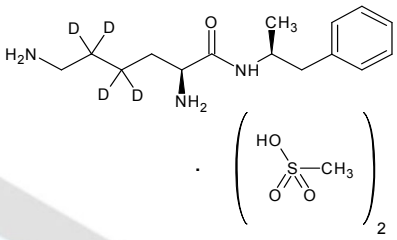
Cerilliant Quality
ISO GUIDE 34
ISO/IEC 17025
ISO 13485
ISO 9001
GMP/GLP

Certificate of Analysis

Lisdexamfetamine-D_4 dimesylate



Catalog Number: L-028
Solution Lot: FE011112-01
Retest Date: May 2016
Solvent: Methanol
Volume per Ampule: Not less than 1 mL
Storage: Store unopened in freezer.
Shipping: Ship cold. See Stability Section.
Intended Use: For R&D/ analytical purposes only. Not suitable for human or animal consumption.
Regulatory: USDEA Exempt | Canadian TK# 61-664 **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 quantitative applications, the minimum sample size for intended use is 1 µL.
- For MS Applications, we advise laboratories not to mix lots during a single sequence.

Component	Solution Purity	Certified Concentration
Lisdexamfetamine-D_4 dimesylate	100.0% (as sum of isomers)	100.0 ± 0.6 µg/mL (as free base)

- 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) Actual Results	Verified Concentration (µg/mL) Acceptance Criteria	%RSD - Homogeneity Actual Results	%RSD - Homogeneity Acceptance Criteria
New Lot	FE011112-01	99.7	± 3%	1.7	≤ 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

October 20, 2015
Date

Standard Solution Assay Parameters

Analysis Method:	HPLC/UV
Column:	Betasil Phenyl, 5 µm, 4.6 x 150 mm
Mobile Phase	Acetonitrile::0.1% Phosphoric acid in Water (10::90)
Flow Rate:	1.0 mL/min
Wavelength:	210 nm

Calibration Curve

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

Neat Material Data

Compound Name:	Lisdexamfetamine-D_4 dimesylate	**Chemical Formula:**	$C_{15}H_{21}D_4N_3O \cdot 2(CH_3SO_3H)$
Compound Lot:	FC121211-02	**CAS Number:**	NA
		Molecular Weight:	459.61

Neat Material Characterization Summary

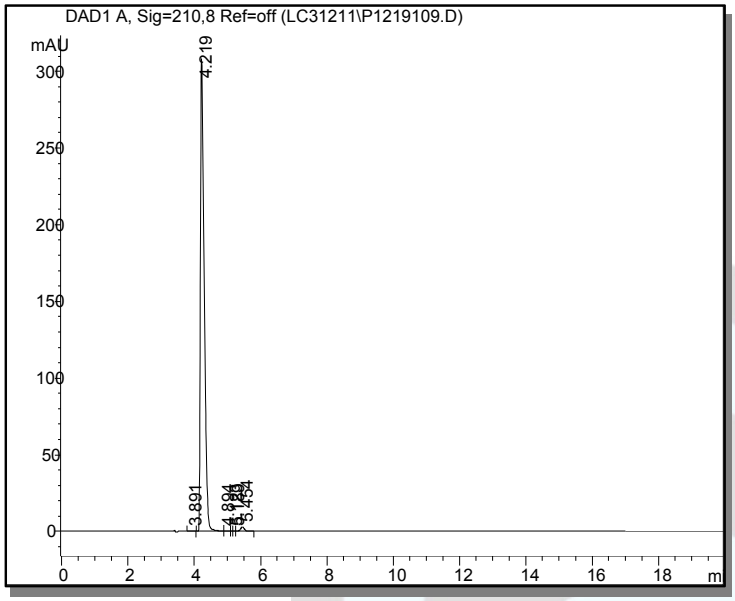
Analytical Test	Method	Results		
Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.9% (sum of isomers)		
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure		
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.48% D_0 vs D_4		
		0.46% D_0	3.85% D_3	
		0.07% D_1	95.55% D_4	
		0.08% D_2		
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	0.21%		
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%		
Elemental Analysis	Outsourced		Calculated	Analyzed
		C	44.43%	44.19%
		H	7.30%	7.32%
		N	9.14%	9.04%
Purity Factor		99.70%		

