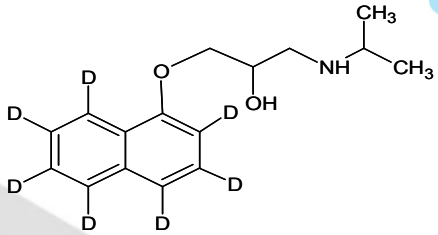
Cerilliant Quality
ISO GUIDE 34
ISO/IEC 17025
ISO 13485
ISO 9001
GMP/GLP

Certificate of Analysis

(±)-Propranolol-D_7 (ring-D_7)



Catalog Number: P-085
Solution Lot: FN052912-02
Retest Date: June 2016
Solvent: Methanol with 5% 1 M HCl
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.
Safety: **Danger. See Safety Data Sheet**

- Retest Date - stability studies ongoing. Certificate of Analysis will be updated upon completion of retest.
- 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.
- For MS Applications, we advise laboratories not to mix lots during a single sequence.
- For quantitative applications, the minimum sample size for intended use is 1 µL.

Component	Solution Purity	Certified Concentration
(±)-Propranolol-D_7	99.7%	100.0 ± 0.6 µg/mL

- 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 (µg/mL)		%RSD - Homogeneity	
		Actual Results	Acceptance Criteria	Actual Results	Acceptance Criteria
New Lot	FN052912-02	100.6	± 3%	1.0	≤ 3%

- 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.

ACLASS ACCREDITED REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

August 24, 2015
Date

Standard Solution Assay Parameters

Analysis Method: UV/Vis
Wavelength: 290 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: (±)-Propanolol-D_7
Compound Lot: PN032012-01

Chemical Formula: $C_{16}H_{14}D_7NO_2$
CAS Number: 344298-99-3
Molecular Weight: 266.39

Neat Material Characterization Summary

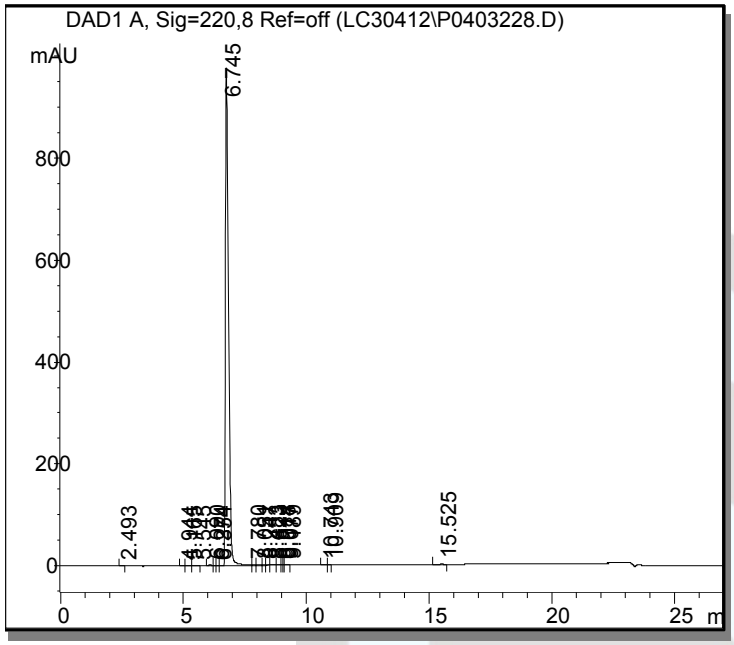
Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.4%	
Secondary Chromatographic Purity by LC/MS Analysis	SP10-0107	97.2%	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.00% D_0 vs D_7	
		0.00% D_0	0.02% D_4
		0.00% D_1	0.69% D_5
		0.00% D_2	11.66% D_6
		0.00% D_3	87.63% D_7
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	USP <921>, SP10-0103	0.10%	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.26%	

- The primary 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 primary chromatographic purity value is used to calculate the Mass Balance 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/UV



Column: Prodigy ODS 3, 5 µm, 4.6 x 250 mm

Mobile Phase: A: Acetonitrile
B: 10 mM Potassium phosphate buffer

Gradient Program:

