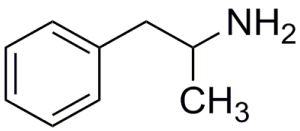
Certified Reference Material - Certificate of Analysis

(±)-Amphetamine, Primary Measurement Standard

1-Phenyl-2-aminopropane

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-007-1ML
Lot No.: FE01202014
Description of CRM: (±)-Amphetamine in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_9H_{13}N$
CAS No.: 300-62-9
Regulatory: USDEA Exempt | Canadian TK # 61-988



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Amphetamine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

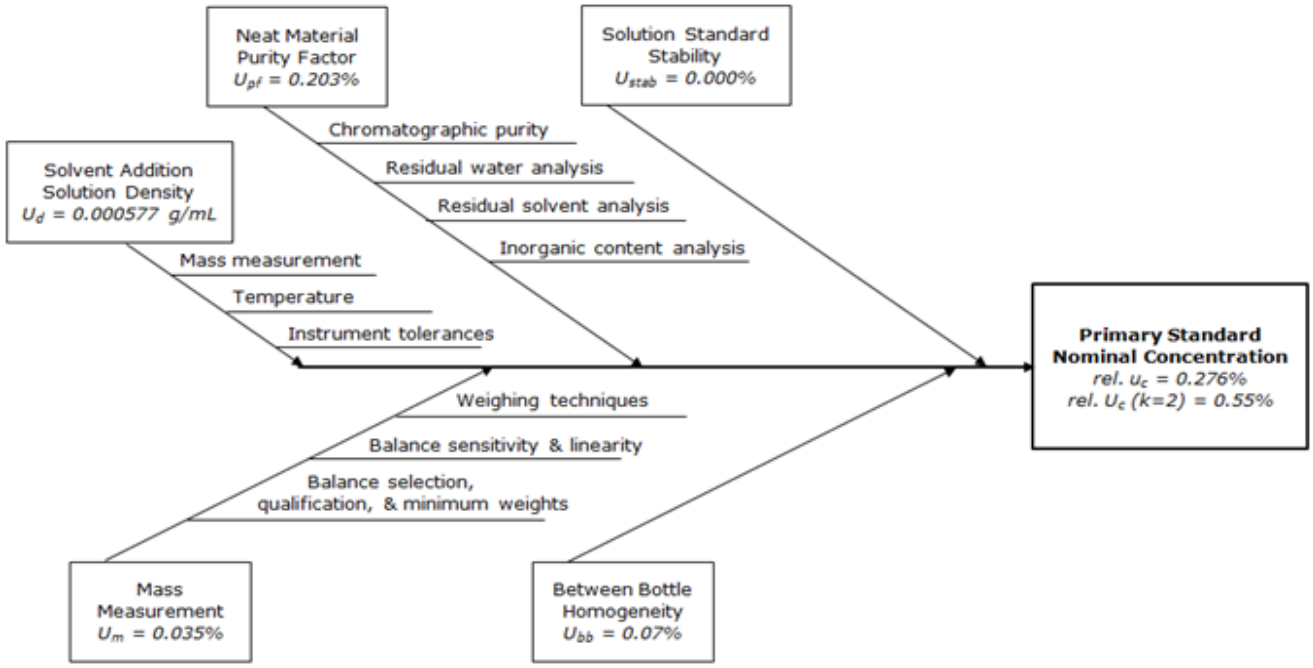
March 10, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms 30 m x 0.53 mm ID, 1.5 µm film thickness	**Number of Points:**	4
Temp Program:	60°C to 260°C at 20°C/min hold 1 min	**Linearity (r) :**	1.000
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01202014	0.985	0.7
Previous Lot	FE04161901	0.982	0.7

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Amphetamine	**Chemical Formula:**	$C_9H_{13}N$
Material Lot:	FC09101802	**CAS Number:**	300-62-9
		Molecular Weight:	135.21

Material Characterization Summary

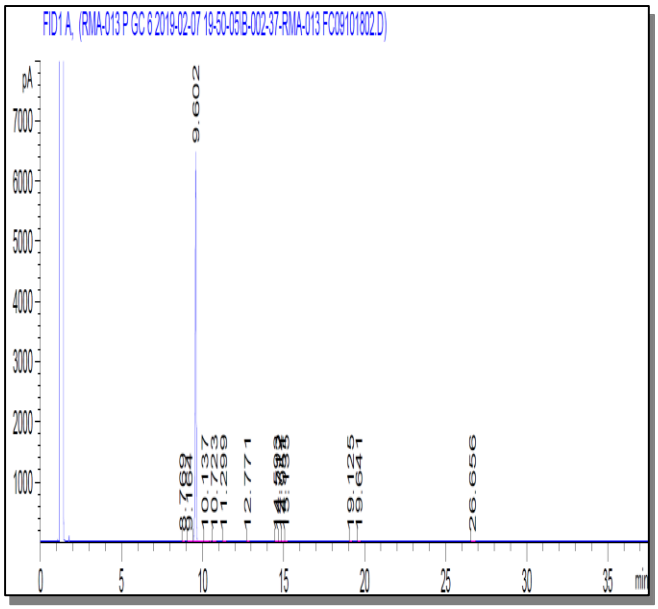
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.5%
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.5%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	0.18%
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.35%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

GC/FID

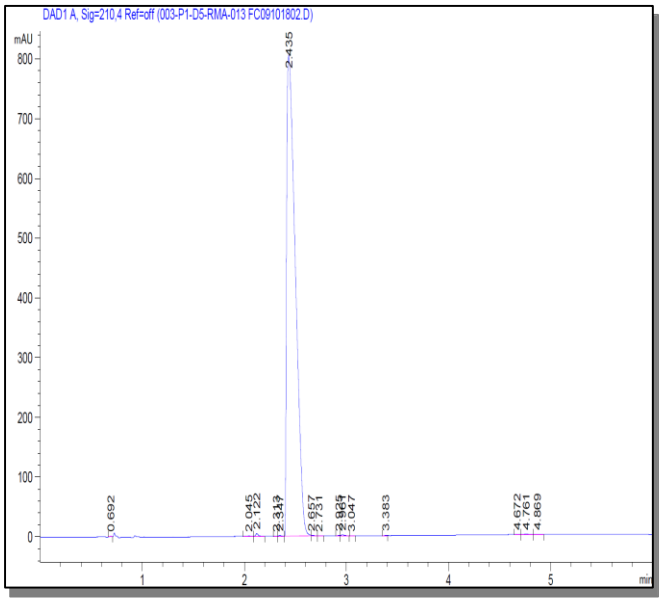


Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 80°C at 40°C/min 80°C to 175°C at 5°C /min 175°C to 300°C at 10°C/min hold 5 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC09101802
Acquired:	February 07, 2019

Peak #	Ret Time	Area %
1	8.77	0.01
2	9.16	0.04
3	9.60	99.53
4	10.14	0.05
5	10.72	0.01
6	11.30	0.16
7	12.77	0.01
8	14.59	0.11
9	14.71	0.04
10	14.95	0.02
11	15.14	0.01
12	19.13	0.00
13	19.64	0.00
14	26.66	0.02

Spectral and Physical Data (cont.)

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.00	5	95
3.50	40	60
5.50	40	60
5.51	5	95

Flow Rate: 0.6 mL/min

Wavelength: 210 nm

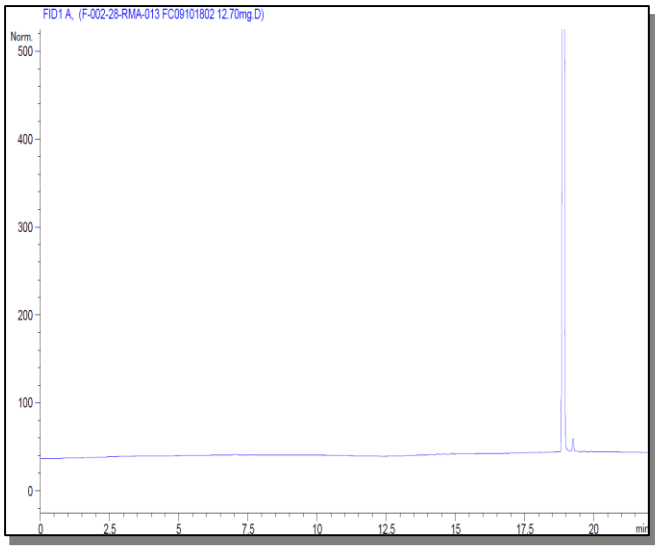
Sample Name: FC09101802

Acquired: January 23, 2019

Peak #	Ret Time	Area %
1	0.69	0.02
2	2.05	0.03
3	2.12	0.18
4	2.31	0.01
5	2.35	0.06
6	2.44	99.45
7	2.66	0.05
8	2.73	0.01
9	2.93	0.01
10	2.96	0.08
11	3.05	0.01
12	3.38	0.00
13	4.67	0.00
14	4.76	0.06
15	4.87	0.02

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



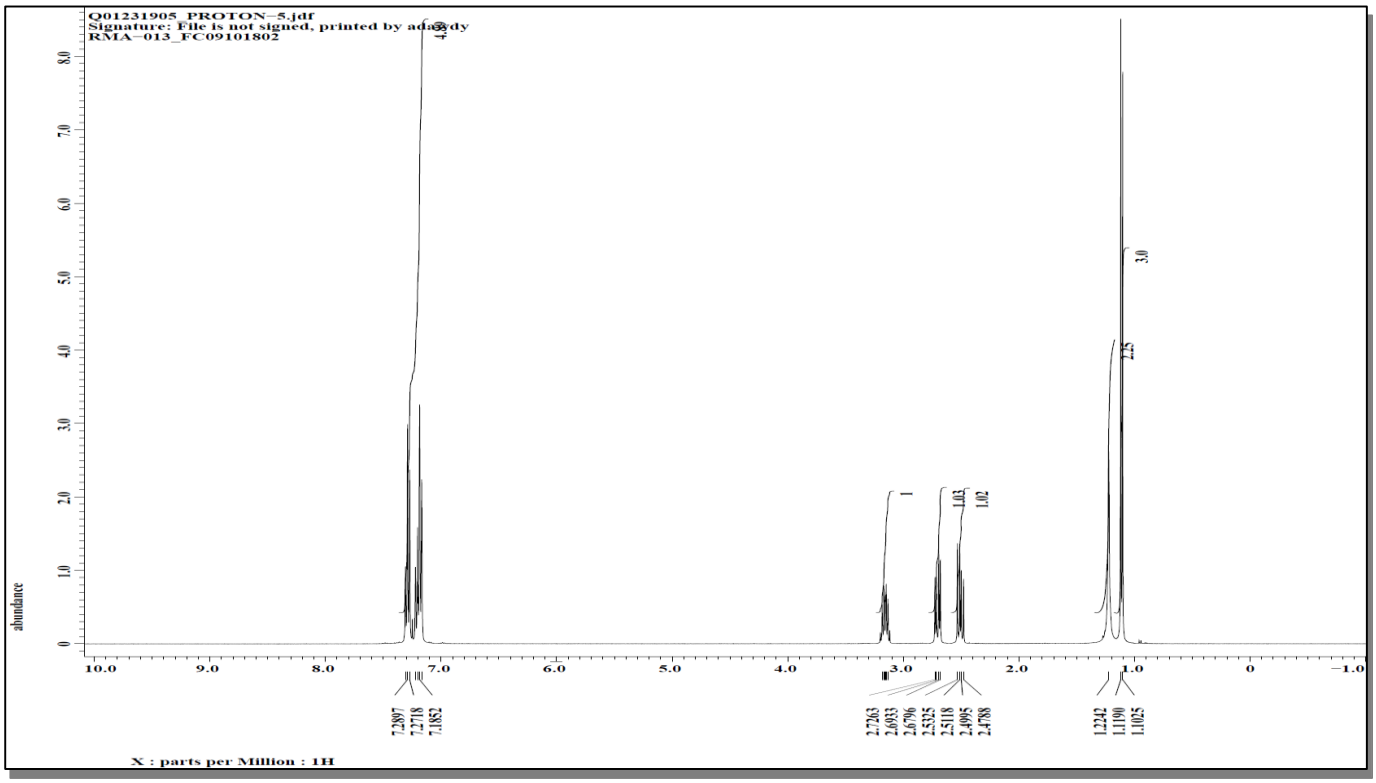
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC09101802
Acquired:	January 23, 2019

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

ND - None Detected

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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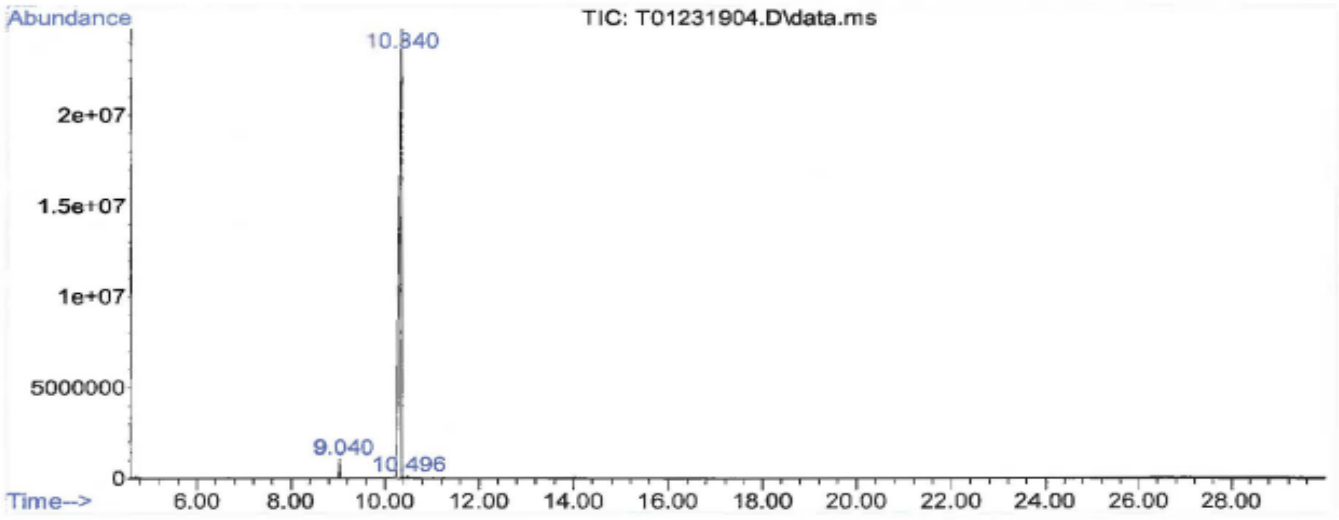
Spectral and Physical Data (cont.)

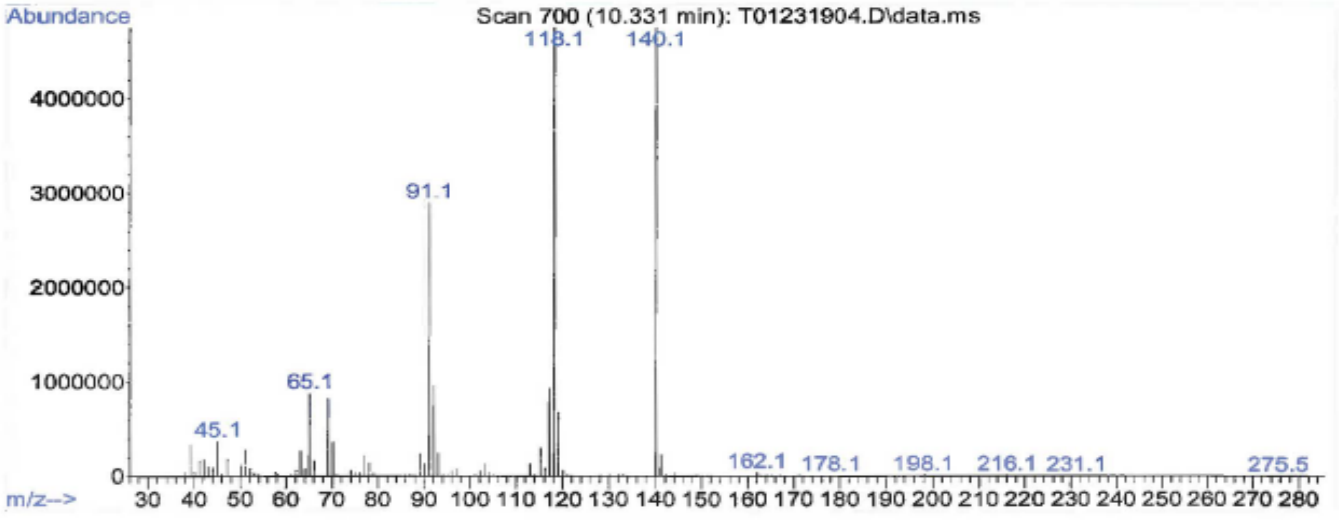
GC/MS

Compound Name	:	(±)-Amphetamine/TFA
Lot Number	:	FC09101802
Instrument	:	Agilent GCMS
Operator	:	ECM(SGIUFFRE)
Date Reported	:	Wed Jan 23 11:11:50 2019
Column Type	:	DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	:	50°C to 300°C @ 10°C/min (hold for 5 min)
Injector Temp.	:	Cool on-column
Carrier Gas	:	Helium
Flow Rate (mL\min)	:	0.80 mL/min
Transfer Line Temp.	:	280°C
Scan Range	:	35-400

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (A-016, (±)-Amphetamine-D_{11}) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 10, 2020	Initial version.