- 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/UV



Column: Prodigy ODS3, 5 µm, 4.6 x 250 mm
Mobile Phase: Acetonitrile::0.1% Phosphoric acid (10::90)
Flow Rate: 1.0 mL/min
Wavelength: 210 nm

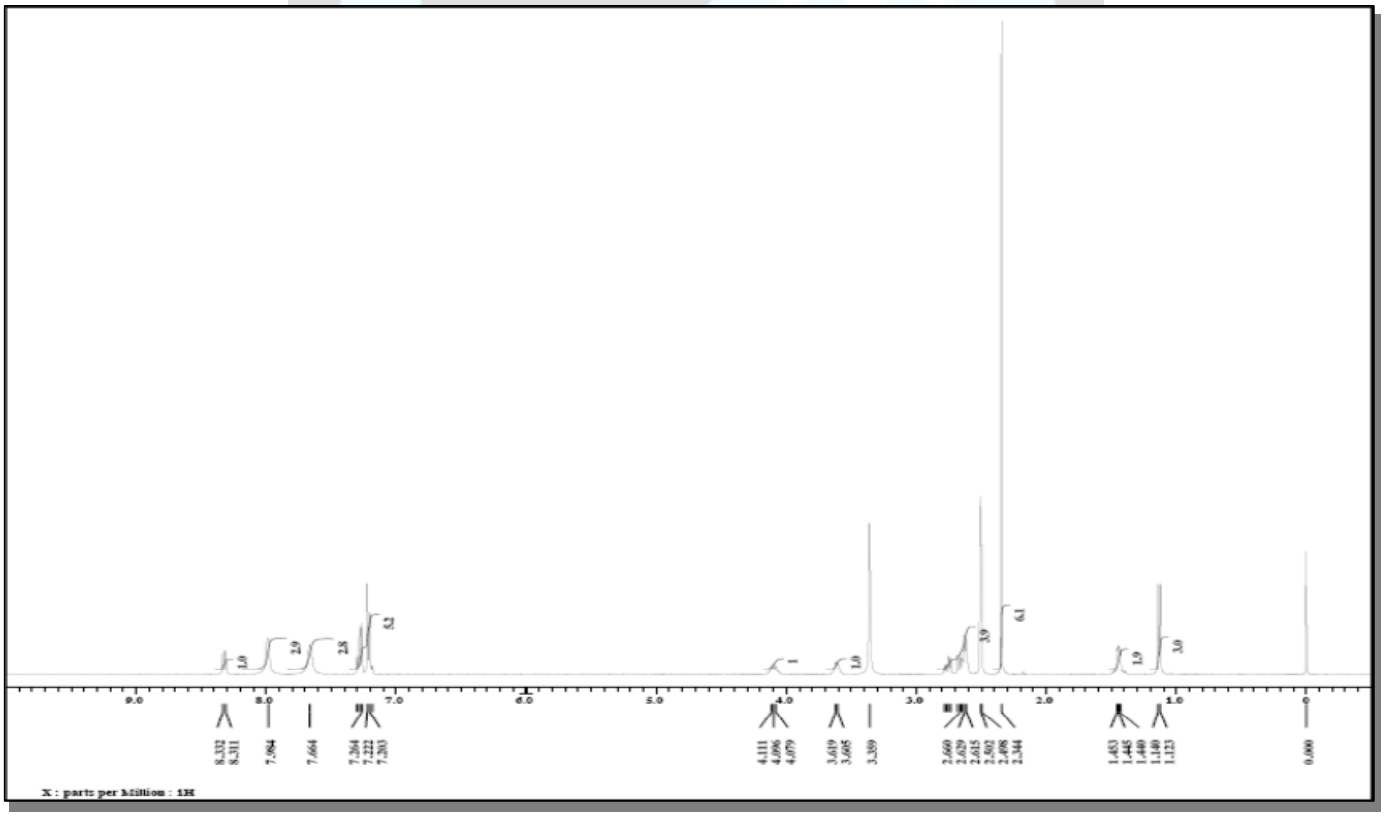
Data File Name: S:\HPLC\HPLC3\2011\LC31211\P1219109.D
Instrument: LC#3
Sample Name: FC121211-02
Acquired: December 19, 2011

