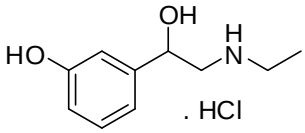
Australian Government

National Measurement Institute

REFERENCE MATERIAL ANALYSIS REPORT

Report ID: M880b.2013.01

Compound Name: **Etilefrine hydrochloride**
Collection Number: M880b
Chemical Formula: $C_{10}H_{15}NO_2$.HCl
CAS Number: 943-17-9
Structure:



Description: Off white solid
Batch Number: 12-D-01
Molecular Weight: 217.7 (HCl), 181.2 (base)
Release Date: 21st February 2012

Synonyms: α-[(Ethylamino)methyl]-3-hydroxy- benzenemethanol hydrochloride
(±)-Ethylphenylephrine hydrochloride
1-(3-Hydroxyphenyl)-2-ethylaminoethanol hydrochloride
Ethylephrine hydrochloride
dl-1-(3-Hydroxyphenyl)-1-hydroxy-2-ethylaminoethanol hydrochloride
α-[(Ethylamino)methyl]-*m*-hydroxybenzylalcohol hydrochloride

Purity (mass fraction): 99.9 ± 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 HPLC with UV detection, thermogravimetric analysis, Karl Fischer analysis and ^{1}H NMR. Supporting evidence is provided by headspace GC-MS analysis of occluded solvent and elemental microanalysis.

HPLC:	Instrument:	Waters Model 1525 Binary pump, 717 plus autosampler
	Column:	Ascentis C-18, 2.7 μm (4.6 mm x 150 mm)
	Column oven:	30 °C
	Mobile Phase:	Water/methanol (60:40) 0.01% Formic acid was present in the aqueous phase
	Flow rate:	0.2 mL/min
	Detector:	Waters PDA 2998 operating at 273.8 nm
	Relative peak area response of main component:	
	Initial analysis:	Mean = 99.98%, s = 0.004% (10 sub samples in duplicate, January 2012)
	Re-analysis:	Mean = 99.99%, s = 0.00% (5 sub samples in duplicate, January 2013)
Thermogravimetric analysis:		The volatile content < 0.1% non volatile residue < 0.2% mass fraction (January 2012)
Karl Fischer analysis:		Moisture content < 0.1% mass fraction (January 2012) Moisture content < 0.1% mass fraction (December 2012)

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 3.5 kV positive ion
	EM voltage:	650 V
	Cone voltage:	5 V
	Peak:	181.9 ($M+H^+$) 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:	Acetone
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3552, 3319, 3213, 3095, 2991, 2802, 2728, 2522, 2448, 2303, 1589, 1476, 1308, 1220, 1164, 1065, 933, 837, 793, 699, 602, 545, 475 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance-III-400
	Field strength:	400 MHz Solvent: D_2O (4.79 ppm)
	Spectral data:	δ 1.31 (3H, t, *J* = 7.2 Hz), 3.16 (2H, q, *J* = 7.3 Hz), 3.25 (1H, dd, *J* = 9.1, 13.0 Hz), 3.31 (1H, dd, *J* = 3.9, 13.0 Hz), 5.00 (1H, dd, *J* = 3.9, 9.0 Hz), 6.89 (1H, m), 6.94 (1H, m), 6.99 (1H, m), 7.34 (1H, d, *J* = 7.9 Hz) ppm
		Acetone estimated at 0.04% mass fraction was observed in the ^{1}H NMR
^{13}C NMR:	Instrument:	Bruker Avance-III-400
	Field strength:	100 MHz Solvent: D_2O
	Spectral data:	δ 10.3, 43.1, 52.5, 68.7, 112.7, 115.5, 117.9, 130.4, 141.5, 155.9 ppm
Melting point:		118-122 °C
Microanalysis:		Found: C = 55.4%; H = 7.6%; N = 6.5% (January, 2012)
		Calc: C = 55.2%; H = 7.4%; N = 6.4% (Calculated for $C_{10}H_{15}NO_2$.HCl)

Expiration of certification
The property values are valid till 21st January 2016, 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.

This material has been given a shelf life of three years from the date of re-certification. 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.

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 HPLC with UV detection on ten randomly selected 1-2 mg sub 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.

Recommended storage
When not in use, this material should be stored at or below 20ºC 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: 20 May, 2013.

Characterisation data and property values specified in this report supersede those in all reports issued prior to 1st February 2013.