Time (min)	%A	%B
0.0	30	70
20.0	70	30
20.1	30	70

Flow Rate: 1.0 mL/min

Wavelength: 220 nm

Data File Name: S:\HPLC\HPLC3\2012\LC30412\P0403228.D

Instrument: LC#3

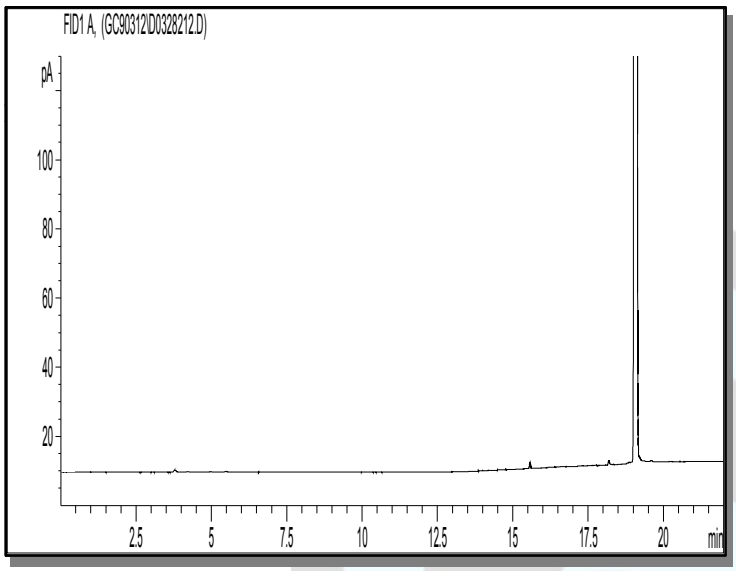
Sample Name: PN032012-01

Acquired: April 03, 2012

Peak #	Ret Time	Area	Height	Area %
1	2.49	2.81	0.48	0.03
2	4.94	0.88	0.12	0.01
3	5.17	1.01	0.10	0.01
4	5.55	0.81	0.12	0.01
5	6.09	7.38	1.32	0.08
6	6.27	1.20	0.20	0.01
7	6.35	0.47	0.12	0.01
8	6.75	8669.10	977.36	99.40
9	7.78	6.71	0.74	0.08
10	8.05	7.63	0.65	0.09
11	8.25	3.21	0.37	0.04
12	8.48	3.01	0.32	0.03