Peak #	Ret Time	Area	Height	Area %
1	3.89	0.24	0.04	0.01
2	4.22	2453.31	308.57	98.93
3	4.89	2.03	0.24	0.08
4	5.12	0.42	0.11	0.02
5	5.19	0.53	0.11	0.02
6	5.45	23.37	2.87	0.94

Note: Purity value is the sum of peaks 2 and 6

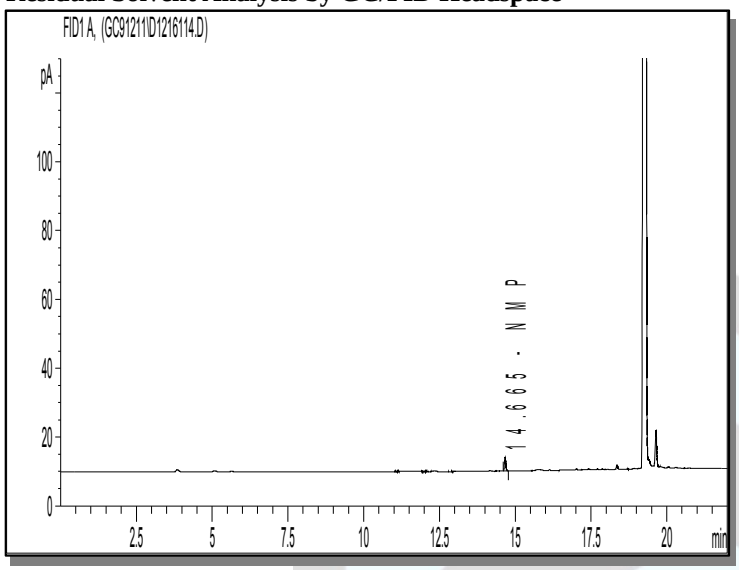
^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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\GC91211\D1216114.D
Instrument:	GC#9
Sample Name:	FC121211-02
Acquired:	December 16, 2011

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

ND - Not Detected

Spectral and Physical Data (cont.)

