

Certificate of Analysis

(±)-Norpropoxyphene-D₅ maleate

α-[2-Methylamino-1-methylethyl]-*α*-pentadeuterophenylbenzeneethanol propanoate maleate

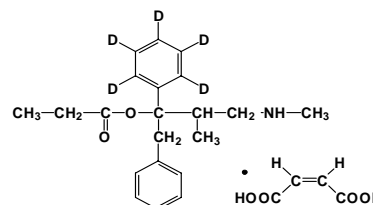
Cerilliant Quality

ISO GUIDE 34
CERTIFICATE AR1353

ISO/IEC 17025
CERTIFICATE AT1352

ISO 9001:2008
CERTIFICATE 3854

Catalog Number: N-919
Solution Lot: FN021011-05
Expiration Date: February 2016
Solvent: Methanol
Volume per Ampule: Not less than 1 mL
Storage: Store in freezer.
Intended Use: For R&D/analytical purposes only. Not suitable for human or animal consumption.
Safety: Flammable, Poison



- Expiration Date has been established through real time stability studies.
- Ampules are overfilled to ensure a minimum 1 mL volume fill. We advise laboratories to use measured volumes of this standard solution before diluting to the desired concentration.

Component	Chromatographic Purity	Certified Concentration
(±)-Norpropoxyphene-D ₅ maleate	99.4%	1.000 ± 0.006 mg/mL (as free base)
<ul style="list-style-type: none"> • Uncertainty of the concentration is expressed as an expanded uncertainty in accordance with ISO 17025 and Guide 34 at the approximate 95% confidence interval using a coverage factor of k = 2 and has been calculated by statistical analysis of our production system and incorporates uncertainty of the purity factor, material density, and balance and weighing technique. • Concentration is corrected for chromatographic purity, residual water, residual solvents and residual inorganics. 		

Solution Standard Verification and Homogeneity

Standard Solution	Lot Number	Verified Concentration (mg/mL)		%RSD - Homogeneity	
		Actual Results	Acceptance Criteria	Actual Results	Acceptance Criteria
New Lot	FN021011-05	1.018	± 3%	0.9	≤ 3%
Previous Lot	FN093010-01	1.008	± 3%	0.5	≤ 3%
<ul style="list-style-type: none"> • Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution. • Homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. The % RSD of samples pulled from across the lot demonstrate homogeneity of the New Lot. • The % RSD of the Previous Lot represents variability of the analysis performed at the time of release. 					

Traceability

- Gravimetrically prepared using qualified balances calibrated semi-annually by Mettler Toledo using NIST traceable weights. Calibration verification performed weekly and prior to each use utilizing NIST traceable weights. Each balance has been assigned a minimum weighing by Mettler Toledo taking into consideration the balance and installed environmental conditions to ensure weighing complies with USP tolerances of no more than 0.1% relative error.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared using balances calibrated to NIST.
- In addition, each neat material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques. Spectral data is provided on subsequent pages of the COA.

Cerilliant certifies that this standard meets the specifications stated in this certificate and warrants this product to meet the stated acceptance criteria through the expiration/retest date when stored unopened as recommended. Product should be used shortly after opening to avoid concentration changes due to evaporation. Warranty does not apply to ampoules stored after opening.



Lara Sparks

Lara Sparks, Quality Assurance Director

May 4, 2011

Date

Standard Solution Assay Parameters

Analysis Method: HPLC/UV
Column: Betasil Phenyl, 4.6 x 150 mm
Mobile Phase: Acetonitrile::0.01M Potassium phosphate buffer
 (70::30)
Flow Rate: 1.0 mL/min
Wavelength: 215 nm

Calibration Curve

Calibration Curve: Linear Regression
Number of Points: 4
Linearity (r): 1.000

Neat Material Data

Compound Name: (±)-Norpropoxyphene-D₅ maleate
Compound Lot: FN020711-02
Chemical Formula: C₂₁H₂₂D₅NO₂·C₄H₄O₄
CAS Number: 136765-47-4
Molecular Weight: 446.54