13	8.62	4.16	0.32	0.05
14	8.91	2.22	0.19	0.03
15	9.02	0.49	0.12	0.01
16	9.08	0.25	0.09	0.00
17	9.19	1.20	0.16	0.01
18	10.74	2.99	0.43	0.03
19	10.91	0.66	0.12	0.01
20	15.53	5.11	0.46	0.06

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



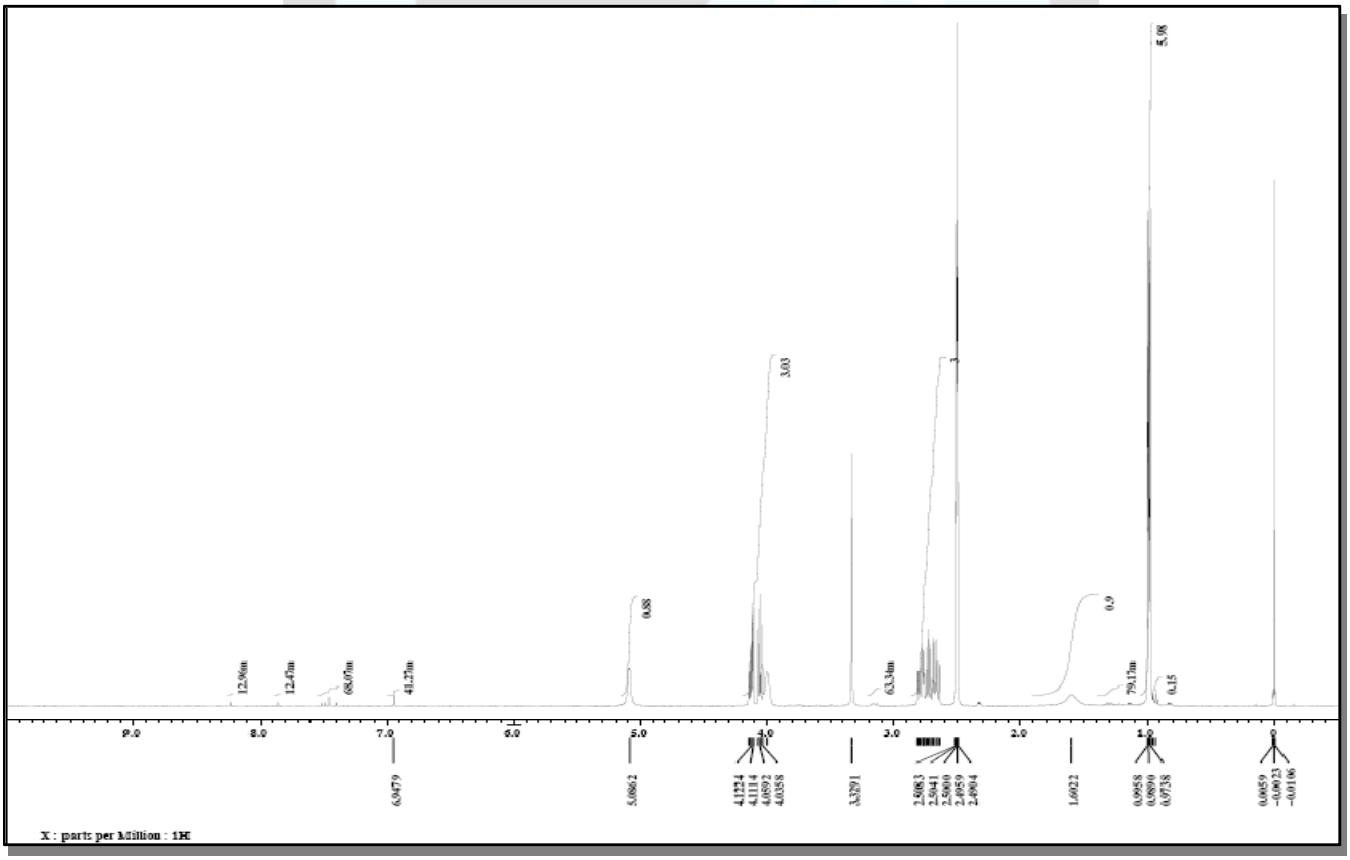
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C (12 min) to 220°C at 40°C/min (5.5 min)
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Data File Name:	C:\CHEM32\1\DATA\GC90312\D0328212.D
Instrument:	GC#9
Sample Name:	PN032012-01
Acquired:	March 28, 2012

