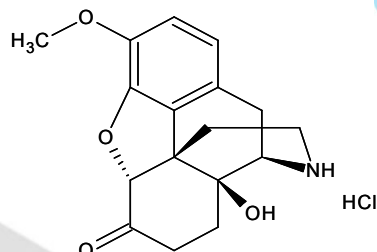


Certificate of Analysis

Noroxycodone HCl

Cerilliant Quality
ISO GUIDE 34
ISO/IEC 17025
ISO 13485
ISO 9001
GMP/GLP



Catalog Number:	N-011
Solution Lot:	FE041212-02
Expiration Date:	April 2017
Solvent:	Methanol
Volume per Ampule:	Not less than 1 mL
Storage:	Store unopened in freezer.
Shipping:	Ambient. See Stability Section.
Intended Use:	For R&D/ analytical purposes only. Not suitable for human or animal consumption.
Regulatory:	USDEA Exempt Canadian TK# 61-155

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	Solution Purity	Certified Concentration
Noroxycodone HCl	99.9%	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. This standard is prepared gravimetrically and mass results are reported on the conventional basis for weighing in air. Concentration is calculated based on: the actual measured mass; Purity Factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C. Concentration is corrected for chromatographic purity, residual water, residual solvents and residual inorganics. 		

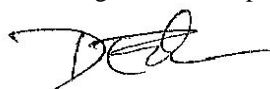
Solution Standard Verification and Homogeneity

Standard Solution	Lot Number	Verified Concentration (mg/mL)		%RSD - Homogeneity	
		Actual Results	Acceptance Criteria	Actual Results	Acceptance Criteria
New Lot	FE041212-02	1.003	± 3%	0.6	≤ 3%
Previous Lot	FE091611-01	1.014	± 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. 					

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.

Darron Ellsworth, Quality Assurance Manager

June 13, 2014

Date

Standard Solution Assay Parameters

Analysis Method: UV/Vis
Wavelength: 280 nm
Slit Width: 1.0 nm
Response: 0.5 s

Calibration Curve

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

Neat Material Data

Compound Name: Noroxycodone HCl
Compound Lot: FC030812-01

Chemical Formula: C₁₇H₁₉NO₄ · HCl
CAS Number: NA
Molecular Weight: 337.80

Neat Material Characterization Summary

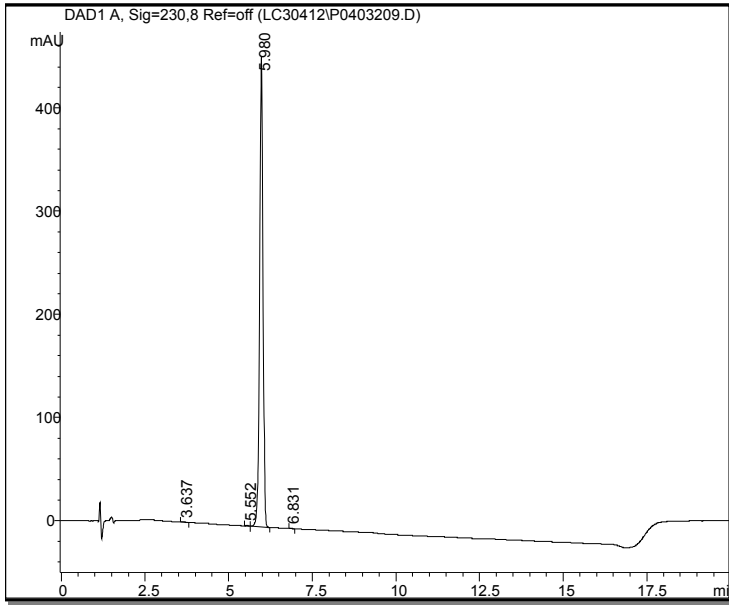
Analytical Test	Method	Results
Chromatographic Purity by HPLC/PDA Analysis	SP10-0102	99.8%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ¹ H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 ¹	1.48%
Residual Water Analysis by Karl Fischer Coulometry	USP <921>, SP10-0103	0.49%
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Purity Factor		97.81%