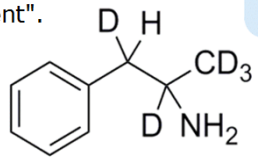
Certified Reference Material - Certificate of Analysis

(±)-Amphetamine-D_5 (SC), Primary Measurement Standard

(±)-1-Phenyl-1,2,3,3,3-pentadeutero-2-aminopropane

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-013-1ML
Lot No.: FE03232004
Description of CRM: (±)-Amphetamine-D_5 (SC) in Methanol (Solution)
Expiration Date: April 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_9H_8D_5N$
CAS No.: 136765-27-0
Regulatory: USDEA Exempt | Canadian TK # 61-993



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Amphetamine-D_5 (SC)	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 08, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

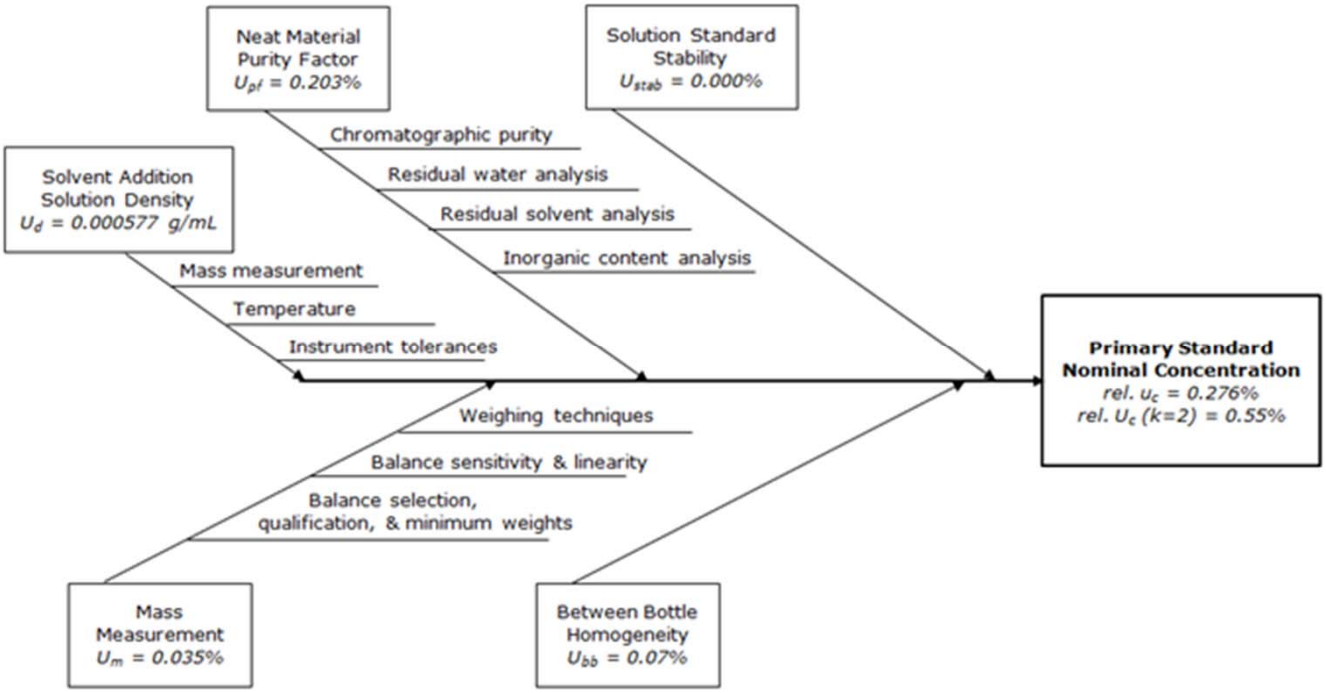
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness	**Number of Points:**	4
		Linearity (r) :	1.000
Temp Program:	60°C to 260°C at 20°C/min hold 1 min		
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03232004	0.989	0.9
Previous Lot	FE06061601	0.983	1.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Amphetamine-D_5 (SC)	**Chemical Formula:**	$C_9H_8D_5N$
Material Lot:	FC08191504	**CAS Number:**	136765-27-0
		Molecular Weight:	140.24

Material Characterization Summary

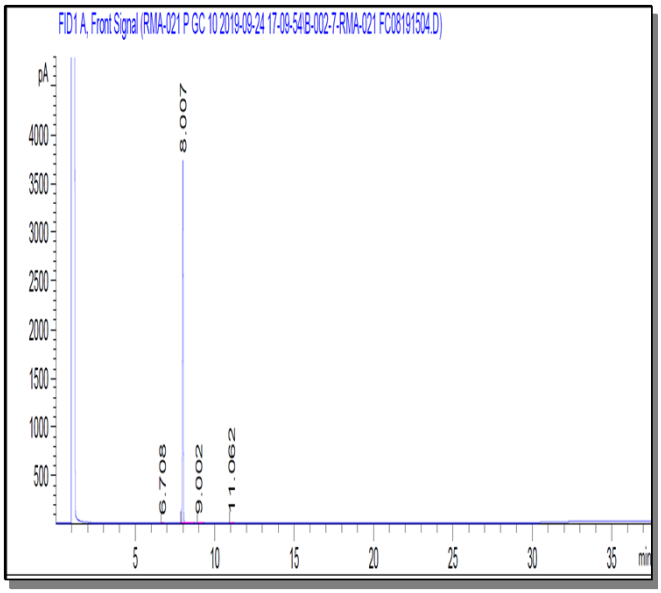
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%	
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.9%	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.00% D_0 vs D_5	
		0.00% D_0	0.16% D_3
		0.03% D_1	4.63% D_4
		0.60% D_2	94.59% D_5
Identity by ^{1}H-NMR Analysis	SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	1.59%	
Mass Balance Purity Factor		98.24%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

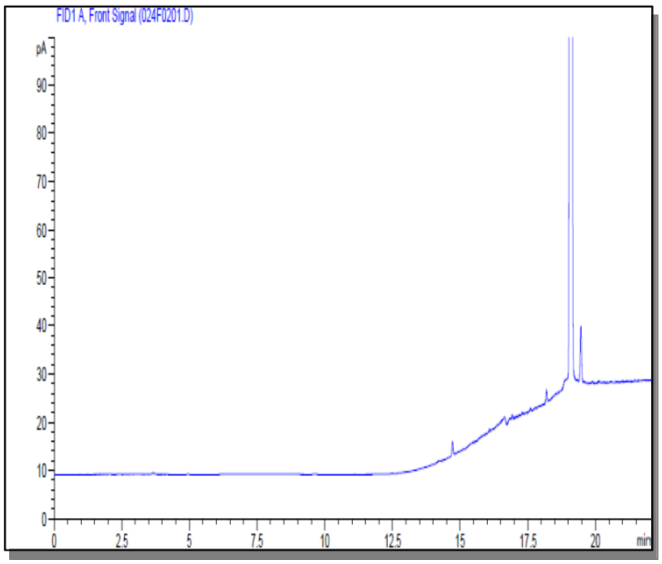
GC/FID



Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 80°C at 40°C/min 80°C to 175°C at 5°C/min 175°C to 300°C at 10°C/min hold 5 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC08191504
Acquired:	September 24, 2019

Peak #	Ret Time	Area %
1	6.71	0.01
2	8.01	99.82
3	9.00	0.16
4	11.06	0.01

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FC08191504
Acquired:	October 28, 2015

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

ND - None Detected

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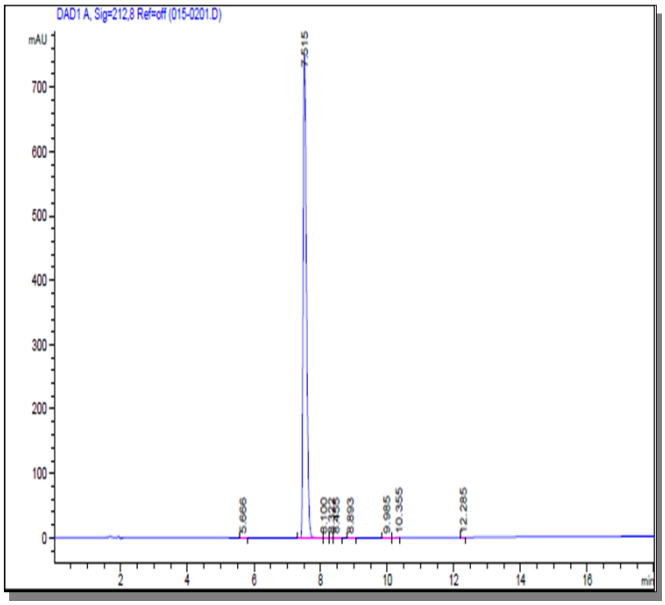
Spectral and Physical Data (cont.)

HPLC / UV



Column:	Zorbax Bonus RP, 3.5 µm, 4.6 x 150 mm
Mobile Phase:	A: Acetonitrile B: 20 mM Sodium perchlorate with 0.02% Phosphoric acid

Gradient:

Time (min)	% A	% B
0.0	10	90
2.0	10	90
12.0	50	50
17.0	50	50
17.1	10	90
23.0	10	90

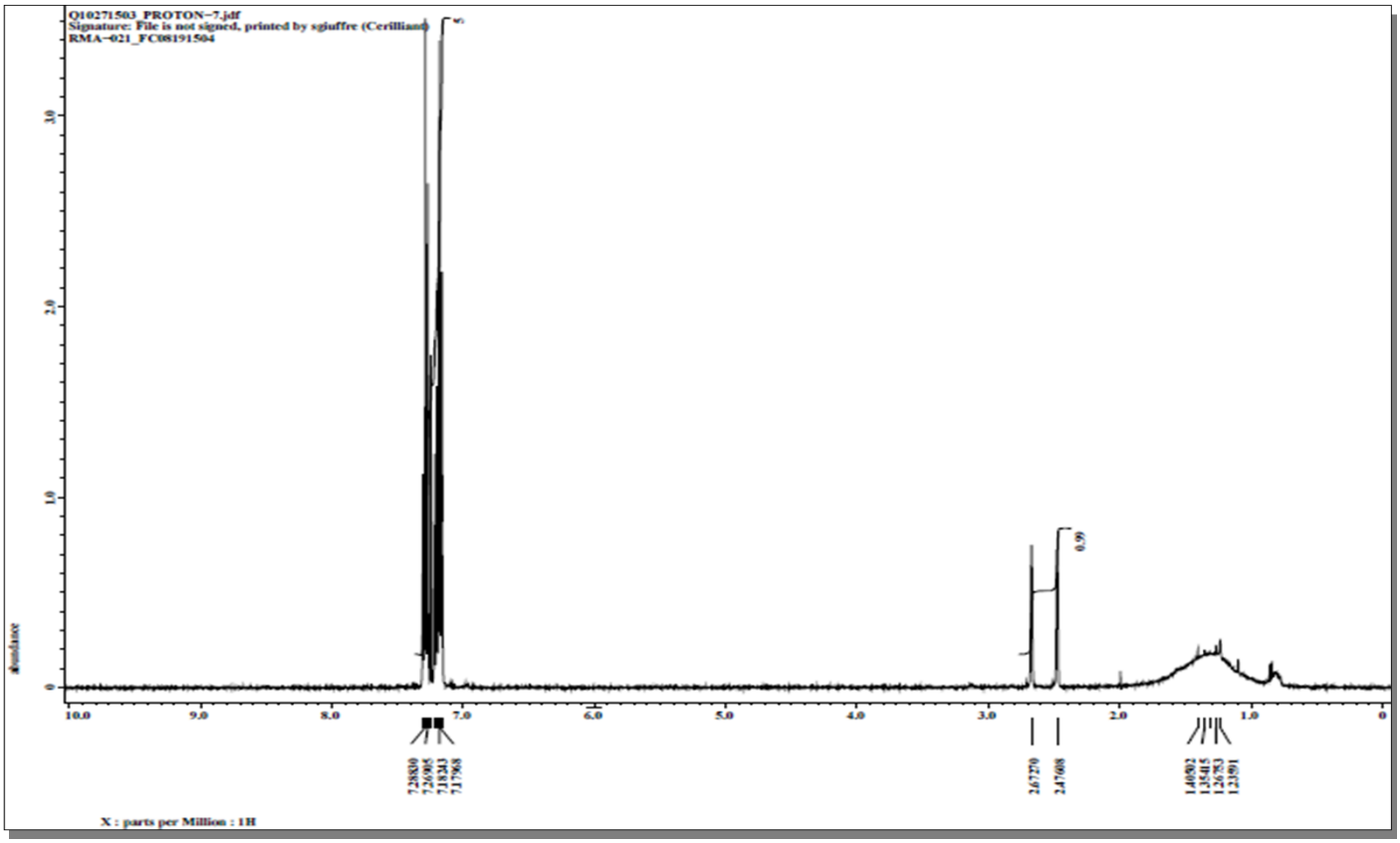
Flow Rate:	1.0 mL/min
Wavelength:	212 nm
Sample Name:	FC08191504
Acquired:	October 27, 2015

Peak #	Ret Time	Area %
1	5.67	0.01
2	7.52	99.94
3	8.10	0.01
4	8.32	0.01
5	8.46	0.01
6	8.89	0.01
7	9.99	0.01
8	10.36	0.00
9	12.29	0.01

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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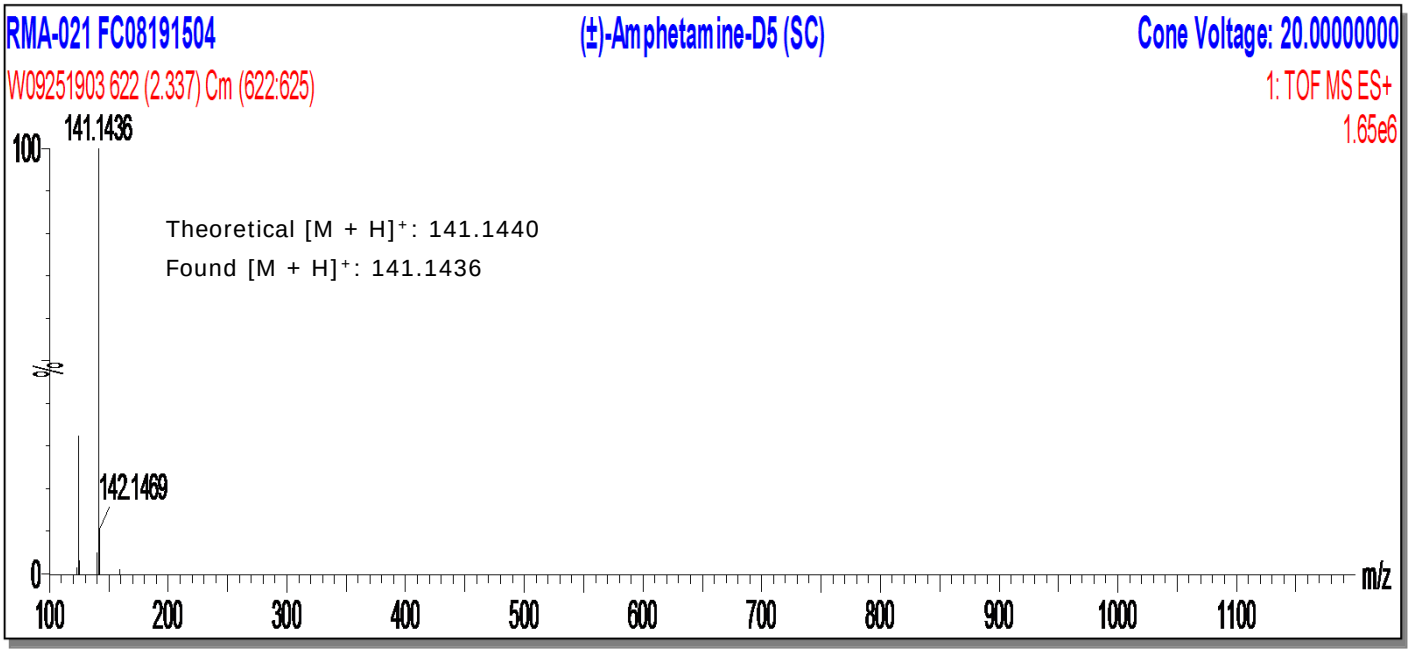
Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	September 25, 2019

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

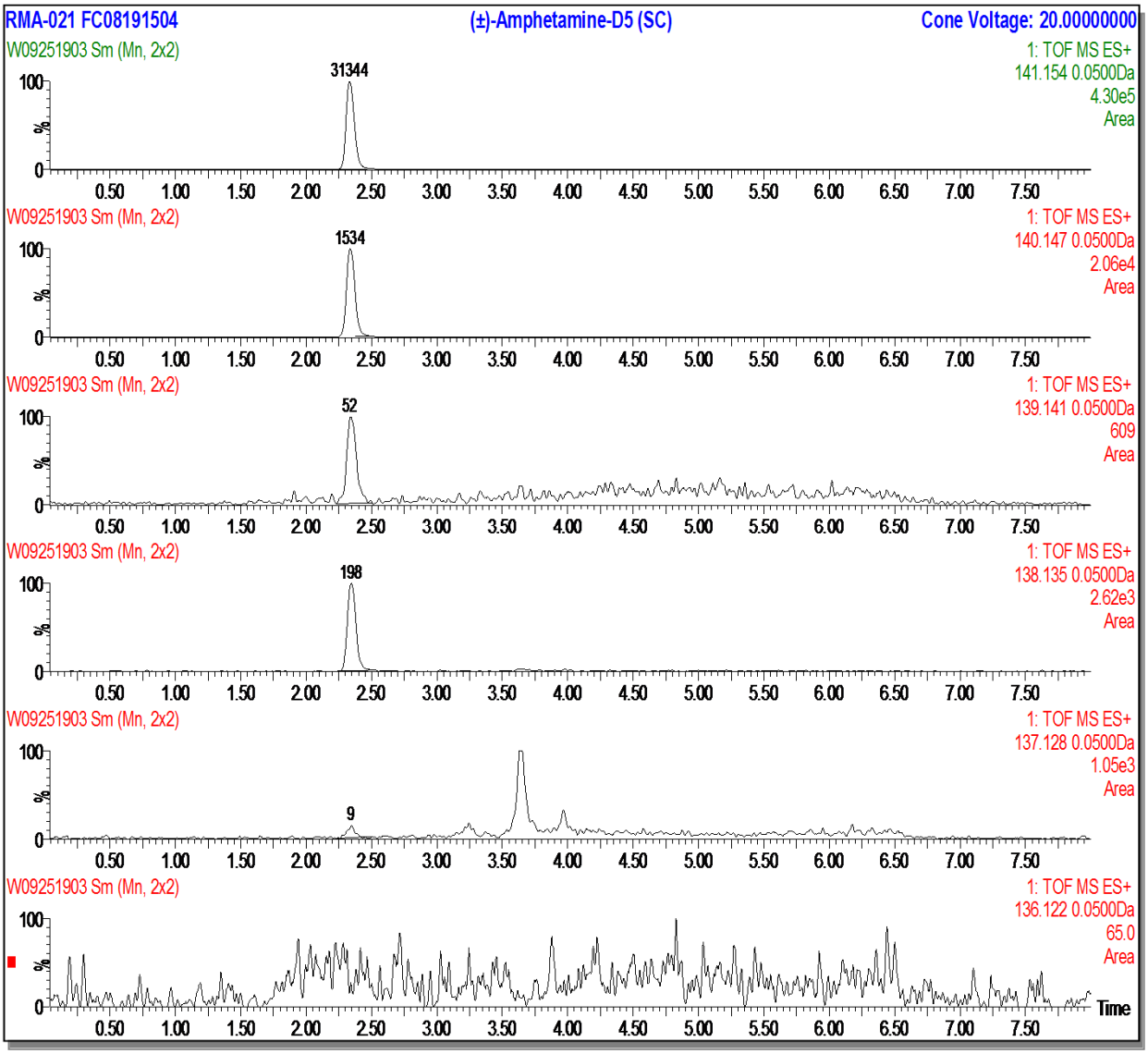
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 136-141 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: September 25, 2019



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (A-016, (±)-Amphetamine-D_{11}) 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 08, 2020	Initial version.