Peak	Compound	Area	Weight %
1	NMP	NA	NA
Total			**ND**

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



Spectral and Physical Data (cont.)

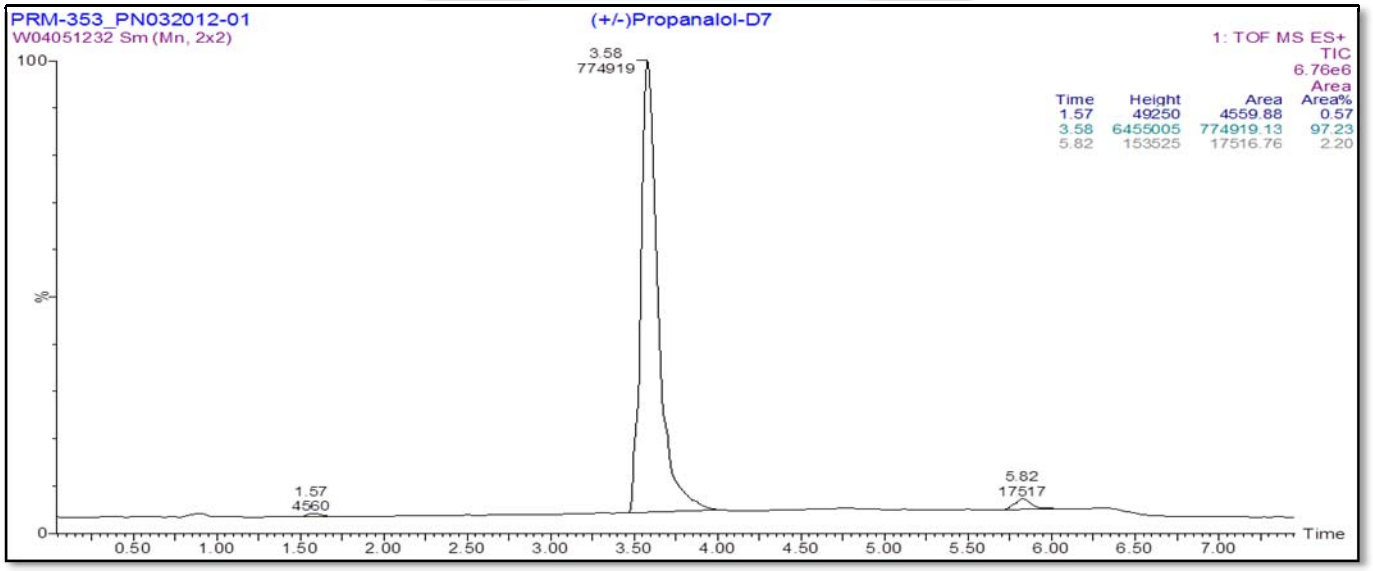
LC/MS

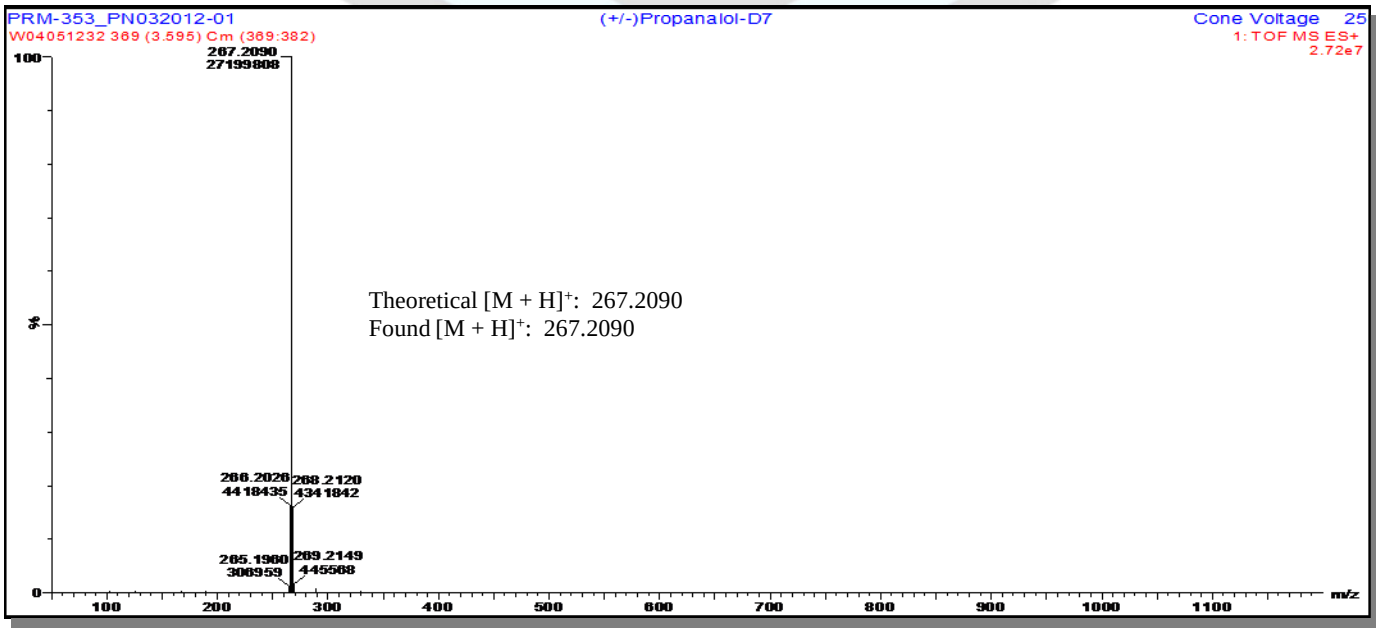
Column: Zorbax Eclipse Plus RRHD C18, 1.8 µm, 2.1 x 50 mm
Mobile Phase: A:: 0.1% Formic Acid in Water
B:: Acetonitrile

Gradient:

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	70	30
5.8	70	30
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 50-1200 amu
Ionization: Electrospray, Positive Ion
Data File Name: W04051232
Instrument: Waters XEVO G2 QTOF
Sample Name: PN032012-01
Acquired: April 05, 2012





Theoretical $[M + H]^+$: 267.2090
Found $[M + H]^+$: 267.2090

Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM Analysis

Column: Zorbax Eclipse Plus RRHD C18, 1.8 µm, 2.1 x 50 mm

Mobile Phase: A:: 0.1% Formic Acid in Water
B:: Acetonitrile

Gradient:

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	70	30
5.8	70	30
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min

