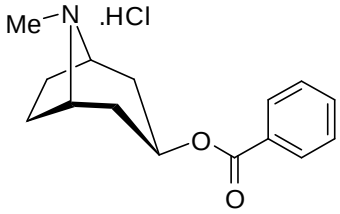
REFERENCE MATERIAL PRODUCT INFORMATION SHEET

Report ID: D846b.2017.01 (Bottled 170822)
This batch of bottles was prepared from the bulk material on 22nd August 2017

Compound Name: **Tropacocaine hydrochloride**
Collection Number: D846b
Chemical Formula: $C_{15}H_{19}NO_2$.HCl
CAS Number: 637-23-0 (HCl salt), 537-26-8 (base)
Structure:



Description: White powder
Batch Number: 14-D-13
Molecular Weight: 281.8 (HCl salt); 245.3(base)
Release date: 27th May 2014

Synonyms: 3-*exo*-8-Methyl-8-azabicyclo[3.2.1]octan-3-ol 3- benzoate hydrochloride
Pseudotropine benzoate hydrochloride

Purity (mass fraction): 99.7 ± 1.3% (95% coverage interval)

The purity value was obtained from a combination of traditional analytical techniques. The purity estimate by traditional analytical techniques was obtained by subtraction from 100% of total impurities by GC-FID, Karl Fischer analysis and ^{1}H NMR. Supporting evidence is provided by headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID:	Instrument:	Varian CP-3800	
	Column:	VF-1ms, 30 m × 0.32 mm I.D. × 0.25 µm	
	Program:	100 °C (1 min), 10 °C/min to 200 °C (3 min), 30 °C/min to 300 °C (3 min)	
	Injector:	250 °C	Detector Temp: 320 °C
	Carrier:	Helium	Split ratio: 20/1
	Relative peak area response of main component as the free base:		
	Initial analysis:	Mean = 99.95%, s = 0.002% (10 sub samples in duplicate, May 2014)	
	Re-analysis:	Mean = 99.9%, s = 0.02% (5 sub samples in duplicate, May 2017)	
GC-FID:	Instrument:	Varian CP-3800	
	Column:	HP-5, 30 m × 0.32 mm I.D. × 0.25 µm	
	Program:	100 °C (1 min), 10 °C/min to 200 °C (3 min), 30 °C/min to 300 °C (3 min)	
	Injector:	250 °C	Detector Temp: 320 °C
	Carrier:	Helium	Split ratio: 20/1
	Relative peak area response of main component as the free base:		
	Initial analysis:	Mean = 99.95%, s = 0.003% (10 sub samples in duplicate, May 2014)	
Karl Fischer analysis:		Moisture content 0.2% mass fraction (May 2014) Moisture content < 0.1% mass fraction (June 2017)	

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973	
	Column:	TG-1MS, 30 m × 0.25 mm I.D. × 0.25 μm	
	Program:	60 °C (1 min), 10 °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 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		
	17.3 min: 245 (M^+, 20), 140 (6), 124 (100), 105 (17), 94 (34), 82 (77), 77 (22), 67 (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:	Ethanol, diethyl ether	
TLC:	Kieselgel $60F_{254}$	Methanol/conc NH_3 (200:3). Single spot observed, R_f = 0.35 Visualisation with UV light (254 nm)	
IR:	Instrument:	BioRad FTS3000MX FT-IR	
	Range:	4000-400 cm^{-1}, KBr powder	
	Peaks:	2959, 2683, 2492, 1711, 1450, 1289, 1118, 1031, 715 cm^{-1}	
^{1}H NMR:	Instrument:	Bruker Avance III -600	
	Field strength:	600 MHz	Solvent: D_2O (4.79 ppm)
	Spectral data:	δ 2.12-2.22 (4H, m), 2.27-2.45 (4H, m), 2.82 (2.72H, s), 3.08 (0.3H, s), 4.04 (2H, t, *J* = 3 Hz), 5.4 (1H, septet, *J* = 6.2 Hz), 7.54 (2H, t, *J* = 7.7 Hz), 7.70 (1H, t, *J* = 7.4 Hz), 8.03 (2H, d, *J* = 7.3 Hz) ppm Two conformational isomers are observed in the ^{1}H NMR spectrum Ethanol and diethyl ether estimated at 0.04 and 0.01% mass fraction were observed in the ^{1}H NMR.	
^{13}C NMR:	Instrument:	Bruker Avance III-600	
	Field strength:	150 MHz	Solvent: D_2O
	Spectral data:	δ 23.7, 25.5, 28.1, 31.5, 34.8, 38.1, 60.2, 63.4, 65.1, 128.7, 129.1, 129.4, 134.0, 167.8 ppm Two conformational isomers are observed in the ^{13}C NMR spectrum.	
Melting point:		280-282 °C	
Microanalysis:		Found: C = 63.8%; H = 7.2%; N = 5.0%; Cl = 12.7 % (May, 2014) Calc: C = 63.9%, H = 7.2%, N = 5.0%; Cl = 12.6 % (Calculated for $C_{15}H_{19}NO_2$.HCl)	

Expiration of certification
The property values are valid till 29th May 2020, i.e. 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.

The long-term stability of the compound in solution has not been examined.

In the absence of 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 10 years.

Homogeneity assessment
The homogeneity of the material was assessed using purity assay by GC-FID 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.

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.

Intended use
For ***in vitro*** laboratory analysis only.

Caution
Treat as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust.

Legal notice
Neither NMI nor any person acting on NMI's behalf assumes any liability with respect to the use of, or for damages resulting from the use of, this reference material or the information contained in this certificate.

Authorised by:

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
Dated: 31 August, 2017.

Characterisation data and property values specified in this report supersede those in all reports issued prior to 31st August 2017.