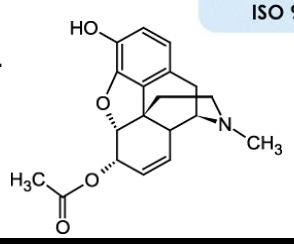
Certified Reference Material - Certificate of Analysis

6-Acetylmorphine, Primary Measurement Standard

7,8-Didehydro-4,5-epoxy-6-acetyl-17-methylmorphinan-3-ol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-009-1ML
Lot No.: FE01142009
Description of CRM: 6-Acetylmorphine in Acetonitrile (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{19}H_{21}NO_4$
CAS No.: 2784-73-8
Regulatory: USDEA Exempt | Canadian TK # 61-990



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
6-Acetylmorphine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
30 minute sonication required before use to ensure accurate concentration.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

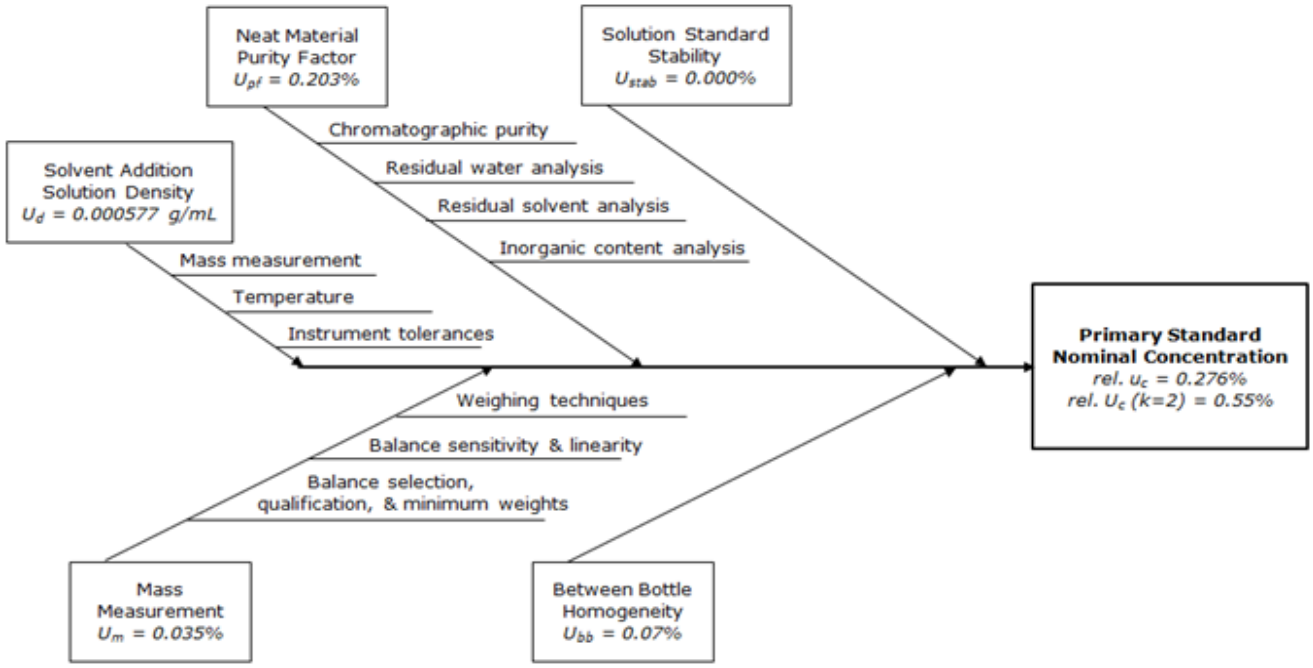
February 28, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (15:85)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	230 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01142009	0.997	0.6
Previous Lot	FE07161901	1.003	0.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	6-Acetylmorphine	**Chemical Formula:**	$C_{19}H_{21}NO_4$
Material Lot:	FC01111902	**CAS Number:**	2784-73-8
		Molecular Weight:	327.37

Material Characterization Summary

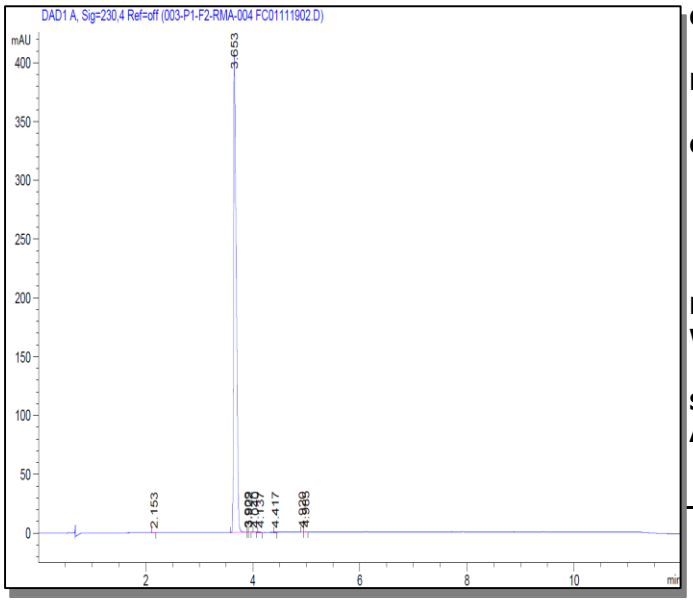
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8% [1]
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.3%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	1.63%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Below Quantitation Limit
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		98.21%

[1] 0.02% Morphine and 0.06% Heroin were detected by HPLC/UV analysis.
[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
8.0	50	50
10.0	50	50
10.1	2	98

Flow Rate: 0.7 mL/min

Wavelength: 230 nm

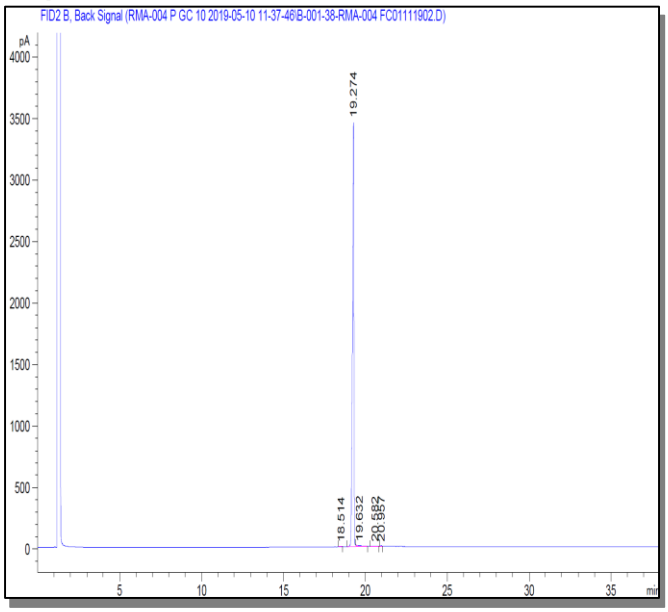
Sample Name: FC01111902

Acquired: May 14, 2019

Peak #	Ret Time	Area %
1	2.15	0.02
2	3.65	99.86
3	3.91	0.01
4	3.92	0.01
5	4.04	0.01
6	4.14	0.01
7	4.42	0.01
8	4.92	0.02
9	4.99	0.06

Peak 1 is identified as Morphine;
Peak 9 is identified as Heroin.

GC/FID



Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C /min
hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

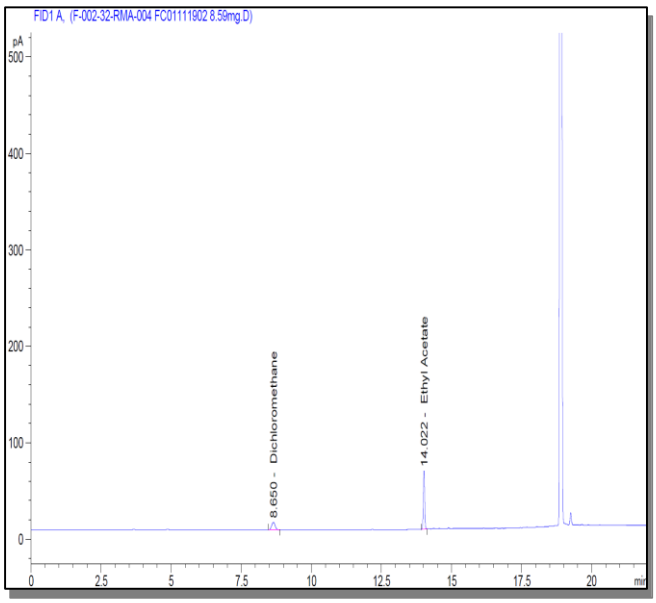
Sample Name: FC01111902

Acquired: May 10, 2019

Peak #	Ret Time	Area %
1	18.51	0.02
2	19.27	99.30
3	19.63	0.43
4	20.58	0.14
5	20.96	0.11

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

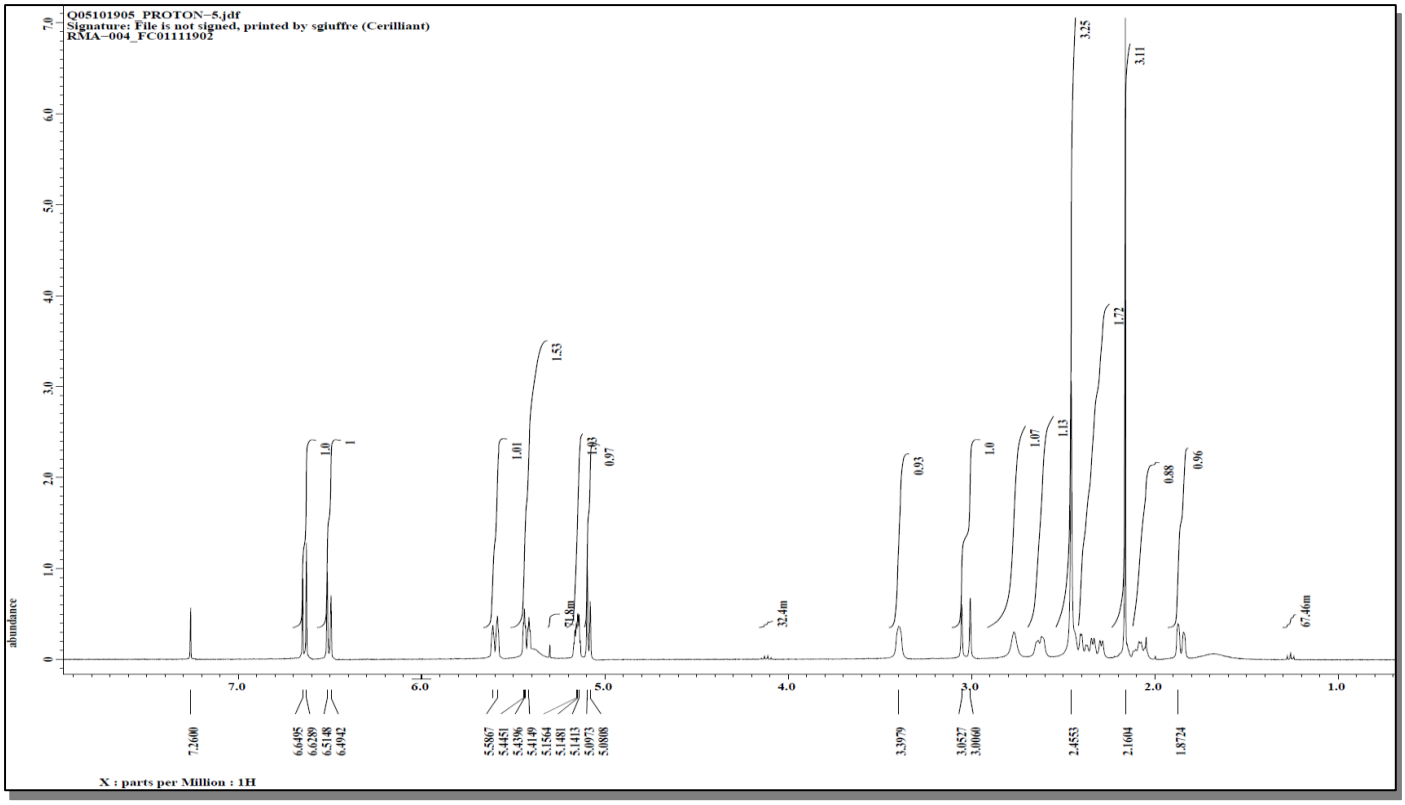


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FN01111902
Acquired:	May 10, 2019

Peak	Compound	Area	Weight %
1	Dichloromethane	69.65	0.93
2	Ethyl acetate	205.72	0.70
3	NMP	NA	NA
Total			**1.63**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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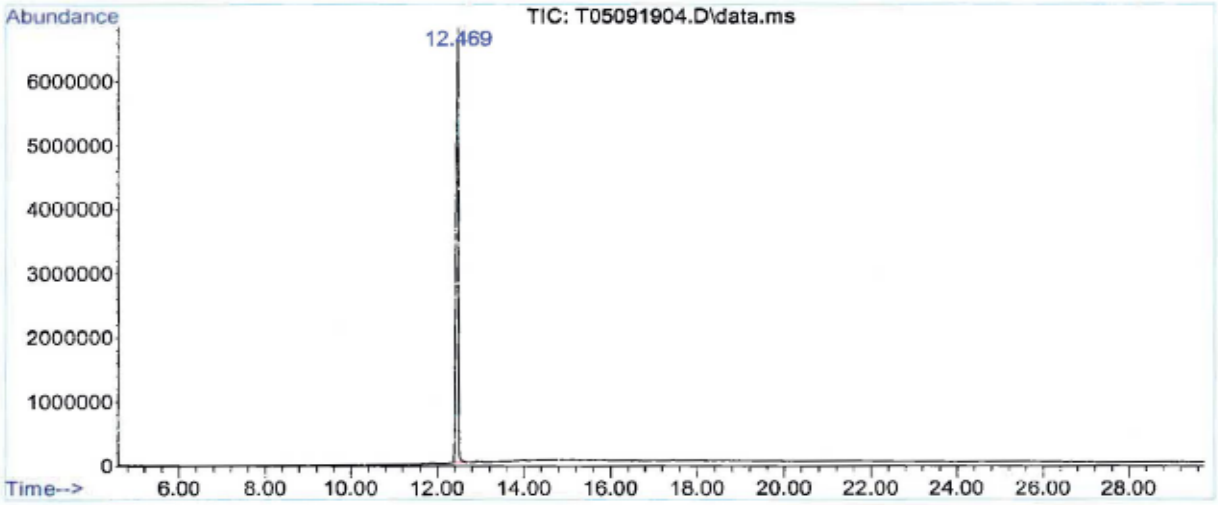
Spectral and Physical Data (cont.)

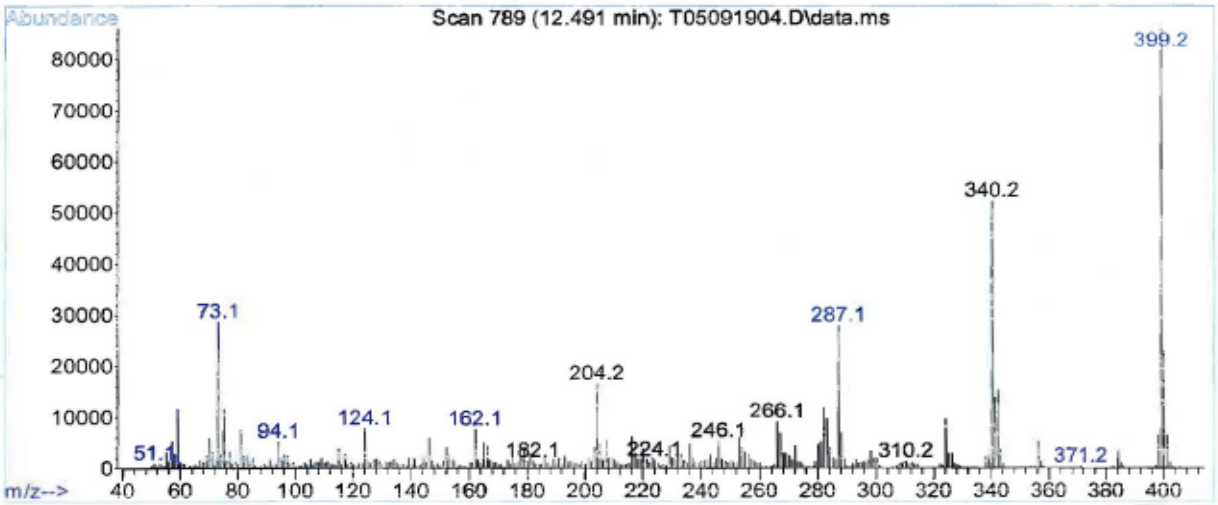
GC/MS

Compound Name	:	6-Acetylmorphine
Lot Number	:	FC01111902
Instrument	:	Agilent GCMS
Operator	:	ECM(SGIUFFRE)
Date Reported	:	Fri May 10 09:24:26 2019
Column Type	:	DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	:	50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.	:	Cool on-column
Carrier Gas	:	Helium
Flow Rate (mL\min)	:	0.80 mL/min
Transfer Line Temp.	:	280°C
Scan Range	:	50-500

Total Ion Chromatogram



Mass Spectrum



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 28, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

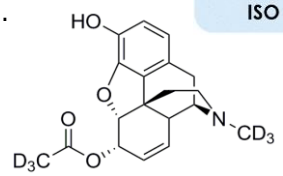
Certified Reference Material - Certificate of Analysis

6-Acetylmorphine-D_6, Primary Measurement Standard

6 α-trideuteroacetoxy-4,5 α-epoxy-17-trideuteromethylmorphin-7-en-3-ol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-027-1ML
Lot No.: FE01202008
Description of CRM: 6-Acetylmorphine-D_6 in Acetonitrile (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{19}H_{15}D_6NO_4$
CAS No.: 152477-90-2
Regulatory: USDEA Exempt | Canadian TK # 61-1000



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
6-Acetylmorphine-D_6	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

45 minute sonication required before use to ensure accurate concentration.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

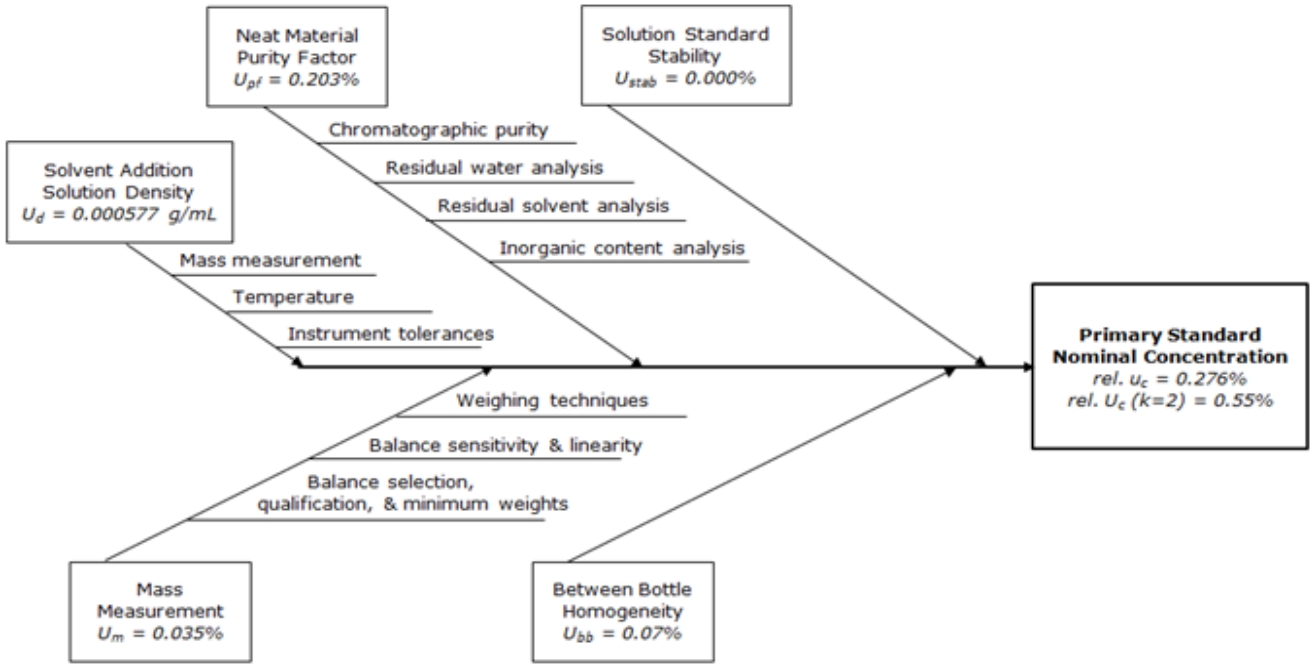
March 02, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (10:90)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	230 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01202008	0.998	0.7
Previous Lot	FE02091605	0.986	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	6-Acetylmorphine-D_6	**Chemical Formula:**	$C_{19}H_{15}D_6NO_4$
Material Lot:	FC05081702	**CAS Number:**	152477-90-2
		Molecular Weight:	333.41

Material Characterization Summary

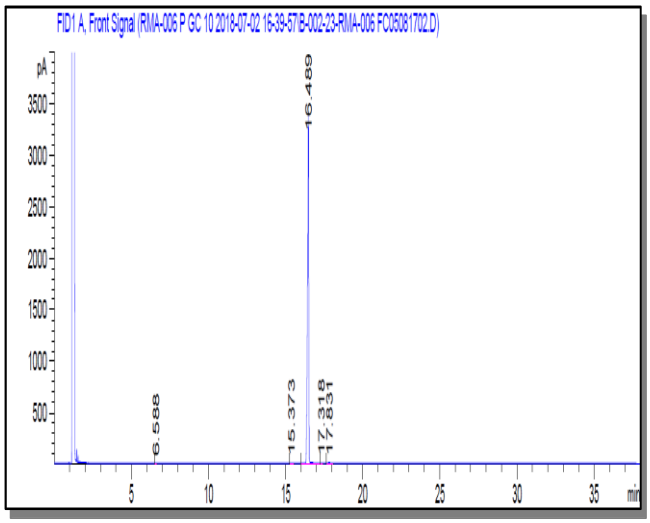
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.7% [1]	
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8% [2]	
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure	
Isotopic Purity and Distribution by GC/MS SIM Analysis	SP10-0105	0.07% D_0 vs D_6	
		0.06% D_0	1.22% D_4
		0.07% D_1	12.27% D_5
		0.08% D_2	86.13% D_6
		0.18% D_3	
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_6	
		0.00% D_0 to D_2	6.07% D_5
		0.01% D_3	93.80% D_6
		0.11% D_4	
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [3]	1.73%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [3]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		97.97%	