Neat Material Characterization Summary

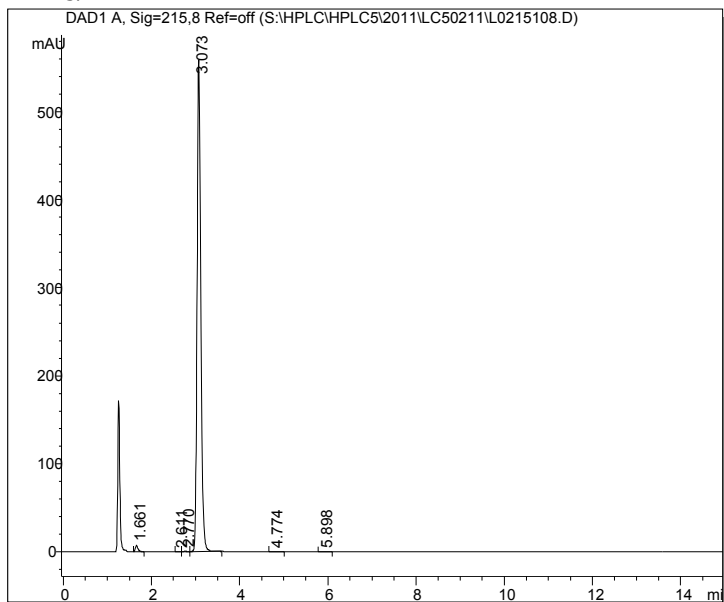
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/PDA Analysis	SP10-0102	99.4%
Secondary Purity Analysis by Thin Layer Chromatography	SP10-0106	Single Spot, R _f = 0.66
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Isotopic Purity by LC/MS SIM Analysis	SP10-0107	0.04% D ₀ vs D ₅
		0.03% D ₀ 0.15% D ₃
		0.00% D ₁ 4.94% D ₄
		0.00% D ₂ 94.88% D ₅
Identity by ¹ H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 ¹	0.38%
Residual Water Analysis by Karl Fischer Coulometry	USP <921>, SP10-0103	Not Detected
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Purity Factor		98.97%

- ♦ Primary purity is calculated as the average of two independently performed analyses utilizing two different methods. Acceptance criteria requires the purity values to be within 0.5% of each other.
- ♦ The primary chromatographic purity value is used to calculate the Purity Factor.
- ♦ A secondary chromatographic purity method is utilized as a control.
- ♦ Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- ♦ Purity factor does not include adjustment for chiral and/or isotopic purity.

