Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

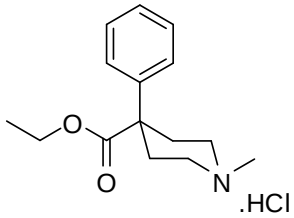
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D443b: Pethidine hydrochloride

Report ID: D443b.2021.03

Chemical Formula: $C_{15}H_{21}NO_2$.HCl

Molecular Weight: 283.8 g/mol (HCl), 247.3 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
07-D-08	50-13-5	99.5 ± 0.3%

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

IUPAC name: Ethyl 1-methyl-4-phenylpiperidine-carboxylate hydrochloride
Synonym: Meperidine hydrochloride

Expiration of certification: The property values are valid till 15 January 2031, i.e. ten 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 solid 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. 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 ten 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 GC-FID on seven randomly selected 1-2 mg samples of the material. The material was judged to be 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 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.
14 September 2022.

This report supersedes any issued prior to 14 September 2022.

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 mass balance from a combination of traditional analytical techniques, including GC-FID, 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.

GC-FID:	Instrument:	Agilent 6890N or Varian CP-3800	
	Column:	HP-1 or VF-1MS, 30 m x 0.32 mm I.D. x 0.25 μm	
	Program:	140 °C (1 min), 10 °C/min to 200 °C, 20 °C/min to 300 °C (3 min)	
	Injector:	250 °C	Detector Temp: 320 °C
	Carrier:	Helium	Split ratio: 20/1
	Relative mass fraction of the main component as the free base:		
	Initial analysis:	Mean = 99.7%, s = 0.01% (7 sub samples in duplicate, July 2007)	
	Re-analysis:	Mean = 99.6%, s = 0.01% (5 sub samples in duplicate, August 2008)	
	Re-analysis:	Mean = 99.7%, s = 0.01% (5 sub samples in duplicate, August 2009)	
GC-FID:	Instrument:	Varian CP3800	
	Column:	VF-1ms, 30 m x 0.32 mm I.D. x 0.25 μm	
	Program:	140 °C (1 min), 3 °C/min to 150°C (8 min), 30 °C/min to 300 °C (3 min)	
	Injector:	250 °C	Detector Temp: 320 °C
	Carrier:	Helium	Split ratio: 20/1
	Relative mass fraction of the main component as the free base:		
	Initial analysis:	Mean = 99.7%, s = 0.002% (5 sub samples in duplicate, July 2010)	
	Re-analysis:	Mean = 99.6%, s = 0.01% (5 sub samples in duplicate, May 2013)	
	Re-analysis:	Mean = 99.7%, s = 0.003% (5 sub samples in duplicate, March 2016)	
	Re-analysis:	Mean = 99.7%, s = 0.01% (5 sub samples in duplicate, January 2021)	
Thermogravimetric analysis:		Volatile content not determined due to the nature of the material	
Karl Fischer analysis:		Moisture content < 0.1% mass fraction (July 2007) Moisture content < 0.2% mass fraction (July 2008 and August 2009) Moisture content < 0.1% mass fraction (July 2010) Moisture content < 0.2 % mass fraction (May 2013, March 2016 and November 2020)	

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 5973 MSD
	Column:	HP-1MS, 30 m × 0.2 mm I.D. × 0.2 μm
	Program:	140 °C (1 min), 10 °C/min to 200°C, 20°C/min to 300 °C (1min)
	Injector:	250 °C
	Transfer line temp:	320 °C
	Carrier:	Helium, 1.5 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.	
	7.53 min:	247 (M^+, 94), 246 (66), 232 (18), 218 (49), 174 (35), 172 (56), 131 (19), 115 (20), 103 (34), 96 (22), 91 (28), 71 (100), 70 (54), 57 (29), 42 (29) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol Single spot observed, R_f = 0.37. Visualization with UV light (254nm)
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400cm^{-1}, KBr powder
	Peaks:	3424, 2964, 2933, 2364, 1721, 1449, 1304, 1224, 1156, 1096, 733, 699 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX500
	Field strength:	500 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	Major isomer δ 1.17 (3H, t, *J* = 7.1 Hz), 2.11 (2H, dt, *J* = 3.9, 14.7 Hz), 2.89 (3H, s), 3.11 (2H, t, *J* = 13.4 Hz), 3.63 (2H, d, *J* = 13.2 Hz), 4.18 (2H, q, *J* = 7.1 Hz), 7.35-7.56 (5H, m) ppm Minor isomer δ 1.12 (3H, t, *J* = 7.1 Hz), 2.38 (2H, bt, *J* = 14.7 Hz), 2.74 (3H, s), 2.93 (2H, t, *J* = 14.6 Hz), 3.49 (2H, bd, *J* = 13.2 Hz), 4.06 (2H, q, *J* = 7.1 Hz), 7.35-7.56 (5H, m) ppm
^{13}C NMR:	Instrument:	Bruker DMX500
	Field strength:	126 MHz
	Solvent:	D_2O
	Spectral data:	δ 12.8, 12.9, 28.6, 30.8, 42.1, 42.8, 46.1, 47.2, 50.4, 52.1, 62.7, 62.9, 125.2, 127.0, 128.1, 129.1, 129.4, 140.3, 153.3, 174.5, 175.5, 183.4 ppm
Melting point:		187-189 °C
Microanalysis:	Found:	C = 63.4%, H = 7.9%; N = 4.9% (July 2007)
	Calculated:	C = 63.5%, H = 7.8%; N = 4.9% (Calculated for $C_{15}H_{21}NO_2$.HCl)