[1] 0.08% Morphine-D_3 and 0.21% Heroin-D_9 detected by GC/FID analysis.
[2] 0.02% Heroin-D_9 detected by HPLC/UV analysis.
[3] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

GC/FID

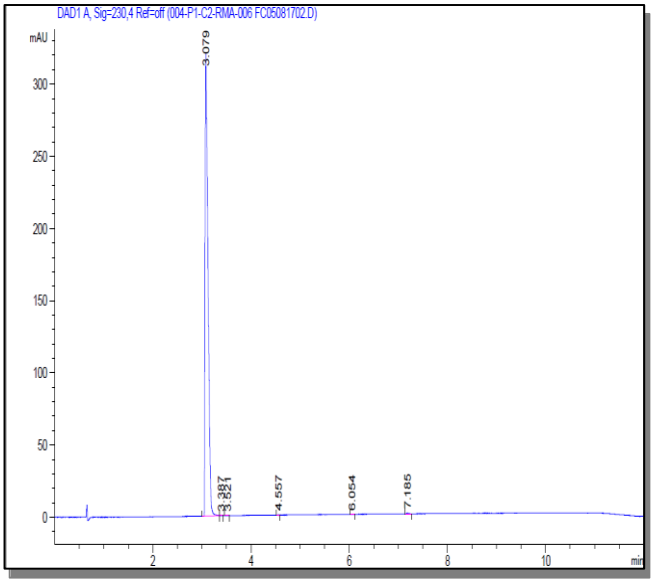


Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC05081702
Acquired: July 02, 2018

Peak #	Ret Time	Area %	
1	6.59	0.01	
2	15.37	0.08	Morphine-D_3
3	16.49	99.69	
4	17.32	0.01	
5	17.83	0.21	Heroin-D_9

HPLC/UV



Column: Ascentis Express C18, 2.7 µm 3.0 x 100 mm
Mobile Phase: A: Acetonitrile
B: 0.1% Phosphoric acid in Water
Gradient:

Time (min)	% A	% B
0.0	5	95
8.0	50	50
10.0	50	50
10.1	5	95

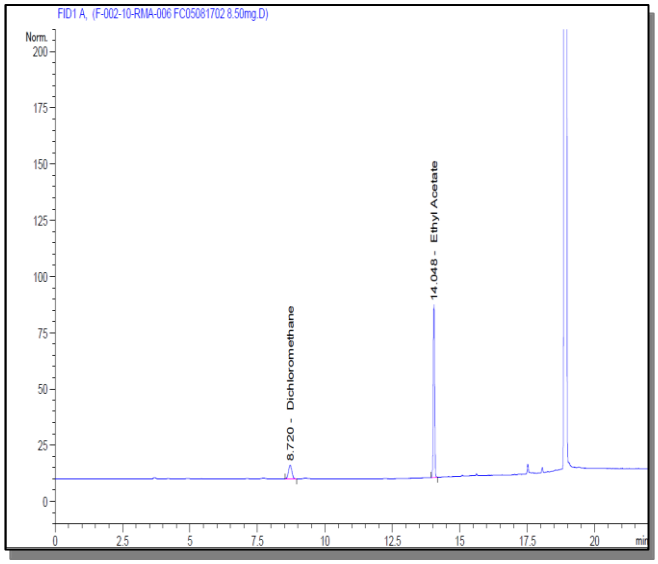
Flow Rate: 0.7 mL/min
Wavelength: 230 nm

Sample Name: FC05081702
Acquired: July 02, 2018

Peak #	Ret Time	Area %	
1	3.08	99.79	
2	3.39	0.03	
3	3.52	0.03	
4	4.56	0.02	Heroin-D_9
5	6.05	0.03	
6	7.19	0.10	

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

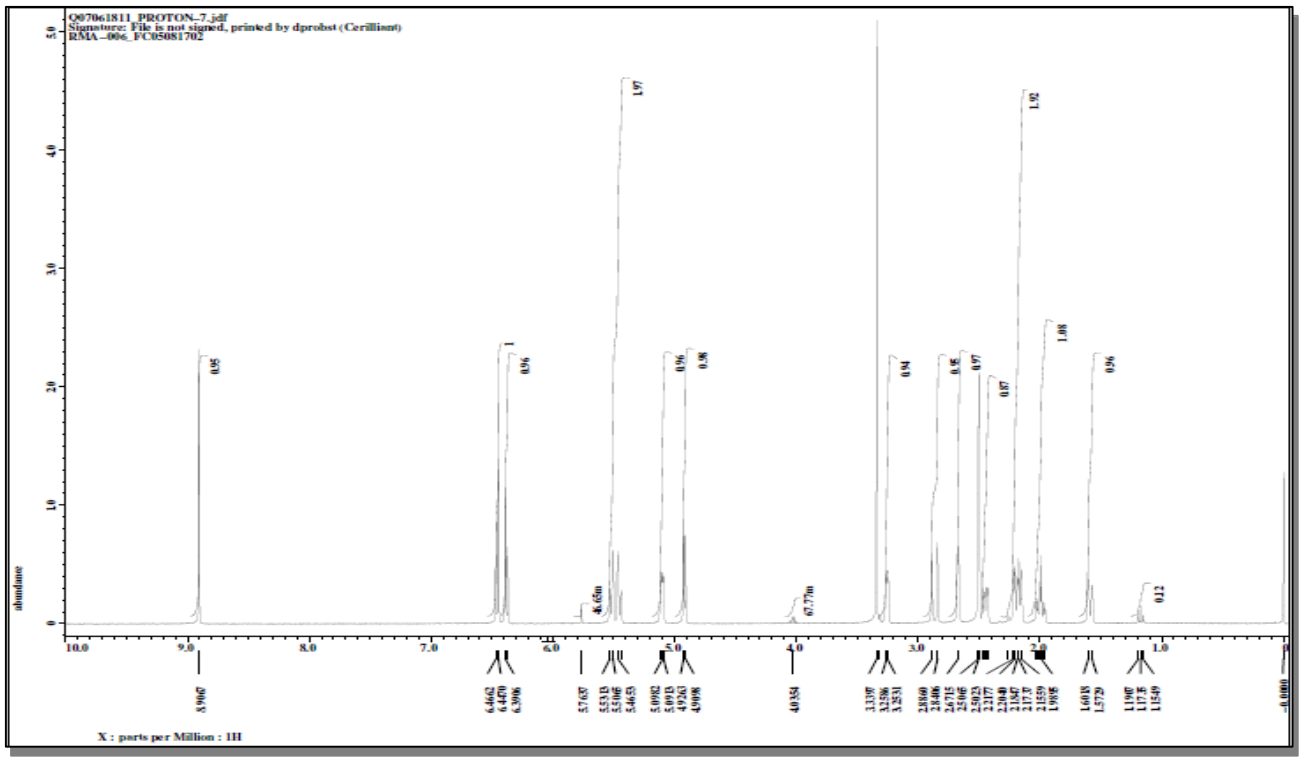


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC05081702
Acquired:	September 13, 2019

Peak	Compound	Area	Weight %
1	Dichloromethane	54.11	0.76
2	Ethyl acetate	259.02	0.97
3	NMP	NA	NA
Total			**1.73**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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Spectral and Physical Data (cont.)

LC/MS

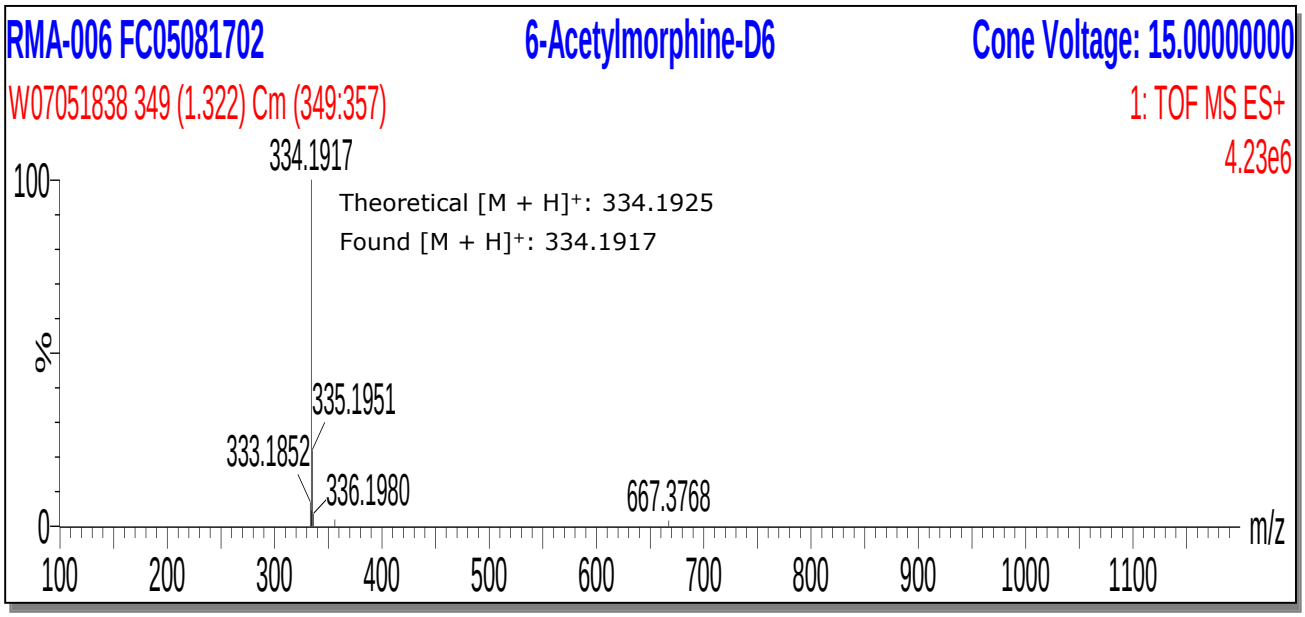
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 100-1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: July 05, 2018



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

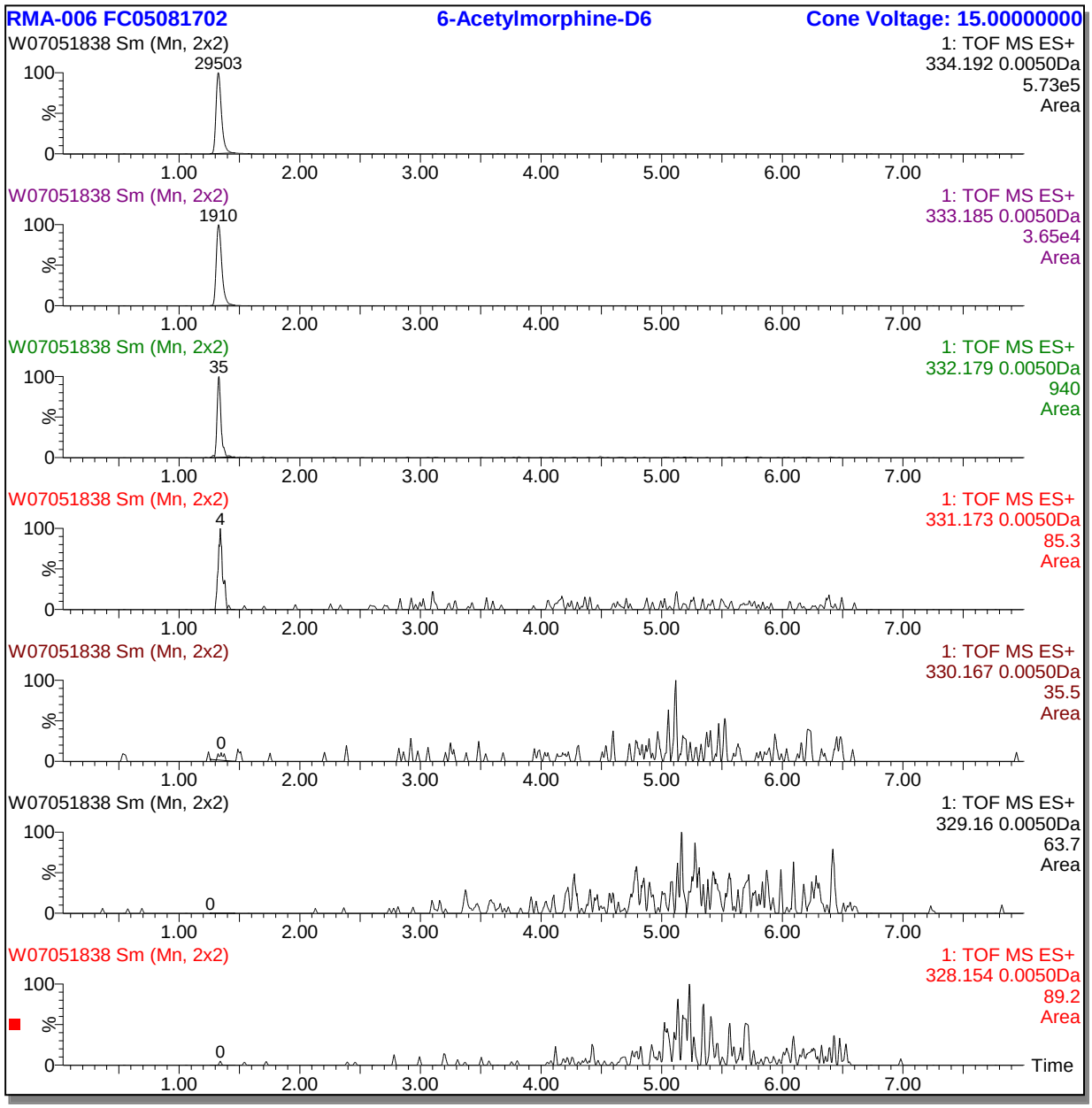
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 328-334 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: July 05, 2018



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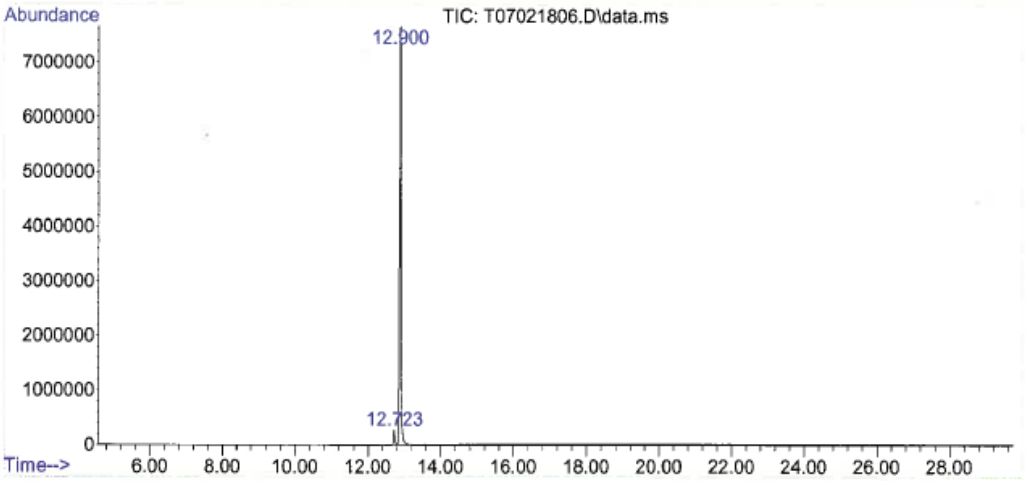
Spectral and Physical Data (cont.)

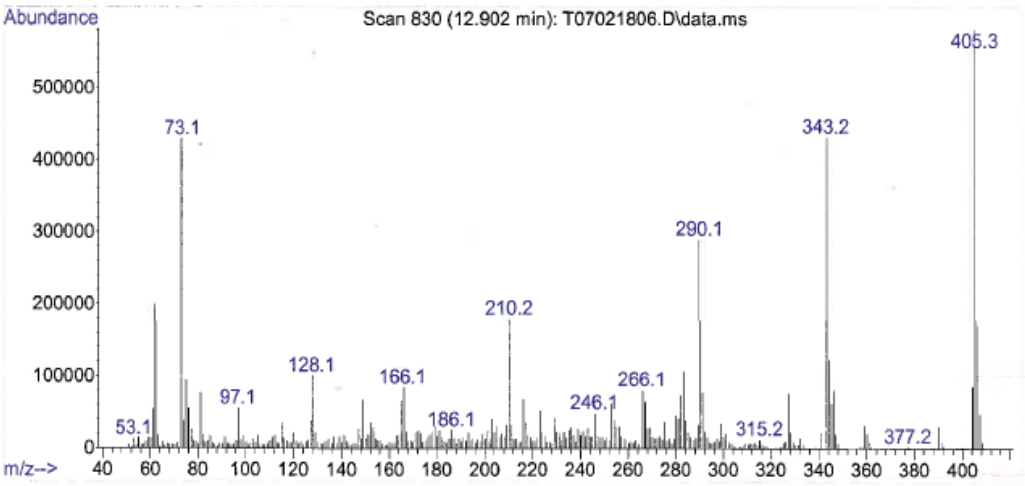
GC/MS

```
Compound Name        : 6-Acetylmorphine-D6
Lot Number           : FC05081702
Instrument           : Agilent GCMS
Operator             : ECM(SGIUFFRE)
Date Reported        : Mon Jul 02 15:43:23 2018
Column Type          : DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program        : 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.       : Cool on-column
Carrier Gas          : Helium
Flow Rate (mL\min)   : 0.80 mL/min
Transfer Line Temp.  : 280°C
Scan Range           : 50-500
```

Total Ion Chromatogram



Mass Spectrum



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (A-006, 6-Acetylmorphine-D_3) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 02, 2020	Initial version.