- ♦ Chromatographic 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 chromatographic purity value is used to calculate the Purity Factor.
- ♦ 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: Ascentis Phenyl 3 μ , 4.6 x 100 mm
Mobile Phase: A: Acetonitrile
 B: 0.1% Trifluoroacetic acid in Water
Gradient Program:

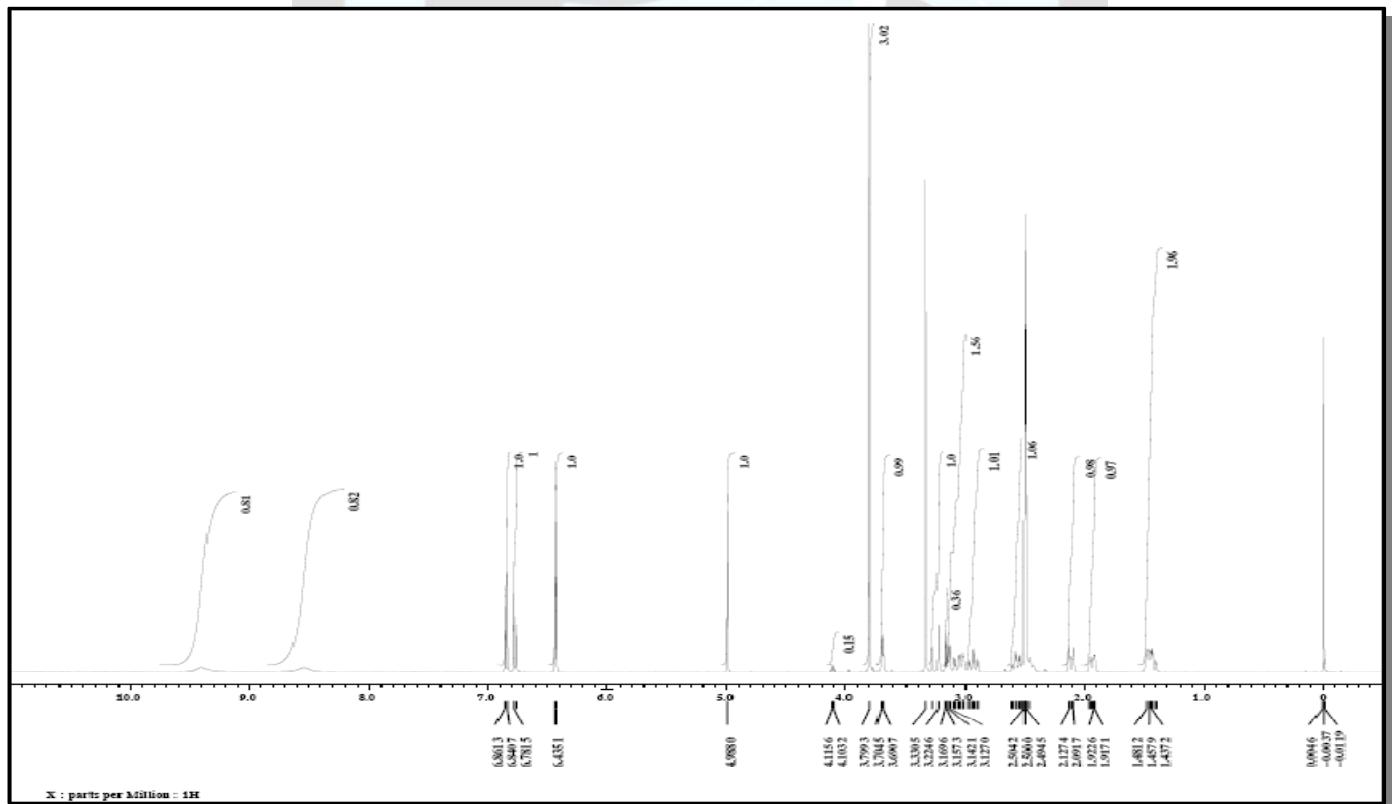
Time (mins)	%A	%B
0	5	95
15	50	50
15.1	5	95