LC/MS

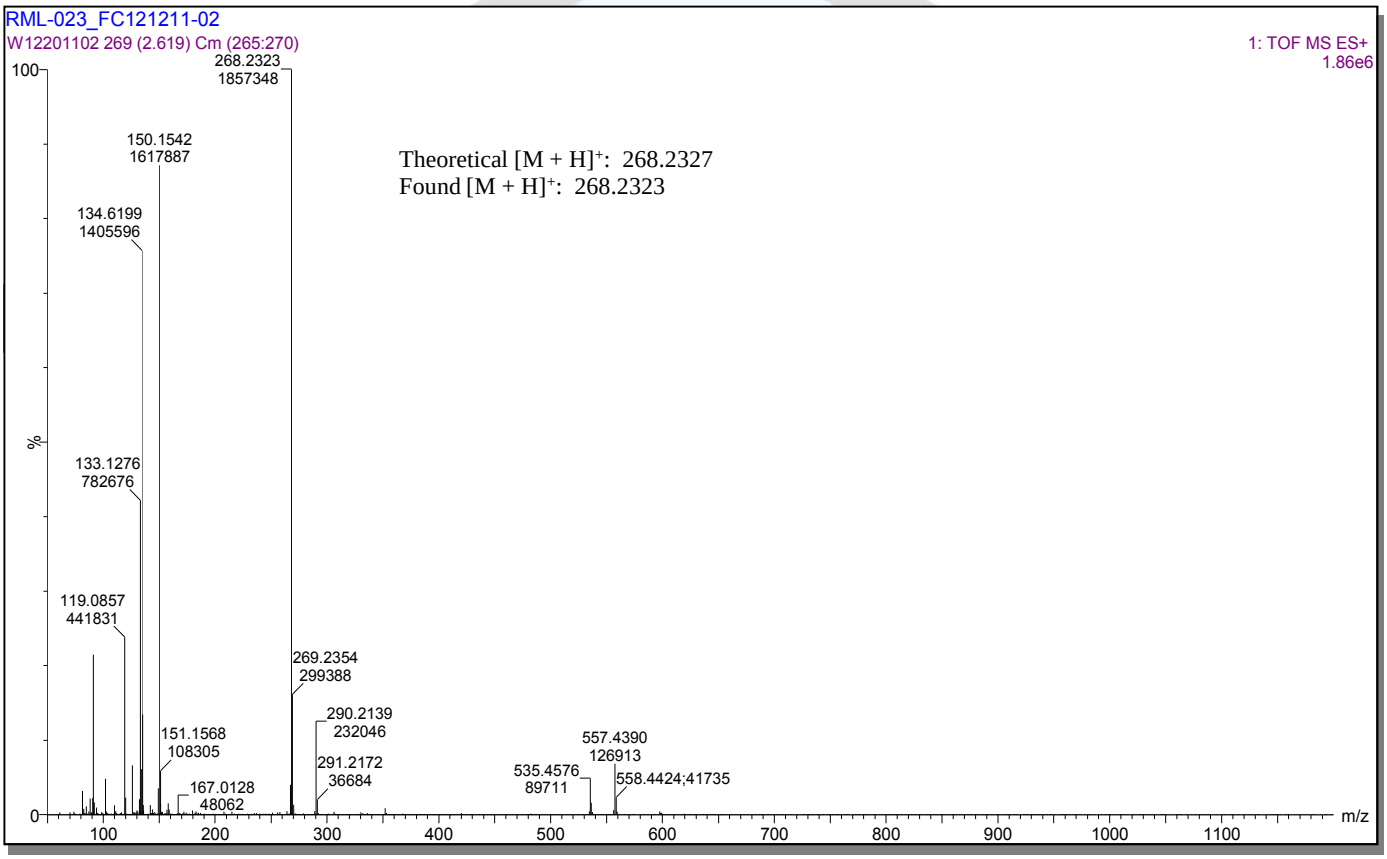
Column: Zorbax Eclipse Plus RRHD, 1.8 µm, 2.1 x 50 mm

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

Gradient:

Time (min)	%A	%B
0.0	99	1
0.5	99	1
4.0	95	5
5.8	95	5
6.0	99	1
8.0	99	1

Flow Rate: 0.4 mL/min
Scan Range: 50-1200 amu
Ionization: Electrospray, Positive Ion
Data File Name: W12201102
Instrument: Waters XEVO G2 QTOF
Sample Name: FC121211-02
Acquired: December 20, 2011



Spectral and Physical Data (cont.)