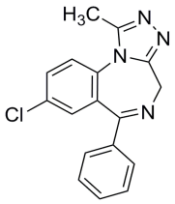
Certified Reference Material - Certificate of Analysis

Alprazolam, Primary Measurement Standard

8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-903-1ML
Lot No.: FE02042004
Description of CRM: Alprazolam in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{13}ClN_4$
CAS No.: 28981-97-7
Regulatory: USDEA Exempt | Canadian TK # 61-1027



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Alprazolam	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

April 01, 2020
Issue Date

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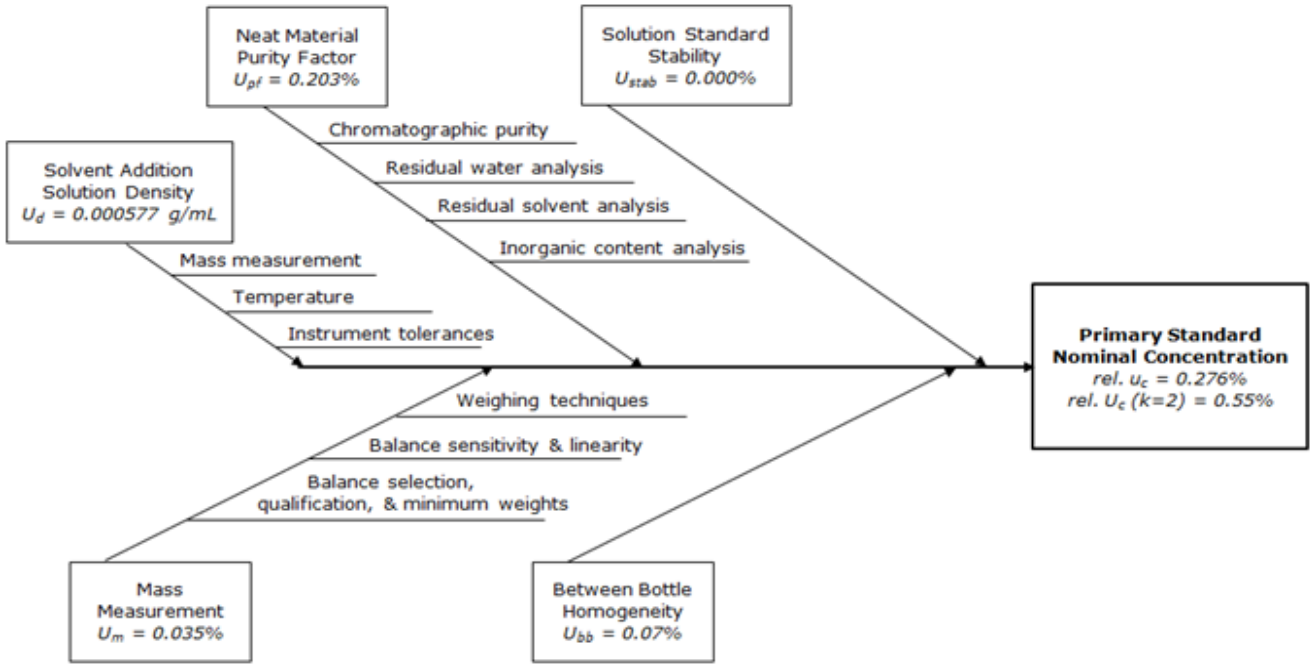
Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Ammonium acetate in Water (50:50)	**Linearity (r) :**	0.999
Flow Rate:	1.0 mL/min		
Wavelength:	238 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02042004	0.994	1.5
Previous Lot	FE07061604	1.011	0.9

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Alprazolam	**Chemical Formula:**	$C_{17}H_{13}ClN_4$
Material Lot:	FC09191907	**CAS Number:**	28981-97-7
		Molecular Weight:	308.76

Material Characterization Summary

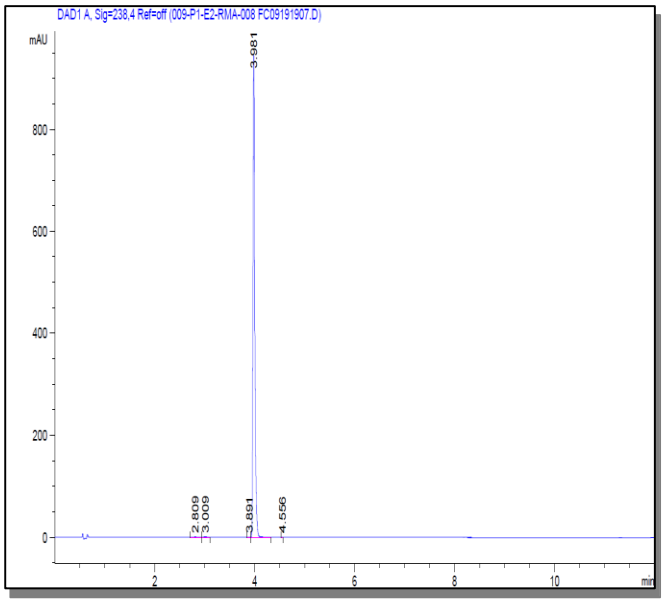
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.9%
Secondary Chromatographic Purity by GC/FID Analysis	20384346	98.2%
Identity by LC/MS Analysis	20384217	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Not Detected
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.87%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl Hexyl, 2.7 µm, 3.0 x 100 mm

Mobile Phase: A: Acetonitrile
B: 0.1% Ammonium acetate in Water

Gradient:

Time (min)	% A	% B
0.0	25	75
8.0	70	30
10.0	70	30
10.1	25	75

Flow Rate: 0.7 mL/min

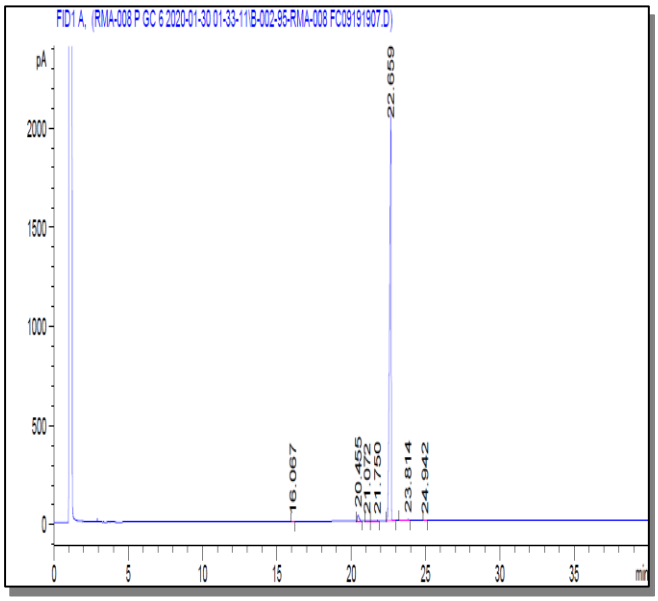
Wavelength: 238 nm

Sample Name: FC09191907

Acquired: January 31, 2020

Peak #	Ret Time	Area %
1	2.81	0.04
2	3.01	0.08
3	3.89	0.01
4	3.98	99.86
5	4.56	0.00

GC/FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 300°C at 5°C/min
hold 16 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

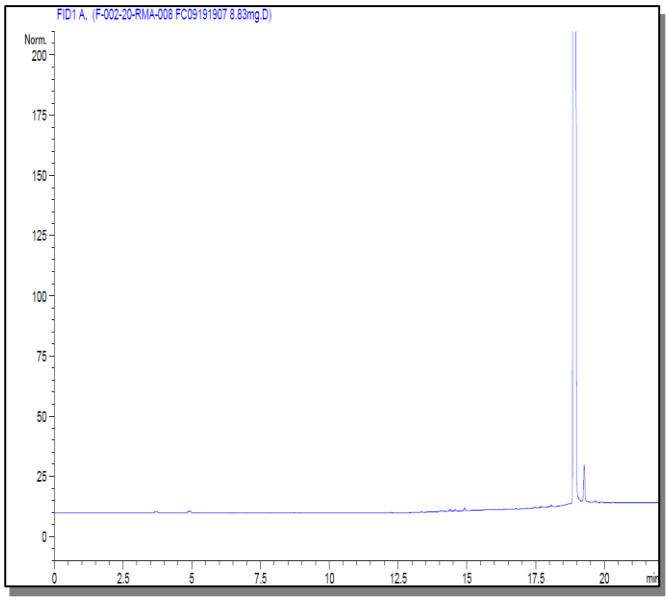
Sample Name: FC09191907

Acquired: January 30, 2020

Peak #	Ret Time	Area %
1	16.07	0.04
2	20.46	1.56
3	21.07	0.05
4	21.75	0.05
5	22.66	98.18
6	23.81	0.11
7	24.94	0.01

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



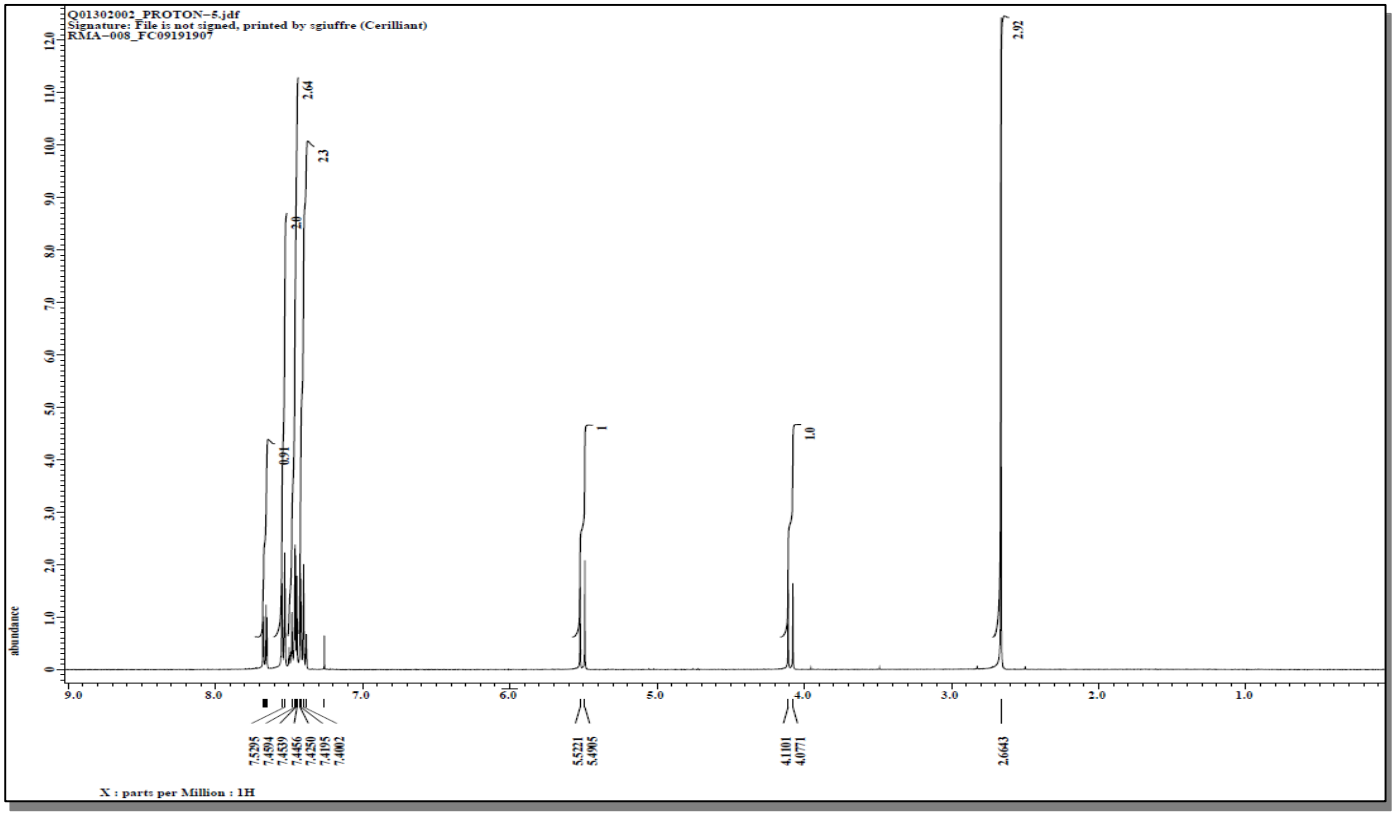
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC09191907
Acquired:	January 31, 2020

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

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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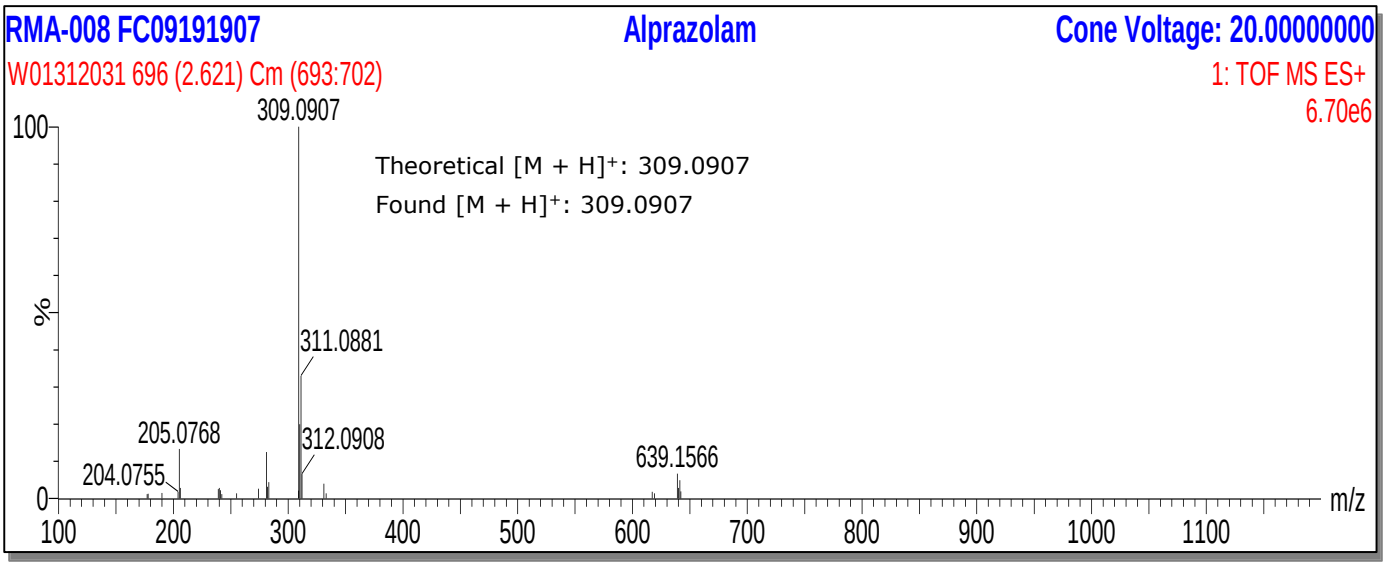
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 31, 2020

Time (min)	% A	% B
0.0	80	20
0.5	80	20
4.0	20	80
5.8	20	80
6.0	80	20
8.0	80	20



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 01, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

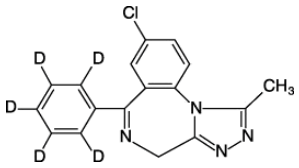
Certified Reference Material - Certificate of Analysis

Alprazolam-D_5, Primary Measurement Standard

8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-α][1,4]benzodiazepine-D_5

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-910-1ML
Lot No.: FE02042006
Description of CRM: Alprazolam-D_5 in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_8ClD_5N_4$
CAS No.: 125229-61-0
Regulatory: USDEA Exempt | Canadian TK # 61-1032



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Alprazolam-D_5	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

March 10, 2020
Issue Date

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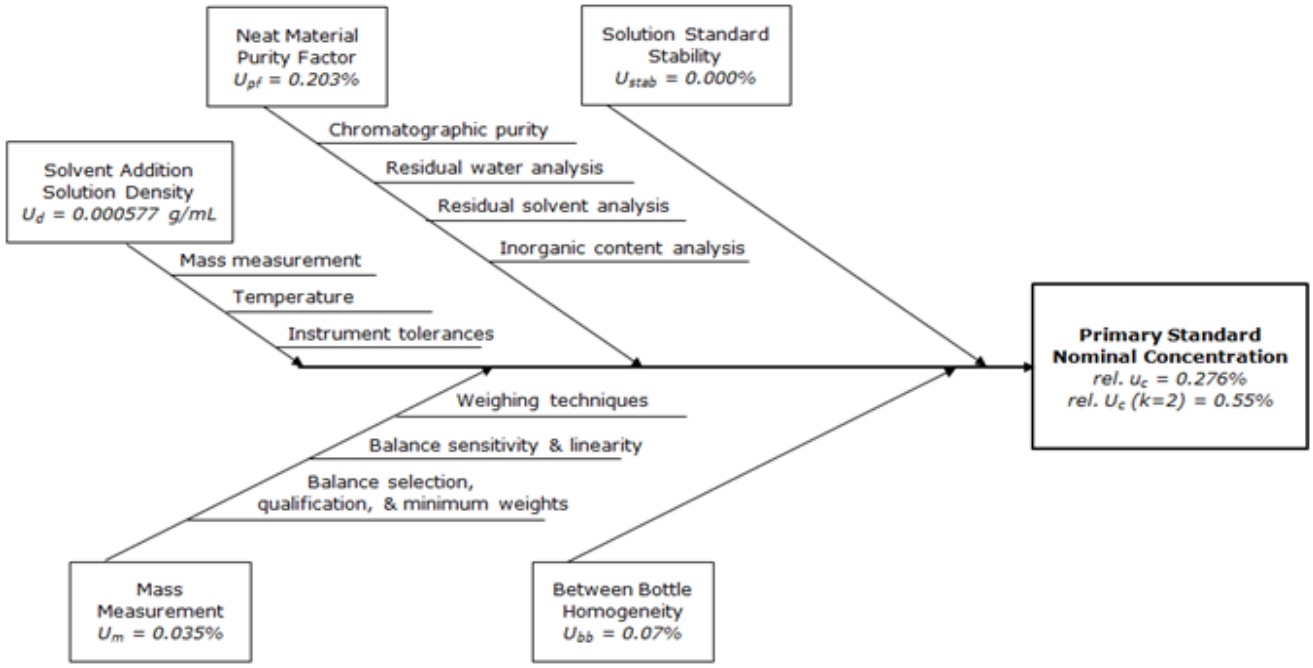
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:Water (50:50)	**Linearity (r) :**	0.999
Flow Rate:	1.2 mL/min		
Wavelength:	238 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02042006	0.991	1.2
Previous Lot	FE08211802	0.994	0.8

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Alprazolam-D_5	**Chemical Formula:**	$C_{17}H_8ClD_5N_4$
Material Lot:	FC05011901	**CAS Number:**	125229-61-0
		Molecular Weight:	313.80

Material Characterization Summary

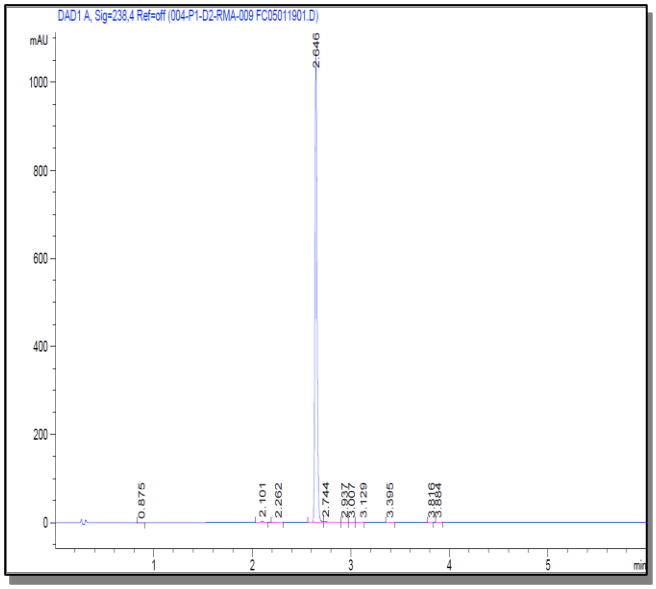
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.5%	
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	98.3%	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.02% D_0 vs D_5	
		0.02% D_0	0.02% D_3
		0.01% D_1	1.83% D_4
		0.01% D_2	98.12% D_5
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.35%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Not Detected	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.15%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: Acetonitrile
B: Water

Gradient:

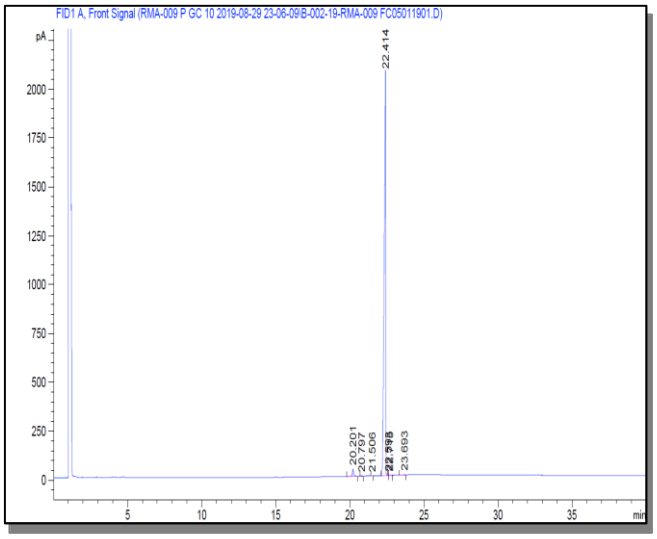
Time (min)	% A	% B
0.0	20	80
4.0	70	30
5.0	70	30
5.1	20	80

Flow Rate: 0.8 mL/min
Wavelength: 238 nm

Sample Name: FC05011901
Acquired: August 21, 2019

Peak #	Ret Time	Area %
1	0.88	0.01
2	2.10	0.20
3	2.26	0.02
4	2.65	99.48
5	2.74	0.22
6	2.94	0.01
7	3.01	0.01
8	3.13	0.01
9	3.40	0.01
10	3.82	0.01
11	3.88	0.03