Flow Rate: 1.2 mL/min
Wavelength: 230 nm
Data File Name: S:\HPLC\HPLC3\2012\LC30412\P0403209.D
Operator: GLR
Instrument: LC#3
Sample Name: FC030812-01
Method File: RMN023-3.M
Acquired: April 3, 2012 12:41 PM

Peak #	Ret Time	Area	Height	Area %
1	3.64	1.46	0.23	0.05
2	5.55	3.12	0.59	0.10
3	5.98	3169.79	456.73	99.82
4	6.83	1.03	0.13	0.03

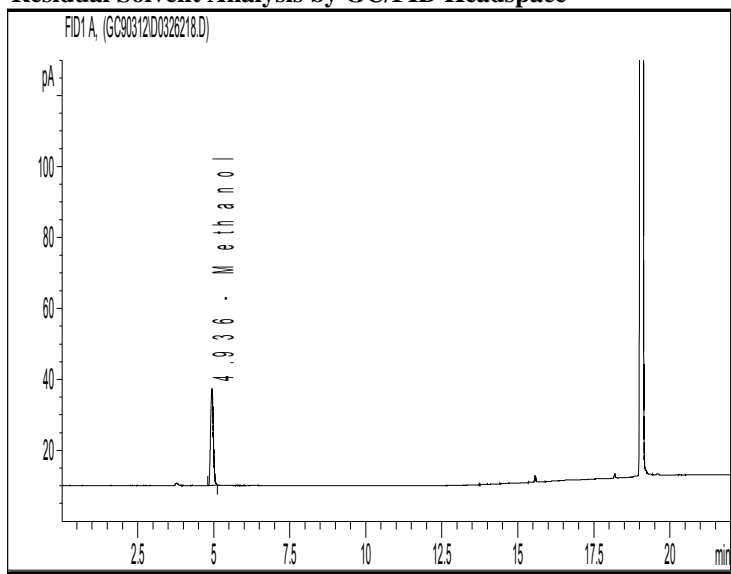
¹H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D₆



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\GC90312\D0326218.D
Operator: BD
Instrument: GC#9
Sample Name: FC030812-01
Acquired: March 27, 2012 12:29 PM