¹ Validated analytical method

Spectral and Physical Data

HPLC/PDA

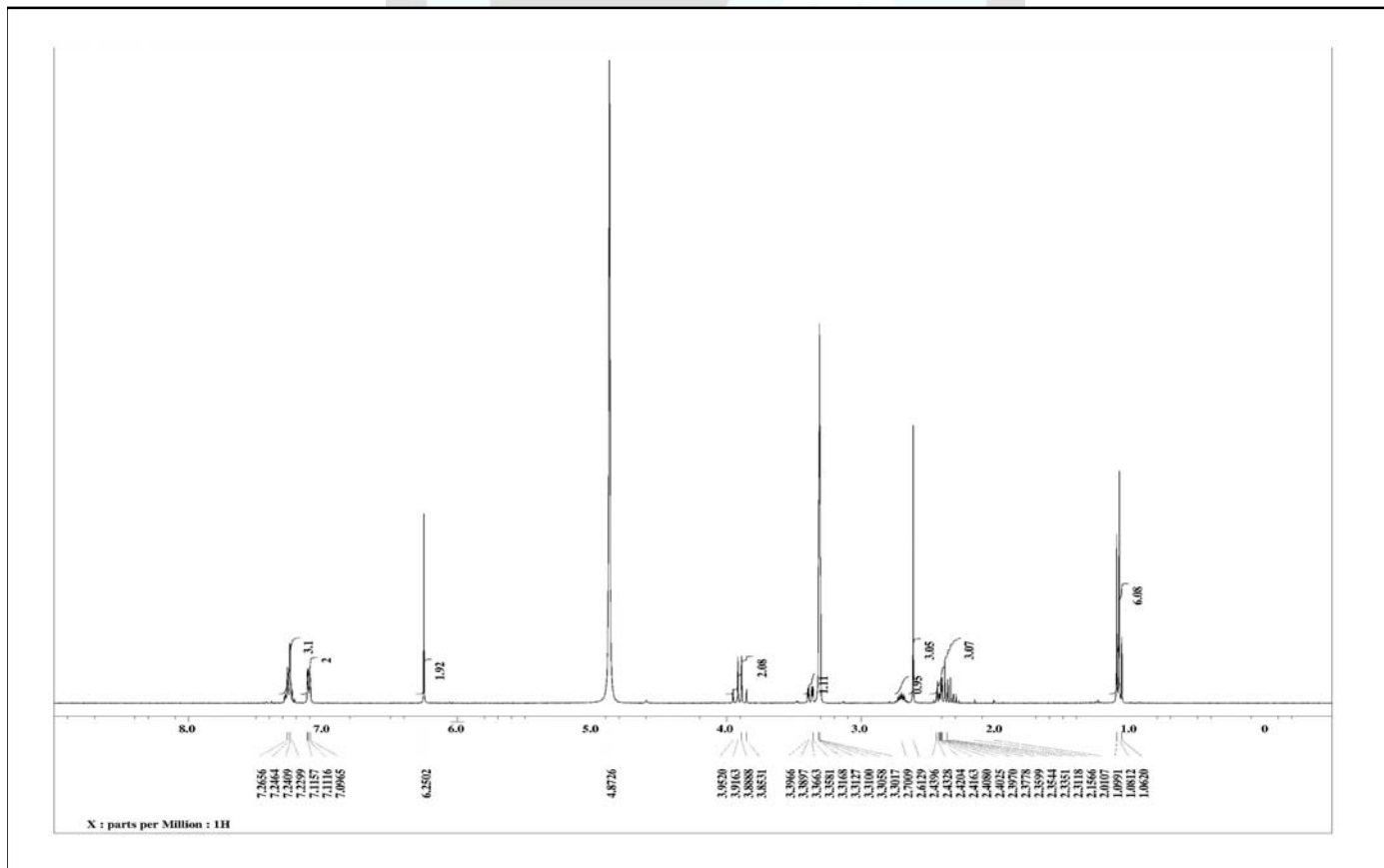


Column: Betasil Phenyl, 4.6 x 150 mm
Mobile Phase: Acetonitrile:10 mM Potassium phosphate buffer (70::30)
Flow Rate: 1.0 mL/min
Wavelength: 215 nm
Data File Name: S:\HPLC\HPLC5\2011\LC50211\L0215108.D
Operator: TNT
Instrument: LC#5
Sample Name: FN020711-02
Method File: AM1207-1.M
Acquired: February 15, 2011 6:02 PM

Peak #	Ret Time	Area	Height	Area %
1	1.66	25.61	6.78	0.77
2	2.61	0.63	0.14	0.02
3	2.77	1.27	0.26	0.04
4	3.07	3289.55	560.16	99.09
5	4.77	1.72	0.18	0.05
6	5.90	0.86	0.10	0.03

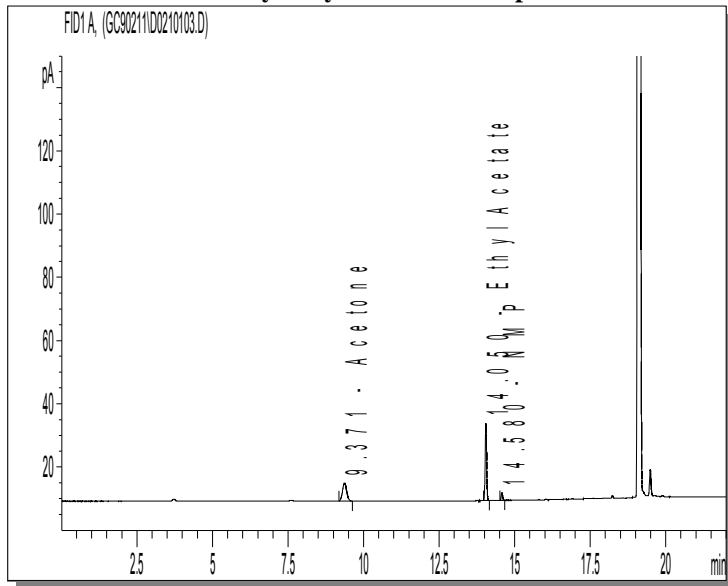
¹H NMR

Instrument: JEOL ECS 400
Solvent: Methanol-D₄



Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



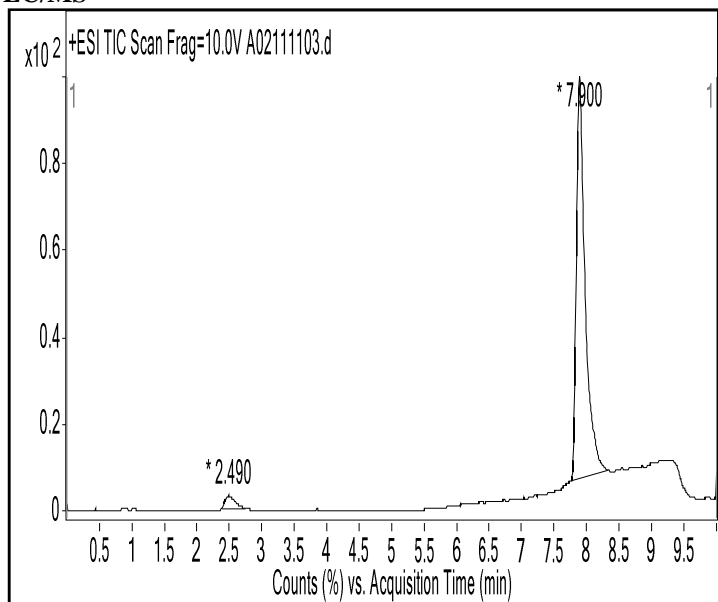
Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C (12 min) to 220°C at 40°C/min (5.5 min)
Carrier Gas: Helium
Flow Rate: 2.0 mL/min
Detector Heater Temp: 250°C
Injector: Headspace Sampler
HS Oven Temp: 60°C
Vial Equilibration: 10 minutes