GC/FID



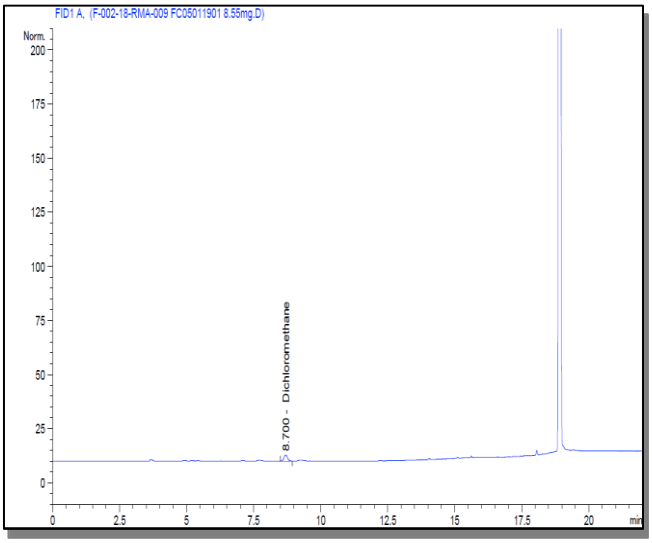
Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 300°C at 5°C/min
hold 16 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC05011901
Acquired: August 29, 2019

Peak #	Ret Time	Area %
1	20.20	1.43
2	20.80	0.07
3	21.51	0.02
4	22.41	98.32
5	22.59	0.02
6	22.72	0.05
7	23.69	0.10

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

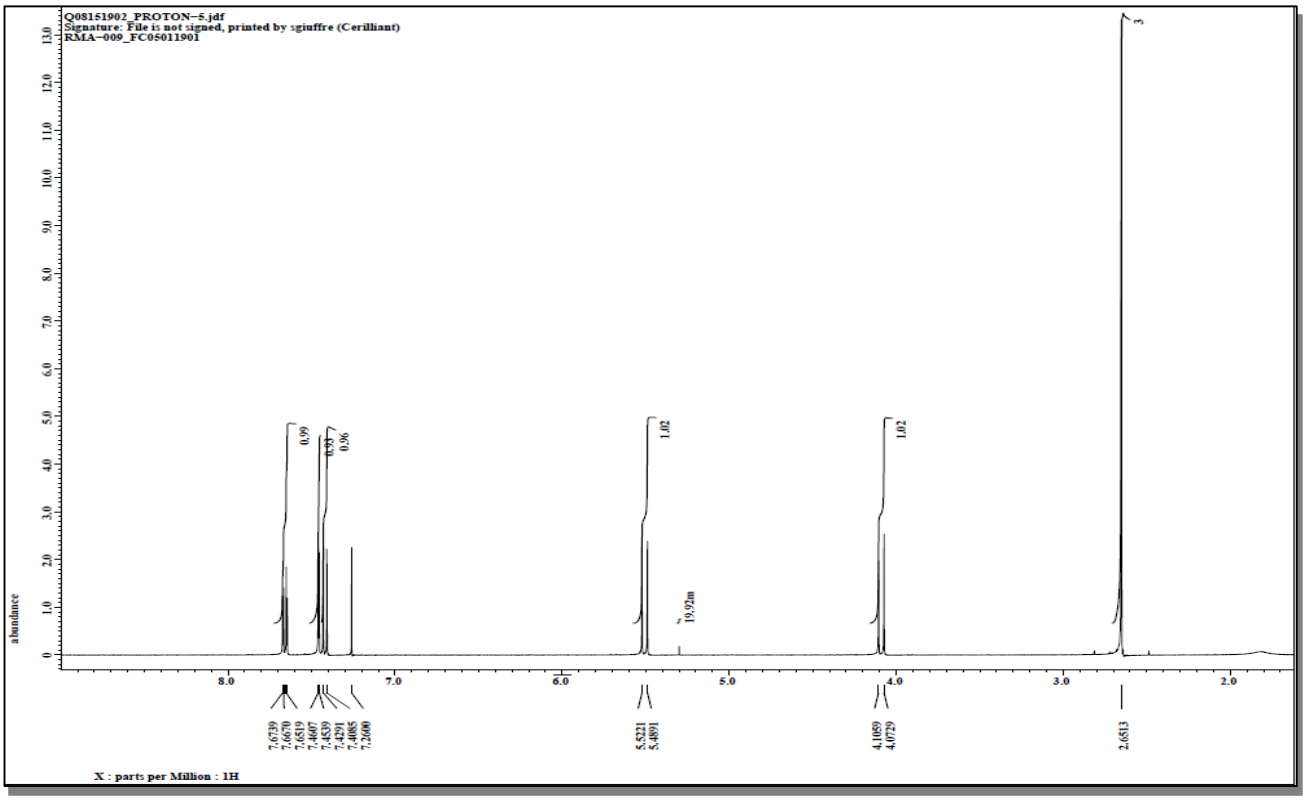


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC05011901
Acquired:	August 16, 2019

Peak	Compound	Area	Weight %
1	Dichloromethane	25.00	0.35
2	NMP	NA	NA
Total			**0.35**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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Spectral and Physical Data (cont.)

LC/MS

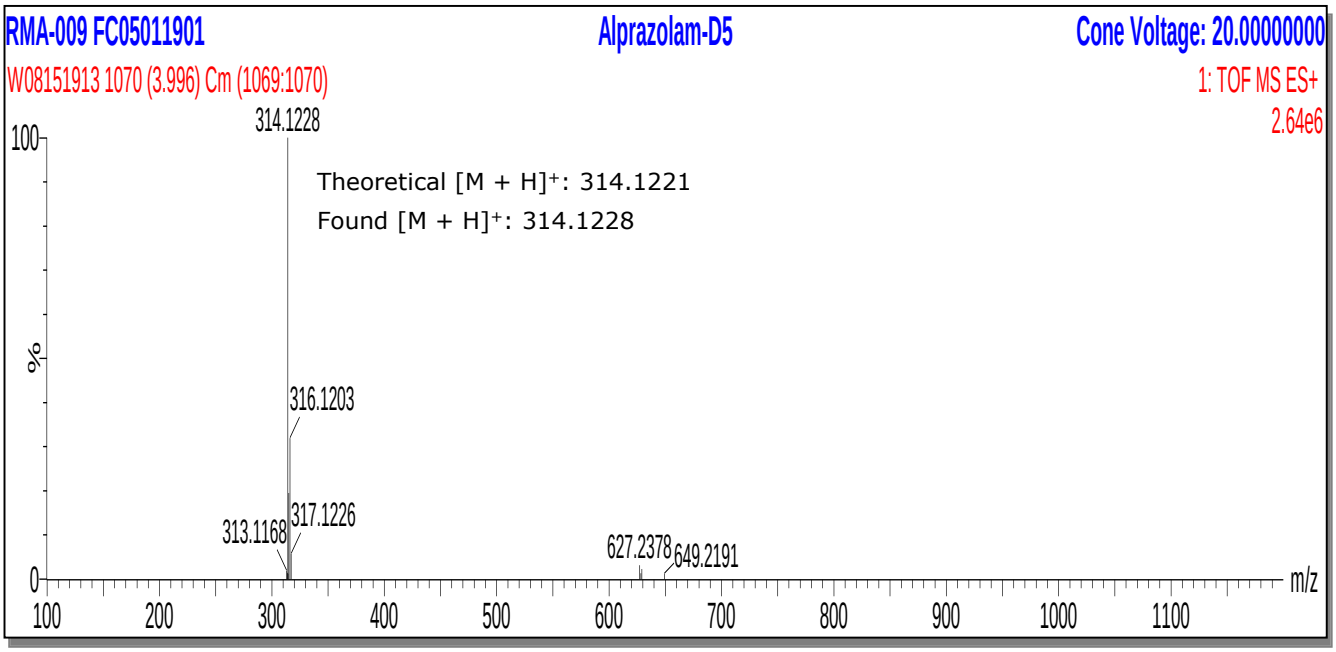
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 100-1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: August 15, 2019



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

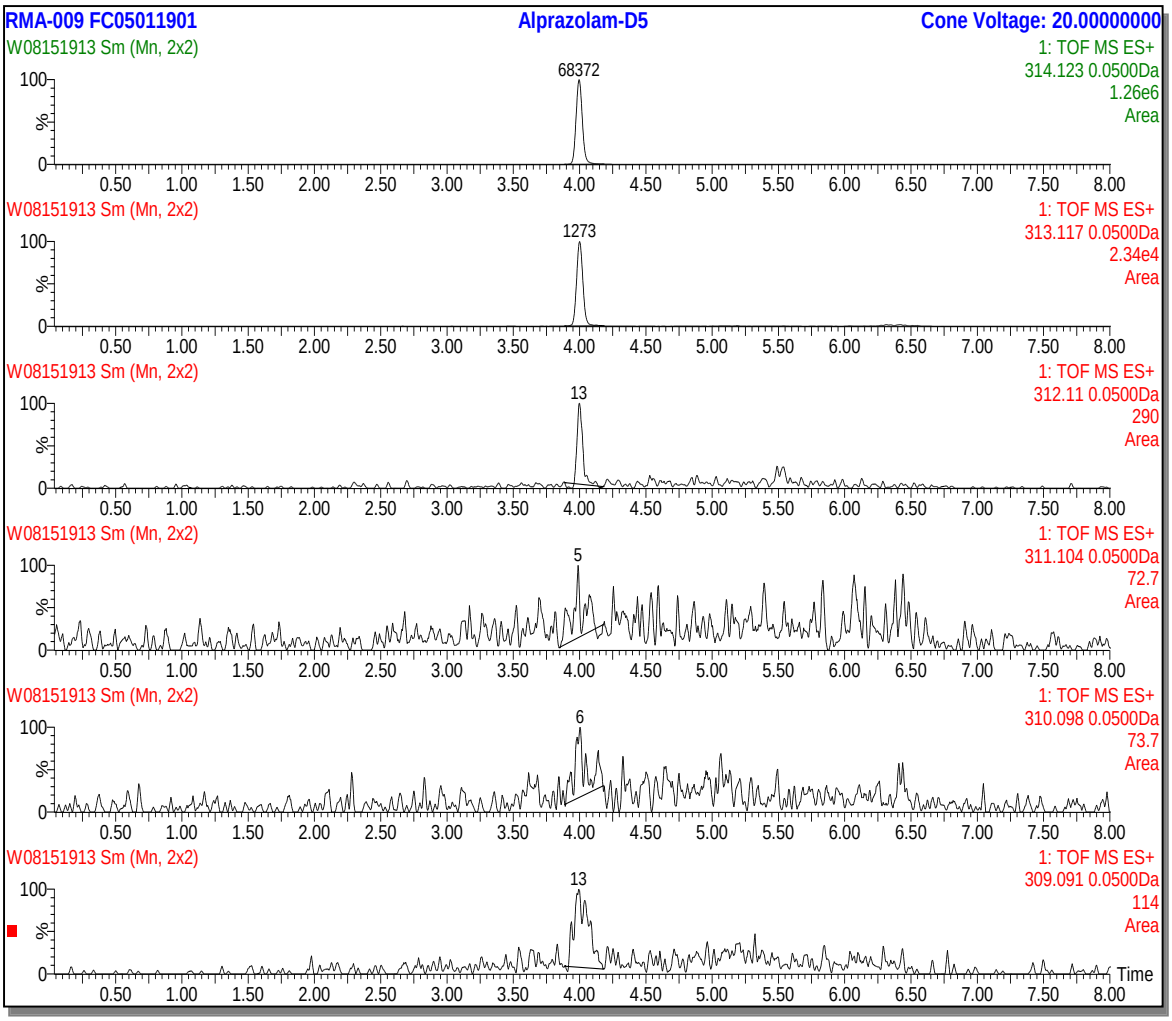
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 309-314 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: August 15, 2019



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (A-903, Alprazolam) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 10, 2020	Initial version.

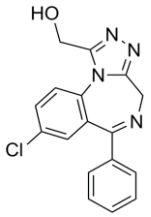
Certified Reference Material - Certificate of Analysis

alpha-Hydroxyalprazolam, Primary Measurement Standard

(8-chloro-6-phenyl-4H-[1,2,4]triazolo[4,3-α][1,4]benzodiazepin-1-yl)methanol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-907-1ML
Lot No.: FN02042005
Description of CRM: alpha-Hydroxyalprazolam in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{13}ClN_4O$
CAS No.: 37115-43-8
Regulatory: Canadian TK # 61-1030



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
alpha-Hydroxyalprazolam	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

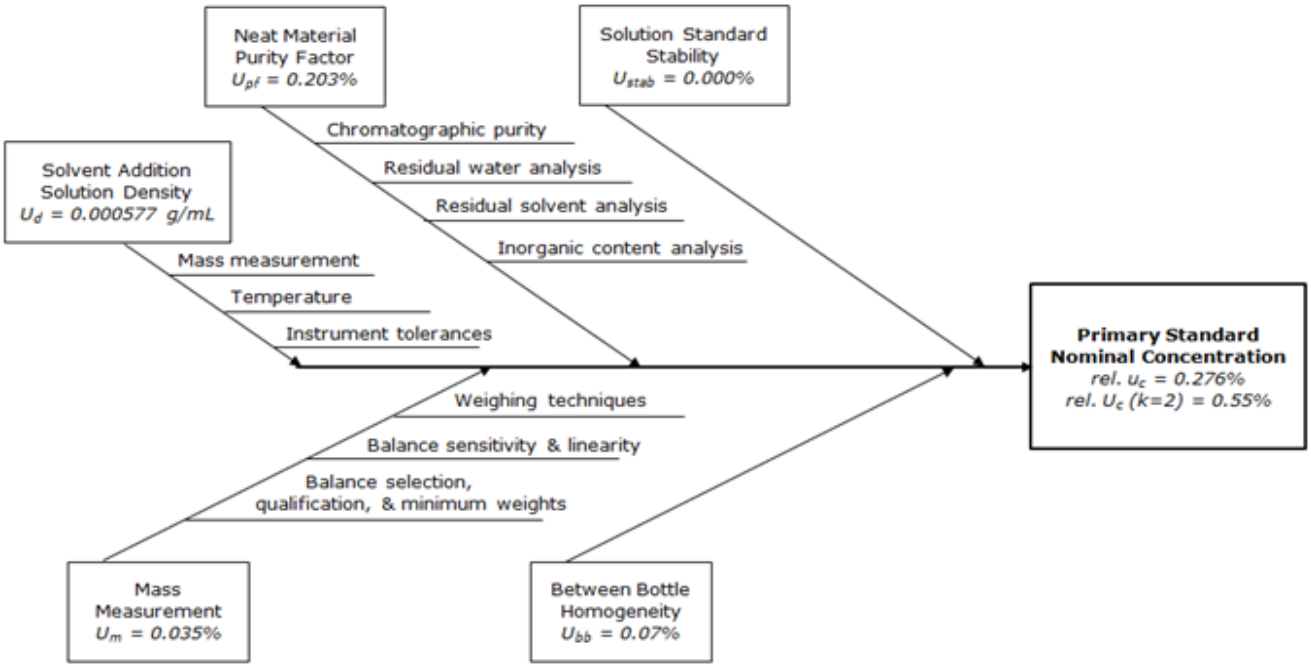
March 09, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Ammonium acetate in Water (40:60)	**Linearity (r) :**	1.000
Flow Rate:	1.2 mL/min		
Wavelength:	238 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN02042005	0.993	0.5
Previous Lot	FN07051601	0.996	0.7

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	alpha-Hydroxyalprazolam	**Chemical Formula:**	$C_{17}H_{13}ClN_4O$
Material Lot:	FN03311612	**CAS Number:**	37115-43-8
		Molecular Weight:	324.76

Material Characterization Summary

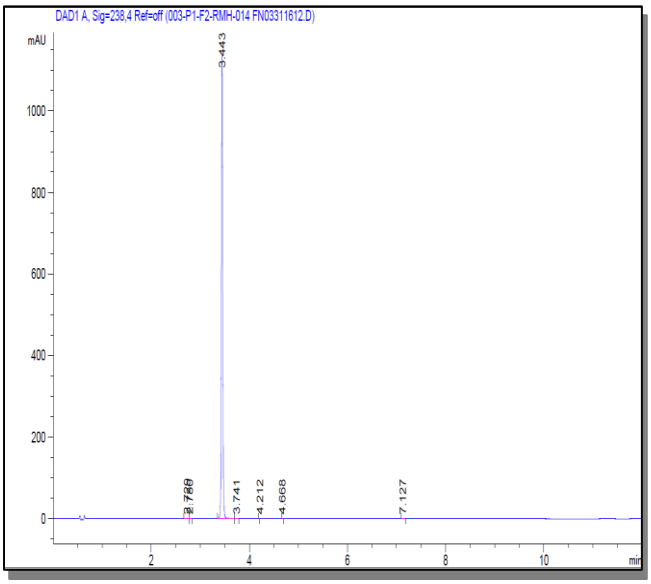
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.9% [1]
Secondary Chromatographic Purity by LC/MS Analysis	20384217	98.7%
Identity by LC/MS Analysis	20384217	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [2]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	20398075 [2]	Below Quantitation Limit
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.91%

[1] 0.02% Estazolam detected by HPLC/UV analysis; no Alprazolam detected.
[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm
Mobile Phase:	A: Acetonitrile B: 0.1% Ammonium acetate in Water

Gradient:

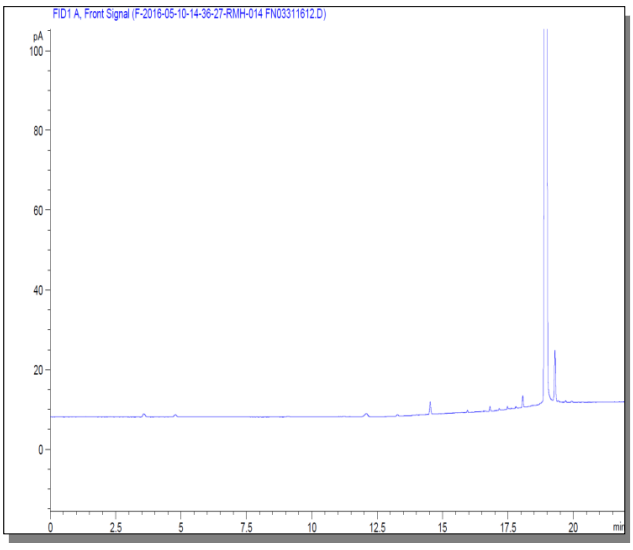
Time (min)	% A	% B
0.0	25	75
8.0	70	30
10.0	70	30
10.1	25	75

Flow Rate:	0.7 mL/min
Wavelength:	238 nm
Sample Name:	FN03311612
Acquired:	October 18, 2019

Peak #	Ret Time	Area %
1	2.73	0.04
2	2.78	0.01
3	3.44	99.92
4	3.74	0.02
5	4.21	0.00
6	4.67	0.00
7	7.13	0.01

Peak 4 has been identified as Estazolam

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FN03311612
Acquired:	May 10, 2016