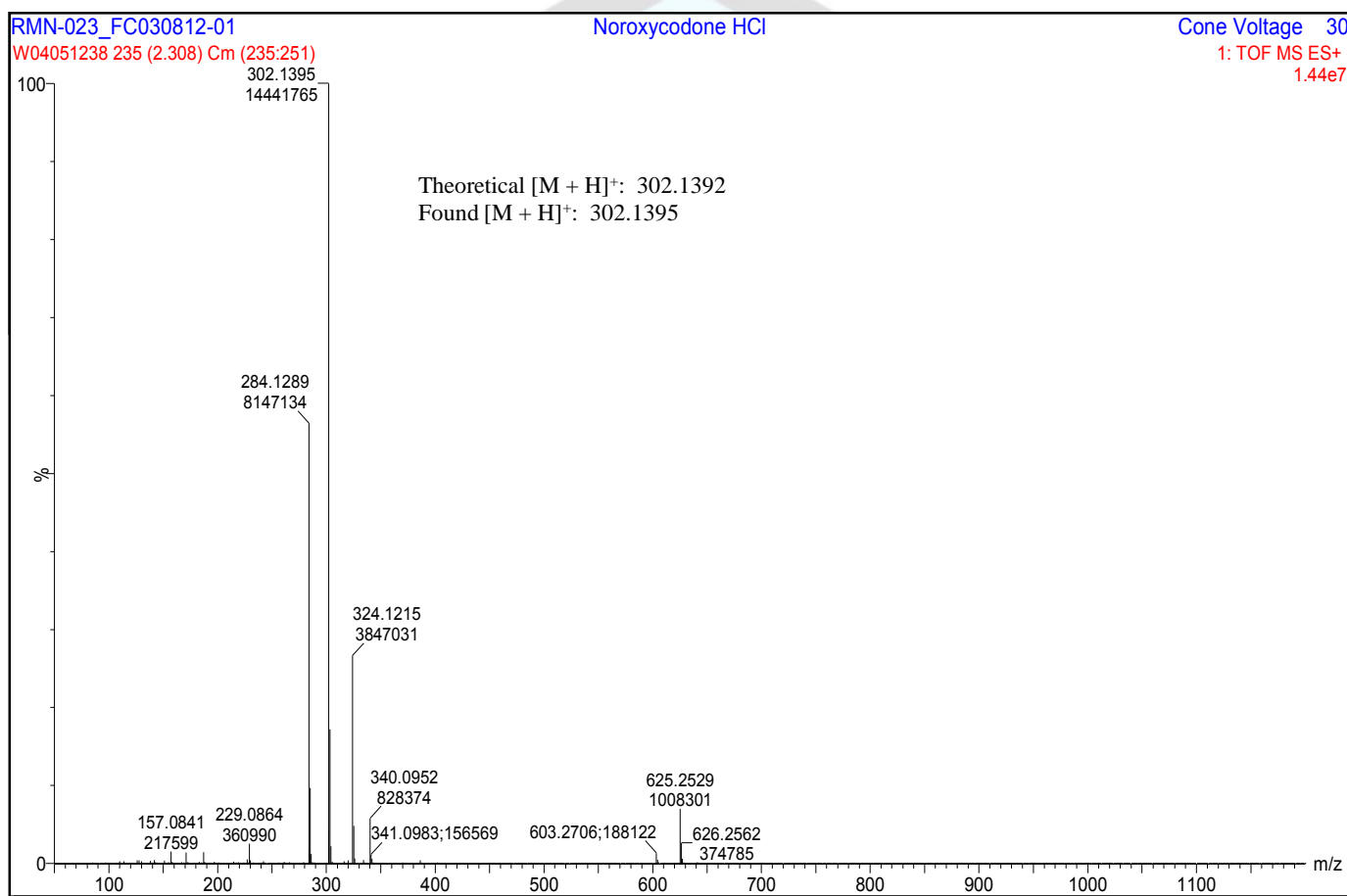
Peak	Compound	Area	Weight %
1	Methanol	168.07777	1.48
2	NMP	NA	NA
Total			1.48

Spectral and Physical Data (cont.)

LC/MS

Column: Zorbax Eclipse Plus C18 RRHD 1.8 μ , 2.1 x 50 mm
Mobile Phase: 0.1% Formic acid in Water::Acetonitrile
(95::5 to 60::40 at 4 mins, to 95::5 at 6.1 mins,
hold 1.9 mins)
Flow Rate: 0.4 mL/min
Scan Range: 50-1200 amu
Ionization: Electrospray, Positive Ion

Data File Name: W04051238
Operator: JDC
Instrument: Waters XEVO G2 QTOF
Sample Name: FC030812-01
Method File: 0595-6040C3
Acquired: April 5, 2012 12:00 AM



Stability

Short term stability studies have been performed under accelerated conditions for periods up to four weeks. Short term data is utilized to predict long term stability and to support transport conditions and normal laboratory use. Real-time stability studies are performed at the recommended storage conditions over the life of the product.

Short Term Stability : A summary of accelerated stability findings for a related product (N-033, Noroxycodone-D3 HCl) is listed below.

Storage Condition	Mean Kinetic Temperature (MKT)	Time Period/Result
Freezer	-15°C	No decrease in purity was noted after four weeks.
Refrigerator	4°C	
Room Temperature	21°C	
40°C	40°C	2.05% decrease in purity was noted after four weeks.

Transport/Shipping : Ship cold.

Short Term Storage: Stability data supports short term storage for no more than 3 months at Refrigerate conditions.

Long Term Stability: Long term stability has been assessed for freezer storage (-10 °C to -25 °C) conditions.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 7, 2012	Initial version
01	June 13, 2014	Update Stability Section to reflect four week stability study.