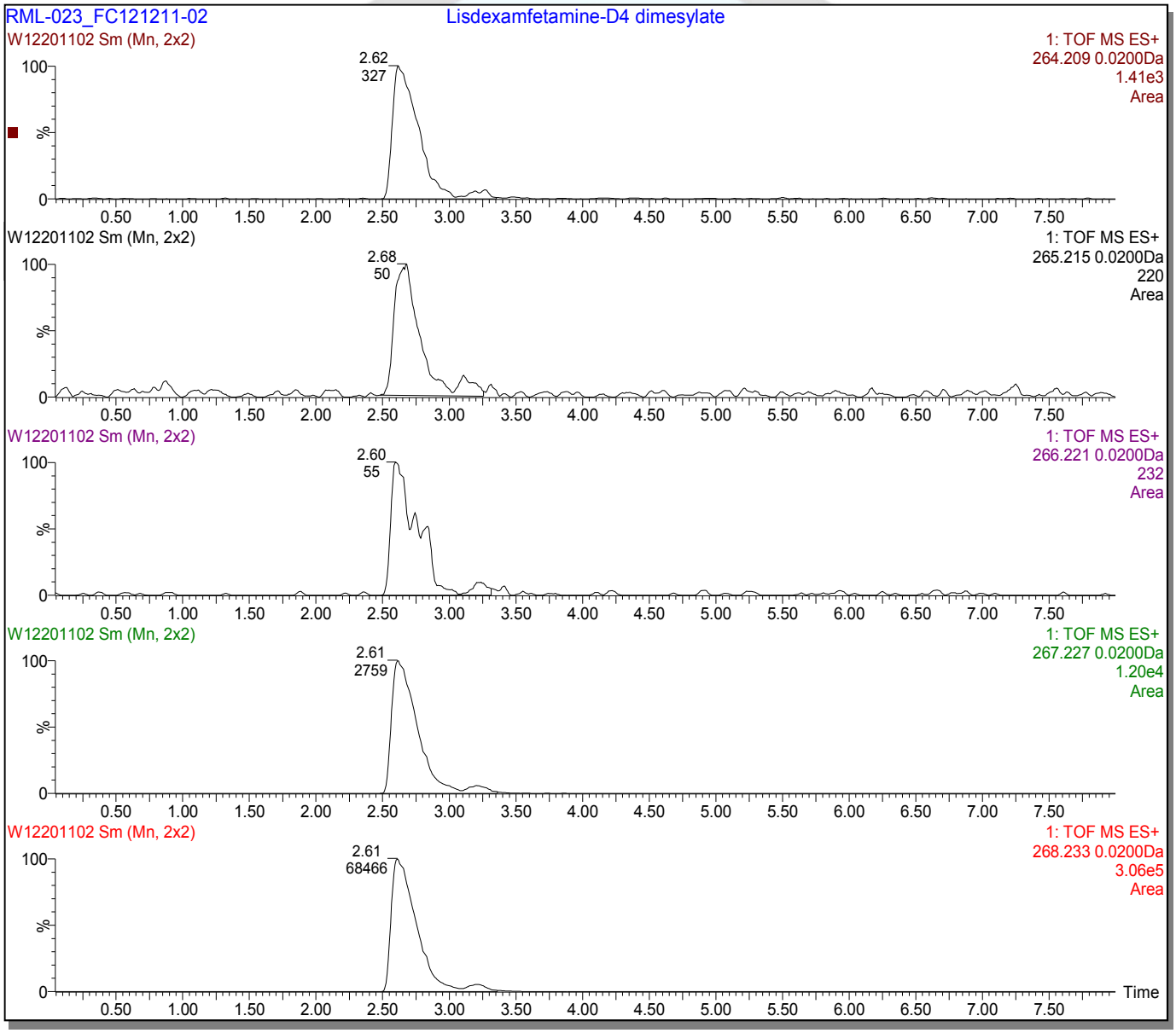
Isotopic Purity by LC/MS SIM Analysis

Column: Zorbax Eclipse Plus RRHD, 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	99	1
0.5	99	1
4.0	95	5
5.8	95	5
6.0	99	1
8.0	99	1

Flow Rate: 0.4 mL/min
Scan Range: 264-268 amu
Ionization: Electrospray, Positive Ion
Data File Name: W12201102
Instrument: Waters XEVO G2 QTOF
Sample Name: FC121211-02
Acquired: December 20, 2011



Stability

Short Term Stability *: A summary of accelerated stability findings for this product 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	5.58% decrease in purity was noted after four weeks.

Transport/Shipping *: Ship cold.*

Short Term Storage: *Stability data supports short term storage of 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 40 months has been established for a related product (L-026, Lisdexamfetamine dimesylate) through real-time stability studies.*

COA Revision History

Revision No.	Date	Reason for Revision
00	January 13, 2012	Initial version
01	September 29, 2012	Revised Retest Date from March 2013 to March 2014.
02	November 11, 2013	Revised Retest Date from March 2014 to May 2015.
03	June 16, 2014	Corrected Retest Date on first page to May 2015.
04	January 08, 2015	Revised Retest Date from May 2015 to May 2016.
		Added minimal sample size and MS application statements to front page.
		Changed Method for Elemental Analysis from SP10-0117 to Outsourced on table on page two.
05	April 22, 2015	Updated Safety Section from "Flammable, Poison" to "Danger. See Safety Data Sheet".
06	September 29, 2015	Updated Short Term Stability with 4-week study data.
07	October 20, 2015	Updated Short Term Stability data from that of related product L-026, Lisdexamfetamine dimesylate, to that of this product.
		Updated Transport/Shipping conditions from ambient to ship cold.