR:	Instrument: Bruker Avance III-500 Field strength: 500 MHz Solvent: MeOH-d ₄ (3.31 ppm) Spectral data: δ 1.82 (1H, dm, <i>J</i> = 13.0 Hz), 2.08 (1H, ddd, <i>J</i> = 5.1, 12.7, 12.7), 2.36 (1H, dd, <i>J</i> = 6.4, 18.8 Hz), 2.45 (1H, ddd, <i>J</i> = 3.4, 12.4, 12.4), 2.60 (1H, dd, <i>J</i> = 4.3, 12.3), 2.65 (1H, septet, <i>J</i> = 2.7 Hz), 3.03 (1H, d, <i>J</i> = 18.8 Hz), 3.39 (1H, dd, <i>J</i> = 3.2, 6.2 Hz), 4.18 (1H, m), 4.81 (1H, dd, <i>J</i> = 1.1, 6.2 Hz), 5.31 (1H, dt, <i>J</i> = 9.9, 2.8 Hz), 5.63 (1H, dm, <i>J</i> = 9.7 Hz), 6.44 (1H, <i>J</i> = 8.1, 8.0 Hz), ppm
¹³ C NMR:	Instrument: Bruker Avance III-500 Field strength: 126 MHz Solvent: MeOH-d ₄ (49.0 ppm) Spectral data: δ 21.6, 36.3, 41.5, 44.4, 47.9, 60.2, 67.9, 92.9, 117.9, 120.5, 127.1, 129.5, 132.0, 133.9, 139.9, 147.4 ppm
Melting point:	256-257 °C
Microanalysis:	Found: C = 66.4%; H = 7.0%; N = 4.7% (March 2022) Calculated: C = 66.6%; H = 7.0%; N = 4.6% (Calculated for C ₁₇ H ₁₆ D ₃ NO ₃ ·H ₂ O)