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

ND - None Detected

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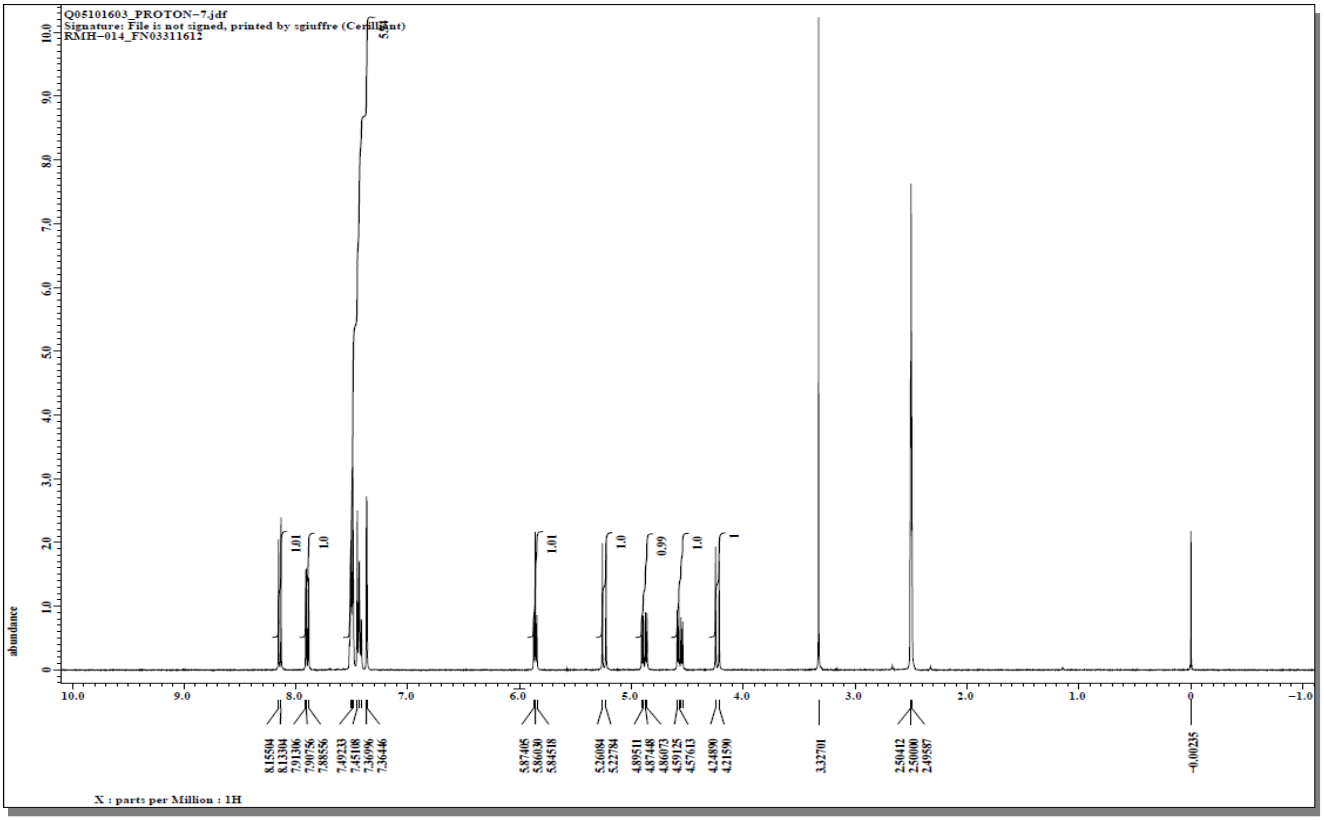
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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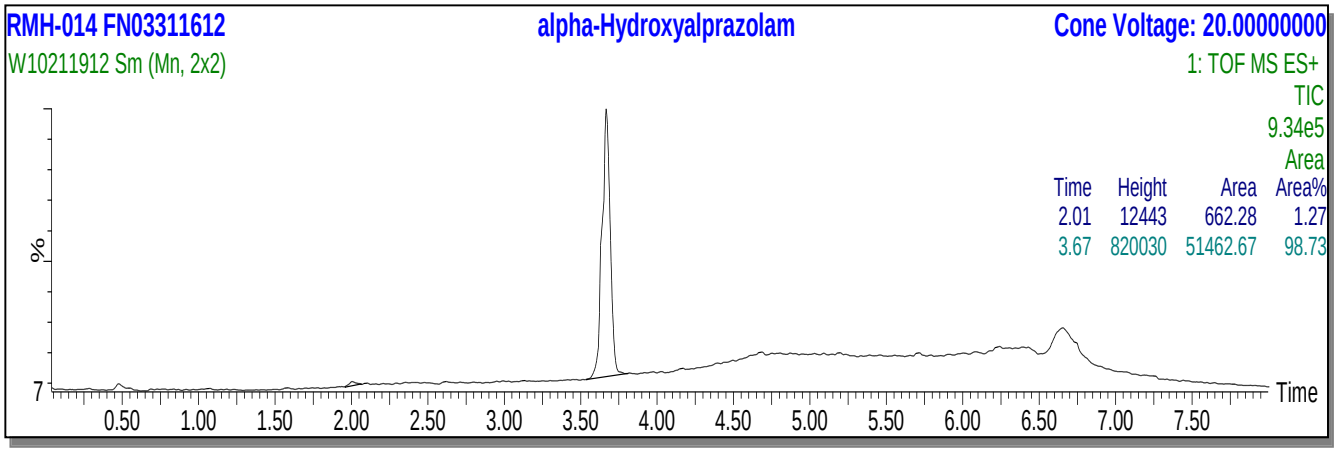
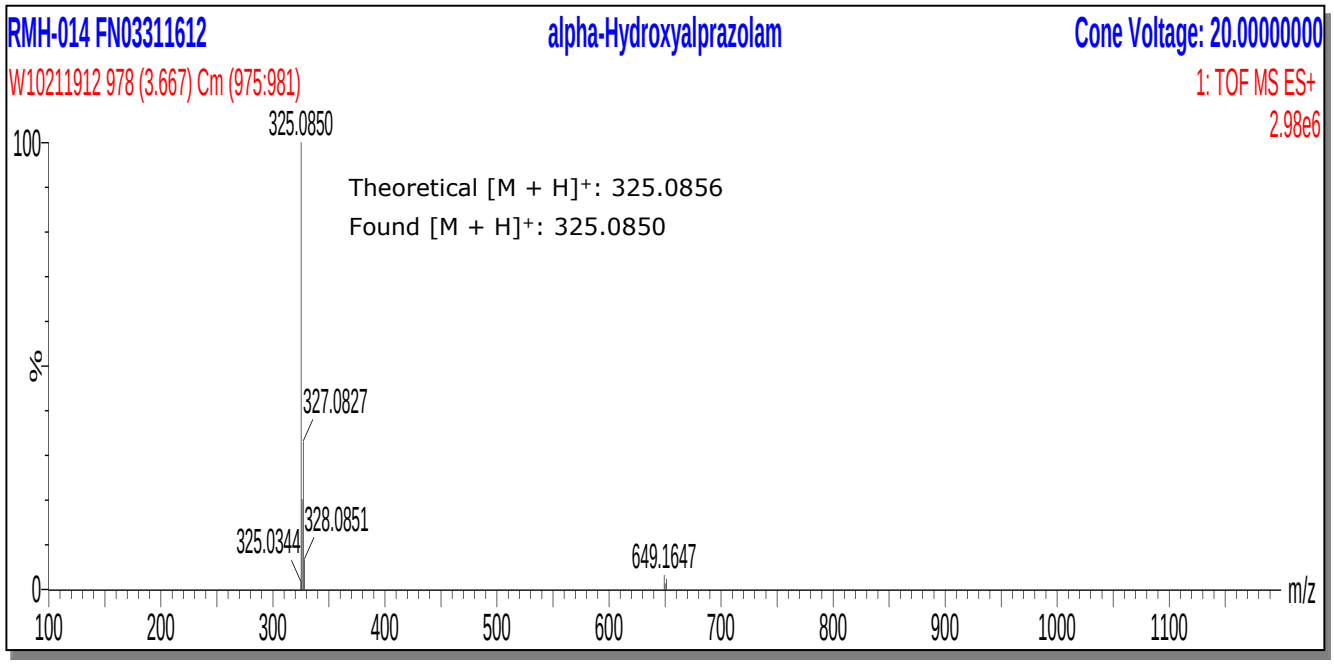
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	October 21, 2019

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10





Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (A-908, alpha-Hydroxyalprazolam-D_5) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 09, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Certified Reference Material - Certificate of Analysis

alpha-Hydroxyalprazolam-D_5, Primary Measurement Standard

(8-chloro-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine-1-yl)Methanol-D_5

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: A-908-1ML
Lot No.: FN02202003
Description of CRM: alpha-Hydroxyalprazolam-D_5 in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_8ClD_5N_4O$
CAS No.: 136765-24-7
Regulatory: Canadian TK # 61-1031

Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
alpha-Hydroxyalprazolam-D_5	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

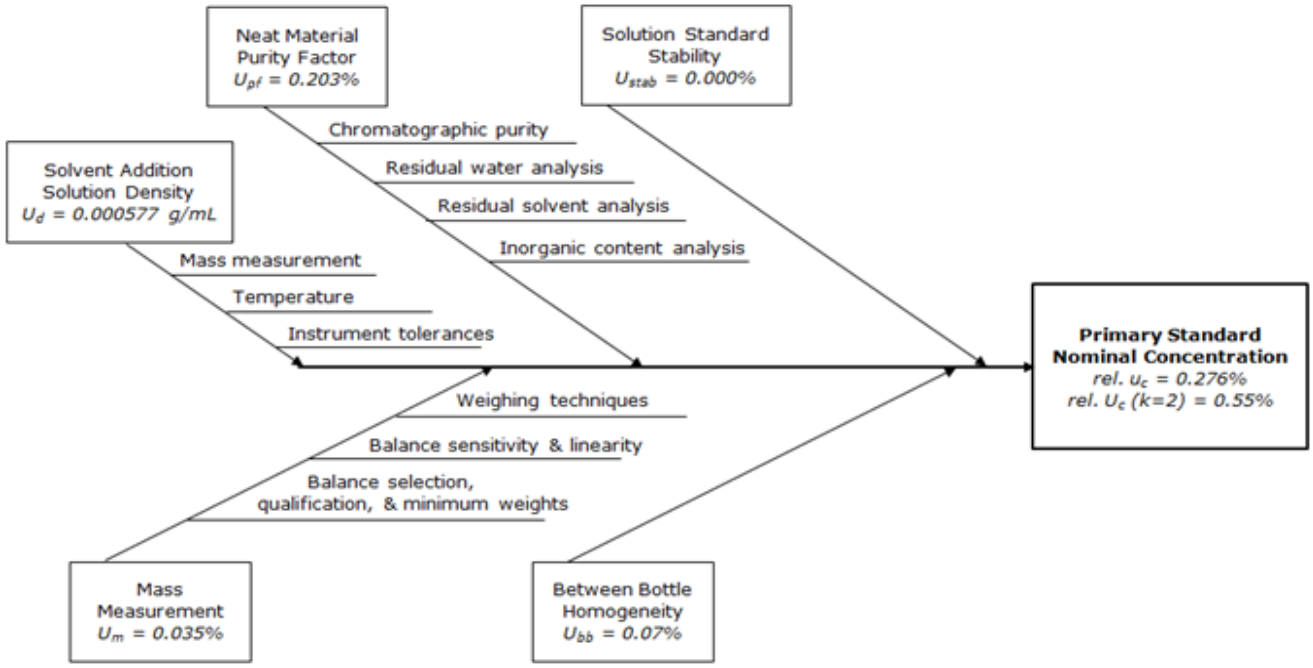
April 20, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:Water (50:50)	**Linearity (r) :**	0.999
Flow Rate:	1.5 mL/min		
Wavelength:	238 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN02202003	1.016	0.5
Previous Lot	FN07311803	1.005	1.5

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	alpha-Hydroxyalprazolam-D_5	**Chemical Formula:**	$C_{17}H_8ClD_5N_4O$
Material Lot:	FN10041908	**CAS Number:**	136765-24-7
		Molecular Weight:	329.80

Material Characterization Summary

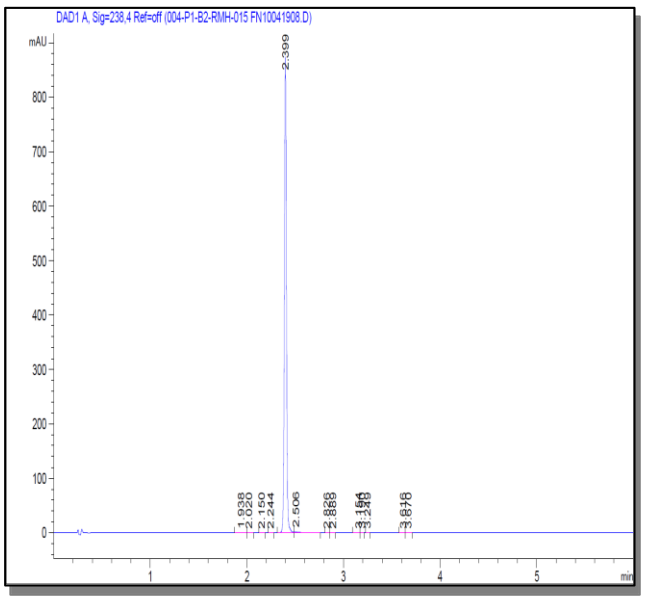
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.5%	
Secondary Chromatographic Purity by LC/MS Analysis	20384217	97.4%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.01% D_0 vs D_5	
		0.01% D_0 to D_2	1.85% D_4
		0.03% D_3	98.09% D_5
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799	0.07%	
Residual Water Analysis by Karl Fischer Coulometry	20398075	Not Detected	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		99.47%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

Mobile Phase: A: Acetonitrile
B: Water

Gradient:

Time (min)	% A	% B
0.0	20	80
4.0	70	30
5.0	70	30
5.1	20	80

Flow Rate: 0.8 mL/min

Wavelength: 238 nm

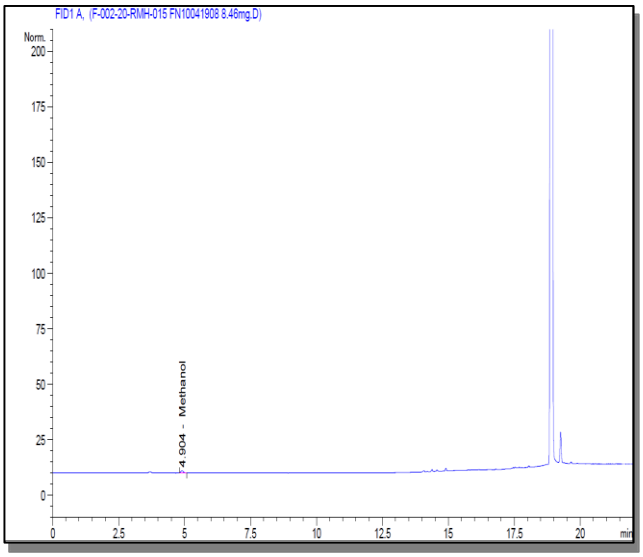
Sample Name: FN10041908

Acquired: January 23, 2020

Peak #	Ret Time	Area %
1	1.94	0.02
2	2.02	0.01
3	2.15	0.01
4	2.24	0.01
5	2.40	99.54
6	2.51	0.35
7	2.83	0.00
8	2.89	0.00
9	3.15	0.00
10	3.19	0.00
11	3.25	0.00
12	3.62	0.01
13	3.67	0.03

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

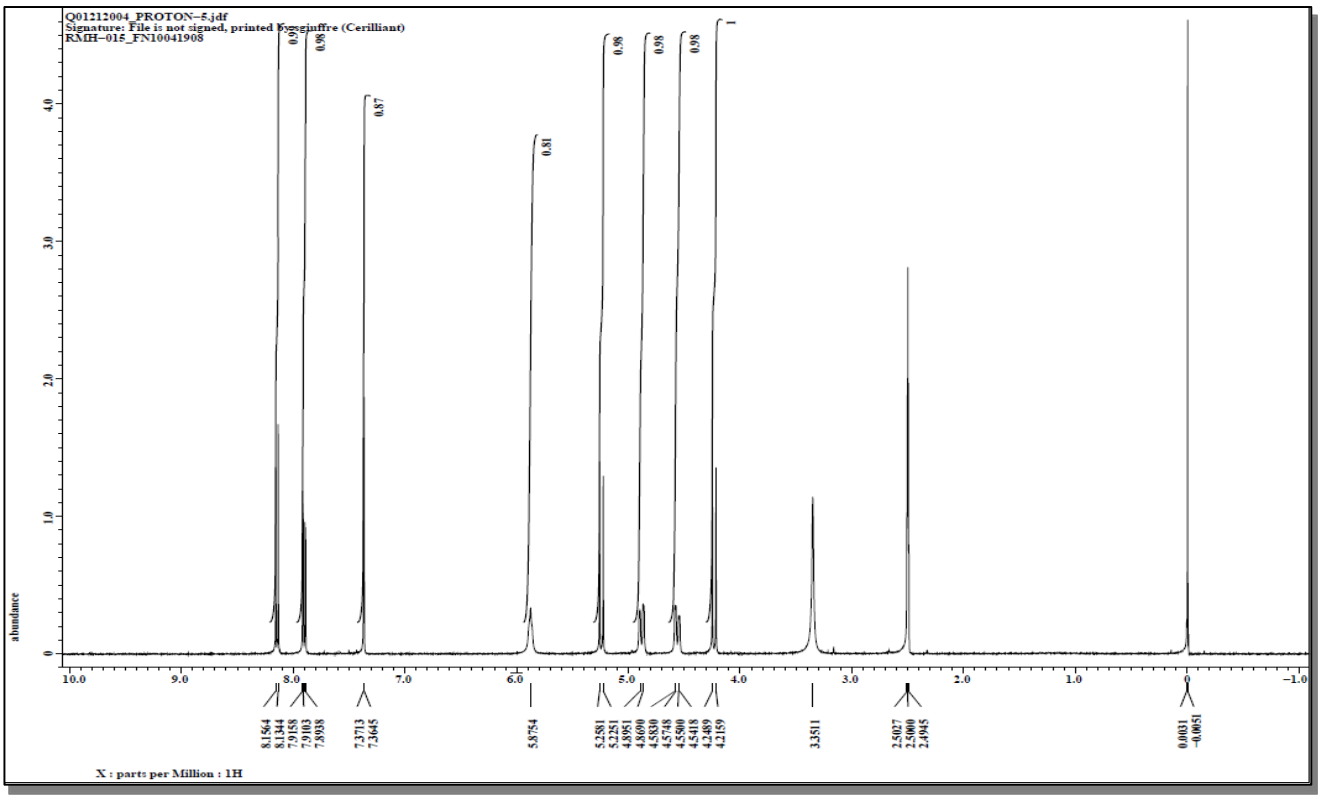


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FN10041908
Acquired:	January 22, 2020

Peak	Compound	Area	Weight %
1	Methanol	7.15	0.07
2	NMP	NA	NA
Total			**0.07**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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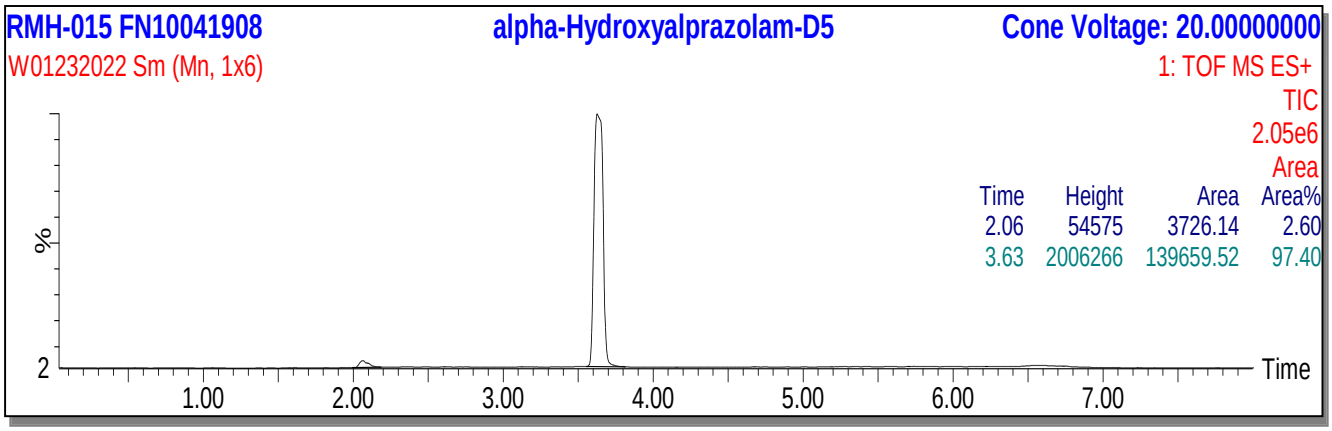
Spectral and Physical Data (cont.)