Data File Name: C:\CHEM32\1\DATA\GC90211\0210103.D
Operator: BD
Instrument: GC#9
Sample Name: FN020711-02
Acquired: February 10, 2011 11:14 AM

Peak	Compound	Area	Weight %
1	Acetone	54.77074	0.11
2	Ethyl acetate	84.69541	0.28
3	NMP	NA	NA
Total			0.38

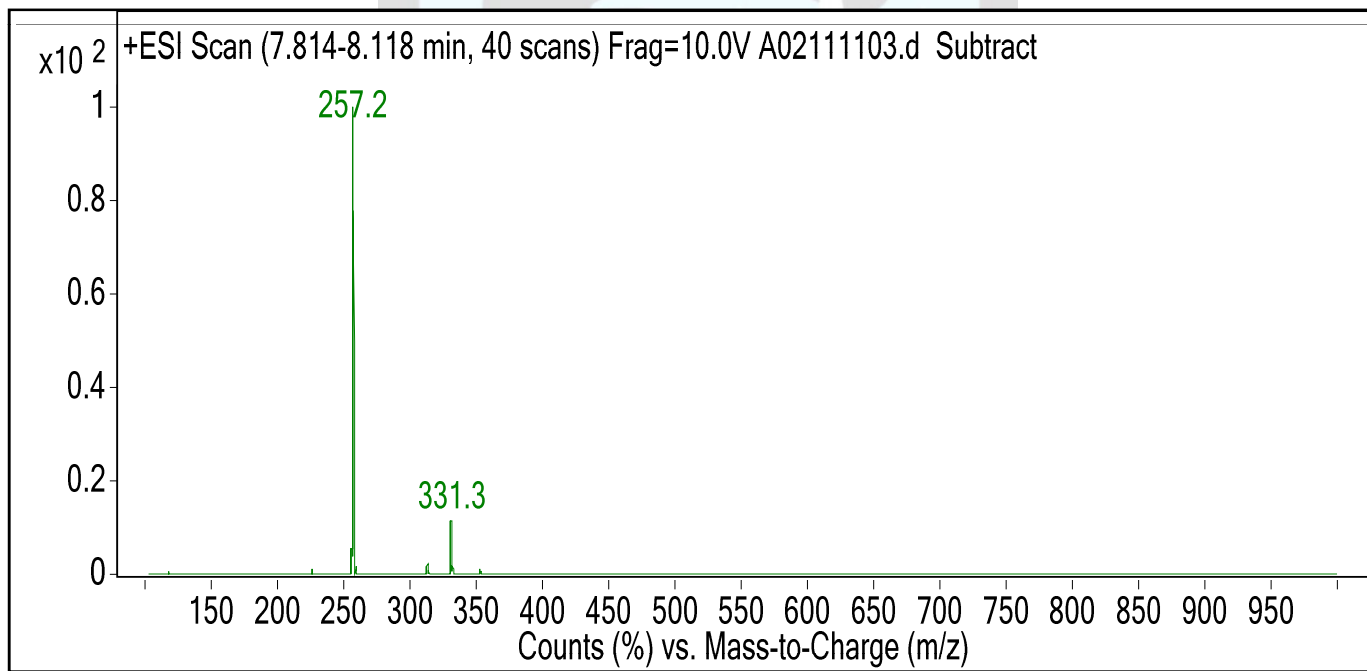
Spectral and Physical Data (cont.)

LC/MS



Column: Luna 3 μ C₁₈, 2.0 x 100 mm
Mobile Phase: Acetonitrile::0.1% Formic acid in Water
(5::95 to 50::50 at 5 mins to 5::95 at 7.5 mins,
hold 2.5 mins)
Flow Rate: 0.3 mL/min
Scan Range: 100-1000 amu
Ionization: Electrospray, Positive Ion

Data File Name: A02111103.d
Operator: JDC
Instrument: LC/MS/MS
Sample Name: FN020711-02
Method File: 0595-55C2P.m
Acquired: February 11, 2011 2:51 PM



Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM Analysis

Column: Luna 3 μ C₁₈, 2.0 x 100 mm
Mobile Phase: Acetonitrile::0.1% Formic acid in Water
(5::95 to 50::50 at 5 mins to 5::95 at 7.5 mins,
hold 2.5 mins)
Flow Rate: 0.3 mL/min
Scan Range: 326-331 amu
Ionization: Electrospray, Positive Ion

Data File Name: A02111104.d
Operator: JDC
Instrument: LC/MS/MS
Sample Name: FN020711-02
Method File: RMN-024a.m
Acquired: February 11, 2011 3:22 PM

