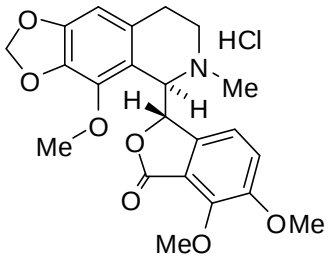
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

# REFERENCE MATERIAL PRODUCT INFORMATION SHEET

## NMIA D791b: Noscapine hydrochloride




Report ID: D791b.2024.01 (Bottled 171005)

Chemical Formula: $C_{22}H_{23}NO_7$.HCl

Molecular Weight: 449.9 (HCl), 413.4 (base) g/mol

## Property value

| Batch No. | CAS No. | Purity estimate |
|---|---|---|
| **17-D-05** | **912-60-7** | **93.6 ± 1.8%** |

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

**IUPAC name:** (3*S*)-6,7-Dimethoxy-3-[(5*R*)-4-methoxy-6-methyl-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl]-2-benzofuran-1(3*H*)-one hydrochloride hydrate.

**Expiration of certification:** The property values are valid till 16 July 2027, three 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 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 reference material is recommended for qualitative analysis 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:** 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.

**Stability:** This material has demonstrated stability over a minimum period of three 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.
26 July 2024

This report supersedes any issued prior to 26 July 2024.

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 purity value was obtained by mass balance from a combination of traditional analytical techniques, including HPLC with UV detection, 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.

| | | |
|---|---|---|
| HPLC: | Instrument: | Shimadzu Binary pump LC-20AB, SIL-20 A HT autosampler |
| | Column: | Alltima C-18, 5 μm (4.6 mm x 150 mm) |
| | Column oven: | 40 °C |
| | Mobile Phase: | Methanol/MilliQ water (65:35 v/v)<br>The aqueous phase contained 0.05% v/v diethylamine |
| | Flow rate: | 1.0 mL/min |
| | Detector: | Shimadzu SPD-M20A PDA operating at 209 nm |
| | Relative peak area of the main component: | |
| | Initial analysis: | Mean = 99.98%, s = 0.007% (10 sub samples in duplicate, June 2017) |
| | Re-analysis: | Mean = 99.96%, s = 0.001% (5 sub samples in duplicate, May 2018) |
| | Re-analysis: | Mean = 99.96%, s = 0.002% (5 sub samples in duplicate, June 2019) |
| | Re-analysis: | Mean = 99.96%, s = 0.004% (5 sub samples in duplicate, March 2022) |
| | Re-analysis: | Mean = 99.93%, s = 0.02 % (5 sub samples in duplicate, July 2024) |
| Thermogravimetric analysis: | | Non volatile residue < 0.2% mass fraction (June 2017). The volatile content (e.g. organic solvents and/or water) could not be determined by thermogravimetric analysis. |
| Karl Fischer analysis: | | Moisture content 2.3% mass fraction (May 2017)<br>Moisture content 3.3% mass fraction (May 2018)<br>Moisture content 2.7% mass fraction (May 2019)<br>Moisture content 3.6% mass fraction (March 2022)<br>Moisture content 3.1% mass fraction (July 2024) |

## Spectroscopic and other characterisation data

| | | |
|---|---|---|
| ESI-MS: | Instrument: | Micromass Quatro LC Micro |
| | Operation: | Positive ion mode, direct infusion at 10 μL/min |
| | Ionisation: | ESI spray voltage at 3.2 kV positive ion |
| | EM voltage: | 650 V |
| | Cone voltage: | 45 V |
| | Peak: | 414.1 ($M+H^+$), 436.2 ($M+Na^+$), 477.1 ($M+Na^++CH_3CN$) *m/z* |
| GC-MS: | Instrument: | Agilent 6890/5973 |
| | Column: | HP-1MS, 30 m x 0.25 mm I.D. x 0.25 μm |
| | Program: | 250 °C (1 min), 30 °C/min to 300 °C (10 min) |
| | Injector: | 250 °C |
| | Transfer line 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 as mass/charge ratios and (in brackets) as a percentage relative to the base peak. | |
| | Free base (6.7 min): | 220 (100), 205 (13), 193 (8), 147 (3), 119 (6) *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: | Propan-2-ol |
| TLC: | Conditions: | Kieselgel $60F_{254}$. tert-Butylmethylether/diethylether/diethylamine (50/45/5) Single spot observed, $R_f$ = 0.9. Visualisation with UV at 254 nm |
| IR: | Instrument: | Biorad FTS 3000 MXFT-IR |
| | Range: | 4000-400$cm^{-1}$, KBr |
| | Peaks: | 400, 2947, 2845, 2518, 1768, 1619, 1490, 1271, 1221, 1104, 1077, 1032, 982, 939, 889, 836 $cm^{-1}$ |
| $^1$H NMR: | Instrument: | Bruker Avance III 500 |
| | Field strength: | 500 MHz |
| | Solvent: | $D_2O$ (4.79 ppm) |
| | Spectral data: | δ 3.04 (5H, bs), 3.27-3.65 (5H, bm), 3.81 (3H, s), 3.88 (3H, s), 5.3 (1H, s), 5.71 (1H, s), 5.82 (1H, s), 6.06 (1H, bs), 6.46 (1H, s), 7.07 (1H, bs), 7.46 (1H, d, *J* = 8.1 Hz) ppm |
| | Propan-2-ol mass fraction 3.2 ± 0.5% (June 2018 – July 2024) by $^1$H NMR. | |
| $^{13}$C NMR: | Instrument: | Bruker Avance III 500 |
| | Field strength: | 126 MHz |
| | Solvent: | $D_2O$ |
| | Spectral data: | δ 22.2 (b), 41.2, 47.0, 56.7, 59.0, 61.1, 62.2, 78.9 (b), 101.4, 102.6, 107.0 (b), 117.0, 119.9, 120.9, 127.8, 133.7, 137.8, 139.6, 146.6, 150.2, 152.7, 168.9 ppm |
| Melting point: | | 210-213 °C |
| Microanalysis: | Found: | C = 57.7%; H = 5.7%; N = 2.9% (June 2017) |
| | Calculated: | C = 58.7%; H = 5.4%; N = 3.1% (Calculated for $C_{22}H_{23}NO_7$.HCl) |
| | Calculated: | C = 57.4%; H = 5.8%; N = 2.9% (Calculated for $C_{22}H_{23}NO_7$.HCl containing 2.3% water and 3.8% isopropanol) |