Scan Range: 260-267 amu

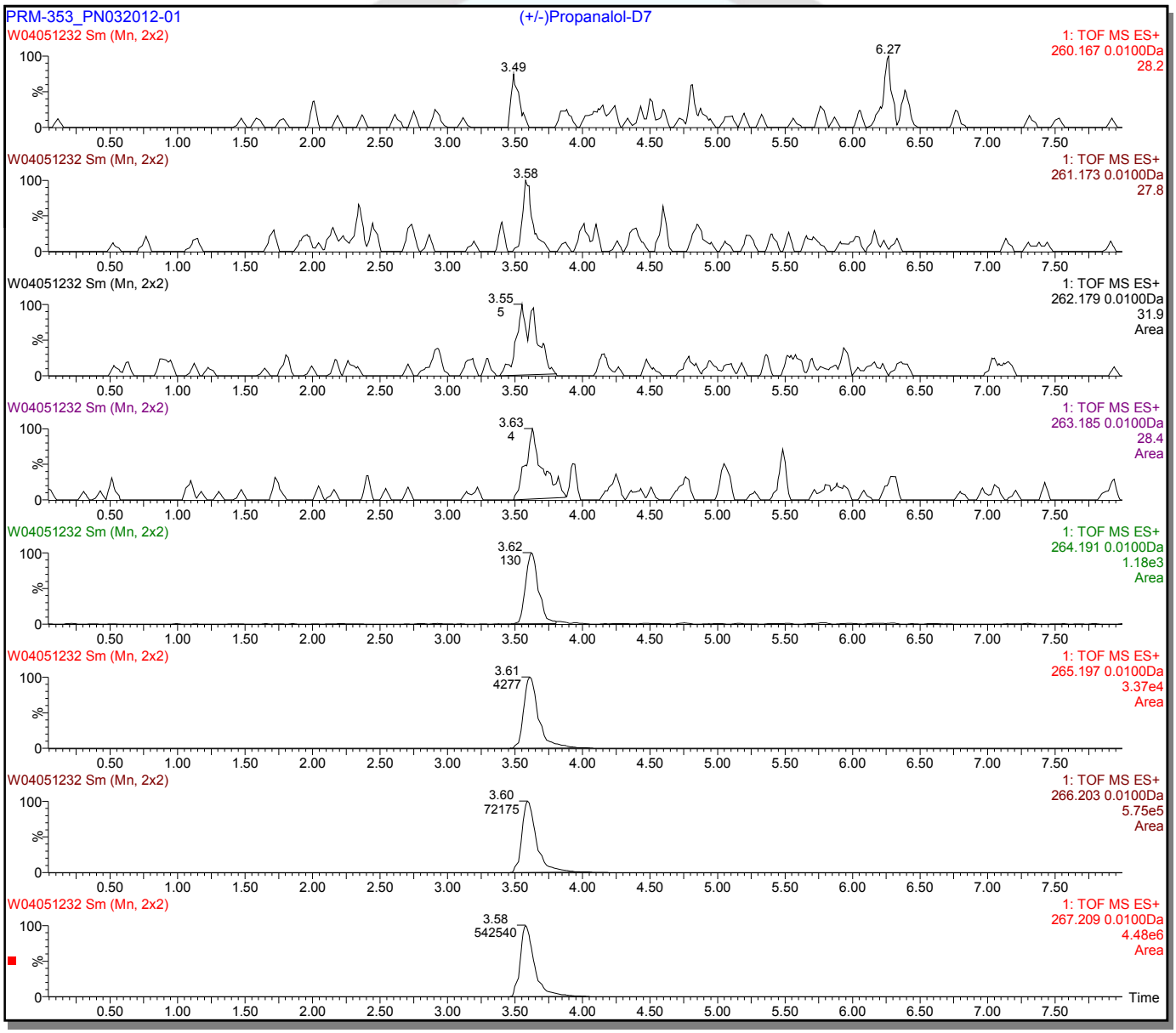
Ionization: Electrospray, Positive Ion

Data File Name: W04051232

Instrument: Waters XEVO G2 QTOF

Sample Name: PN032012-01

Acquired: April 05, 2012



Stability

***Short Term Stability** : A summary of accelerated stability findings for this product is listed below.*		
Storage Condition	**Mean Kinetic Temperature (MKT)**	**Time Period**
Freezer	-15°C	No decrease in purity was noted after four weeks.
Refrigerator	4°C	
Room Temperature	21°C	
40°C	40°C	
***Transport/Shipping** : Stability data supports transport of this product at ambient conditions.*		
***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. Stability of a minimum of 36 months has been established through real-time stability studies.*		

COA Revision History

Revision No.	Date	Reason for Revision
00	June 22, 2012	Initial version
01	July 31, 2013	Revised Retest Date from August 2013 to August 2014.
02	September 10, 2014	Added Long Term Stability Section.
		Revised Retest Date from August 2014 to September 2015.
		Added minimal sample size and MS application statements to front page.
		Added Secondary Chromatographic Purity by LC/MS to table on page two.
		Added Purity by LC/MS chromatogram on page five.
03	April 23, 2015	Updated Safety Section from "Flammable, Poison" to "Danger. See Safety Data Sheet"
04	August 07, 2015	Revised Restest Date from September 2015 to June 2016.
		Revised Long Term Stability from 27 months to 36 months.
05	August 24, 2015	Updated Stability Section to reflect 4-week study data.
		Changed shipping conditions from "Ship cold" to "Ambient."