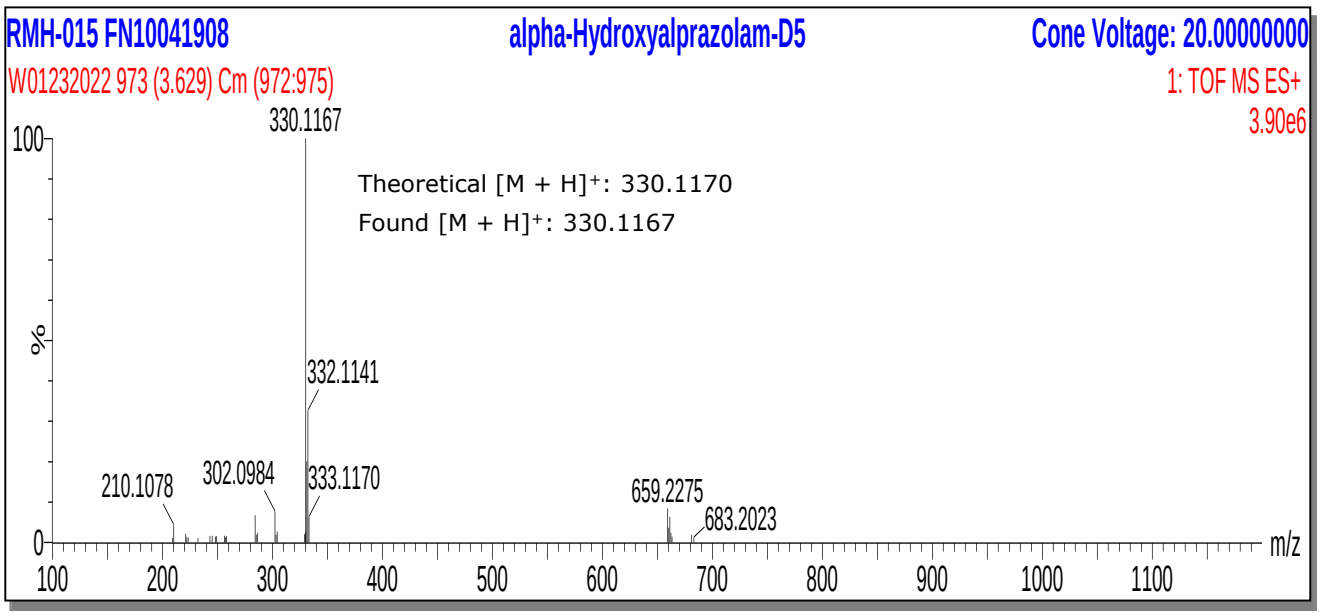
LC/MS

Column: Ascentis Express C18, 2.7 µm, 3.0 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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 100-1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: January 23, 2020





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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

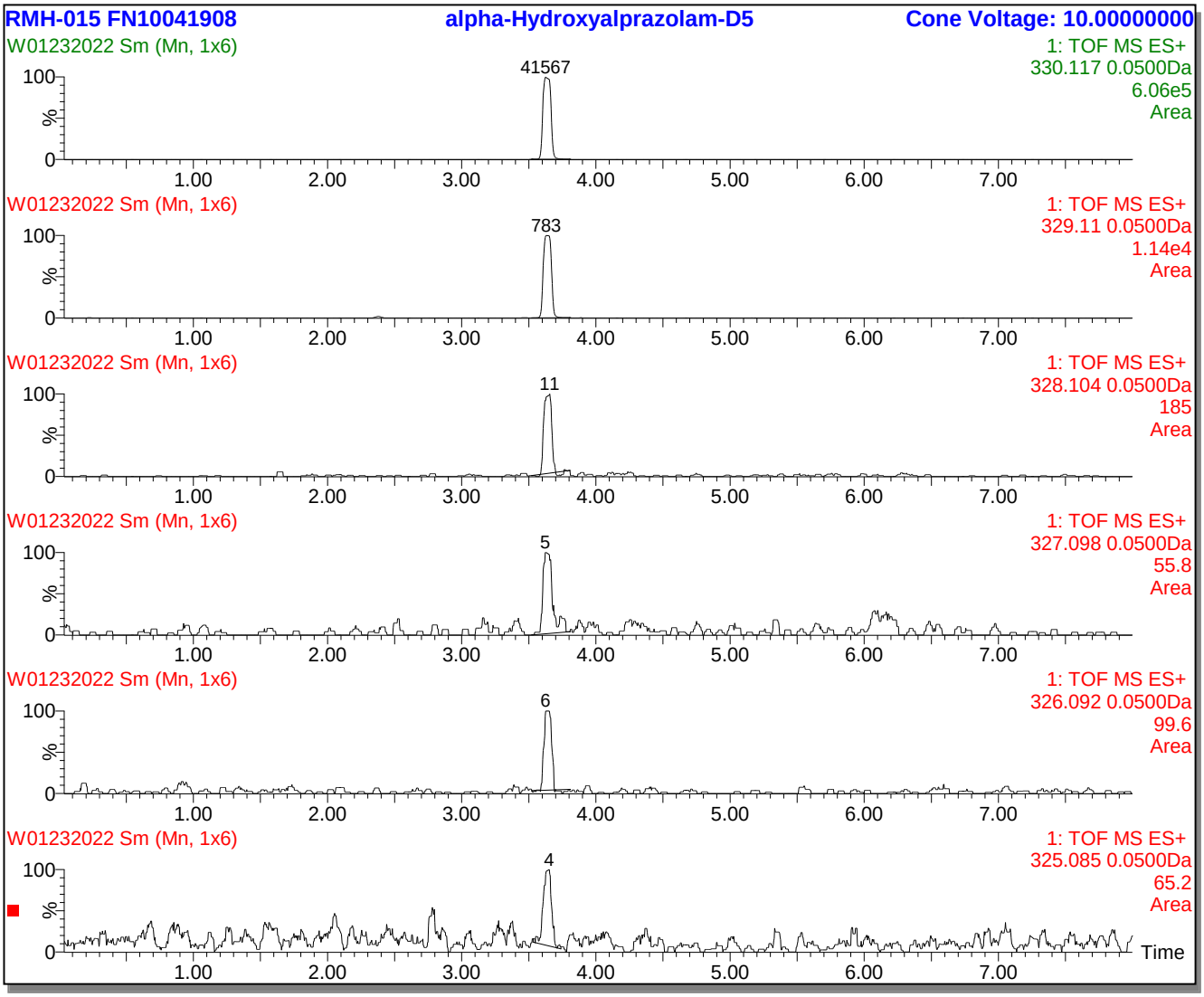
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 325-330 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: January 23, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 20, 2020	Initial version.

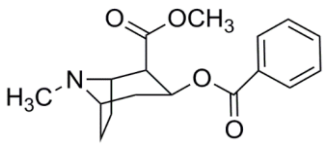
Certified Reference Material - Certificate of Analysis

Cocaine, Primary Measurement Standard

3-(Benzoyloxy)-8-methyl-8-azabicyclo[3,2,1]octane-2-carboxylic acid methyl ester

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: C-008-1ML
Lot No.: FE01202010
Description of CRM: Cocaine in Acetonitrile (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{21}NO_4$
CAS No.: 50-36-2
Regulatory: USDEA Exempt | Canadian TK # 61-1079



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Cocaine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

March 18, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

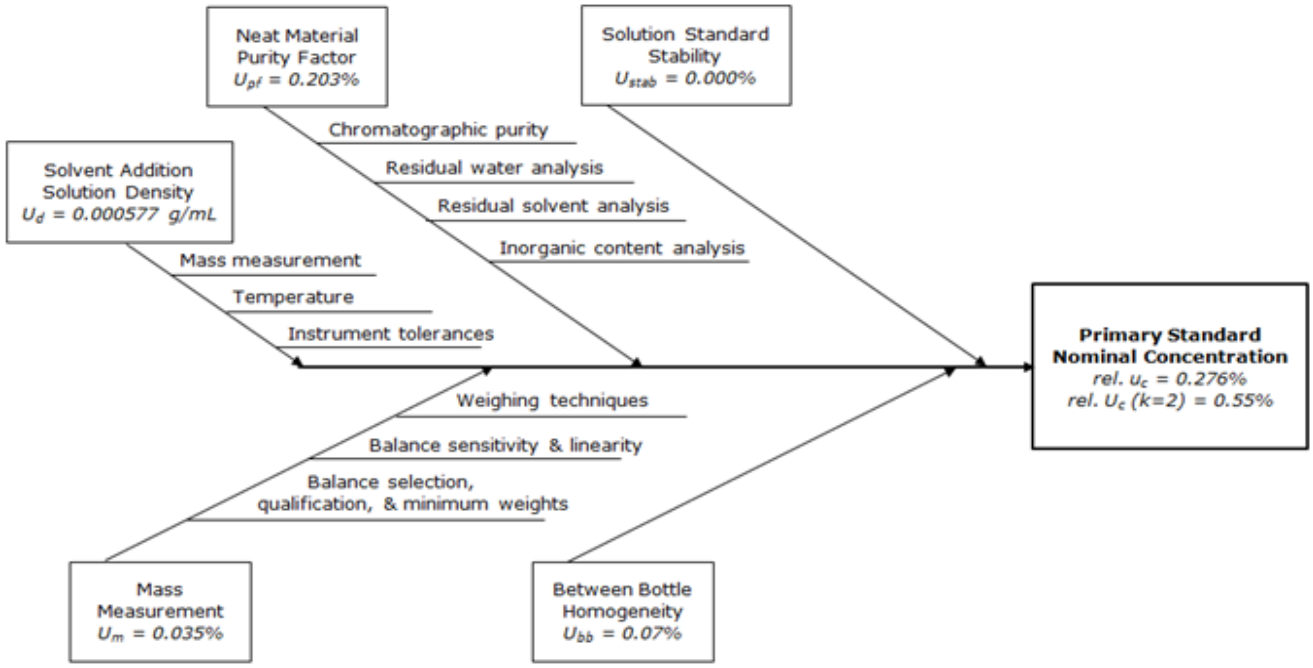
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (25:75)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	235 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01202010	1.001	0.4
Previous Lot	FE09091901	0.997	0.7

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Cocaine	**Chemical Formula:**	$C_{17}H_{21}NO_4$
Material Lot:	FE10301701	**CAS Number:**	50-36-2
		Molecular Weight:	303.35

Material Characterization Summary

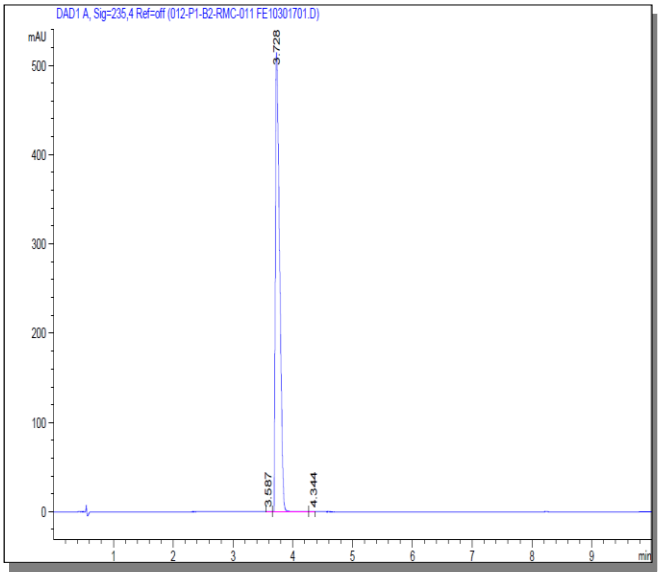
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	> 99.9% [1]
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	> 99.9%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	0.66%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Below Quantitation Limit
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.33%

[1] 0.01% Cocaethylene detected by HPLC/UV analysis.
[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	10	90
1.0	10	90
7.0	60	40
9.0	60	40
9.1	10	90

Flow Rate: 0.8 mL/min

Wavelength: 235 nm

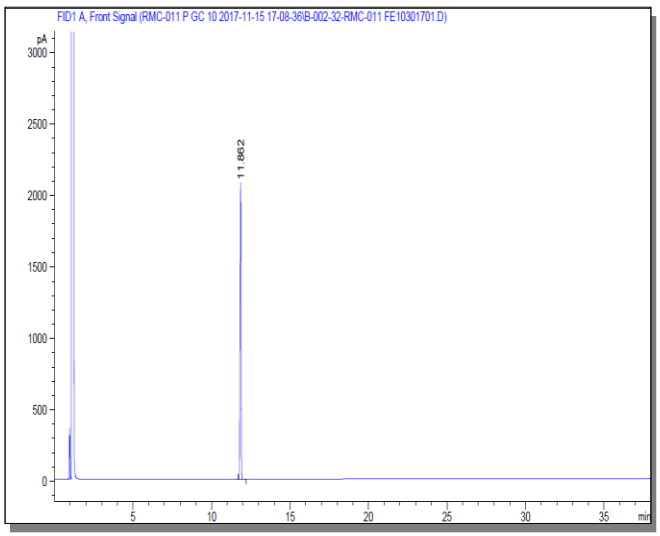
Sample Name: FE10301701

Acquired: November 16, 2017

Peak #	Ret Time	Area %
1	3.59	0.01
2	3.73	99.98
3	4.34	0.01

Peak 3 has been identified as Cocaethylene

GC/FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

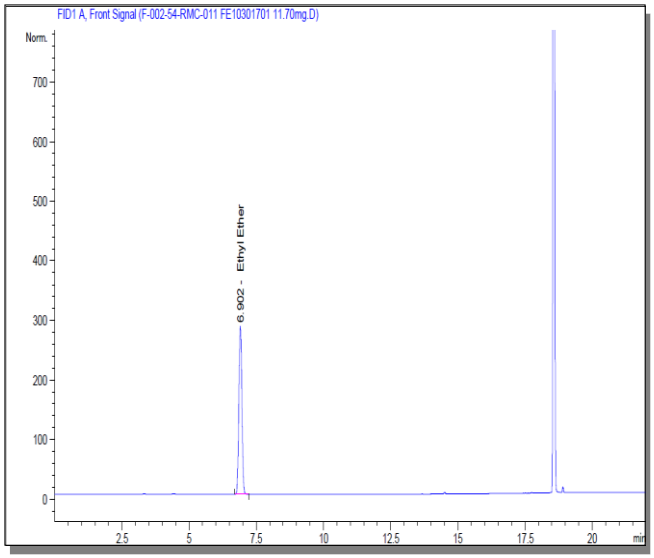
Sample Name: FE10301701

Acquired: November 15, 2017

Peak #	Ret Time	Area %
1	11.86	100.00

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

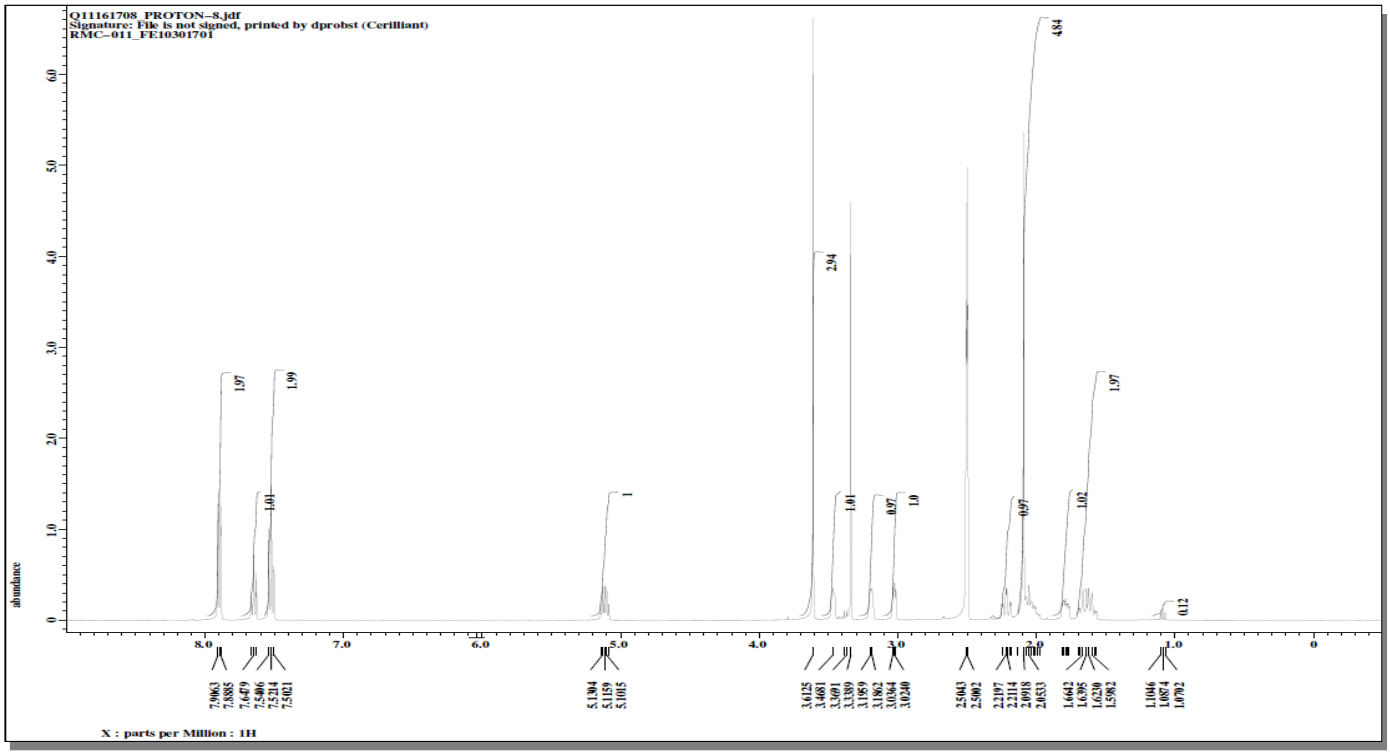


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FE10301701
Acquired:	November 14, 2017

Peak	Compound	Area	Weight %
1	Ethyl ether	2221.29	0.66
2	NMP	NA	NA
Total			**0.66**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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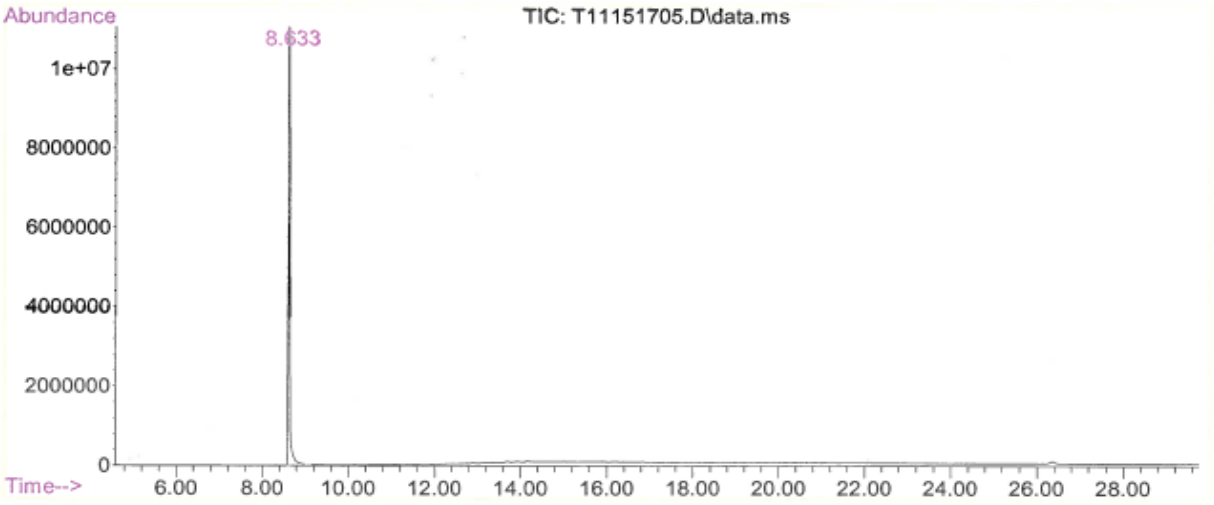
Spectral and Physical Data (cont.)

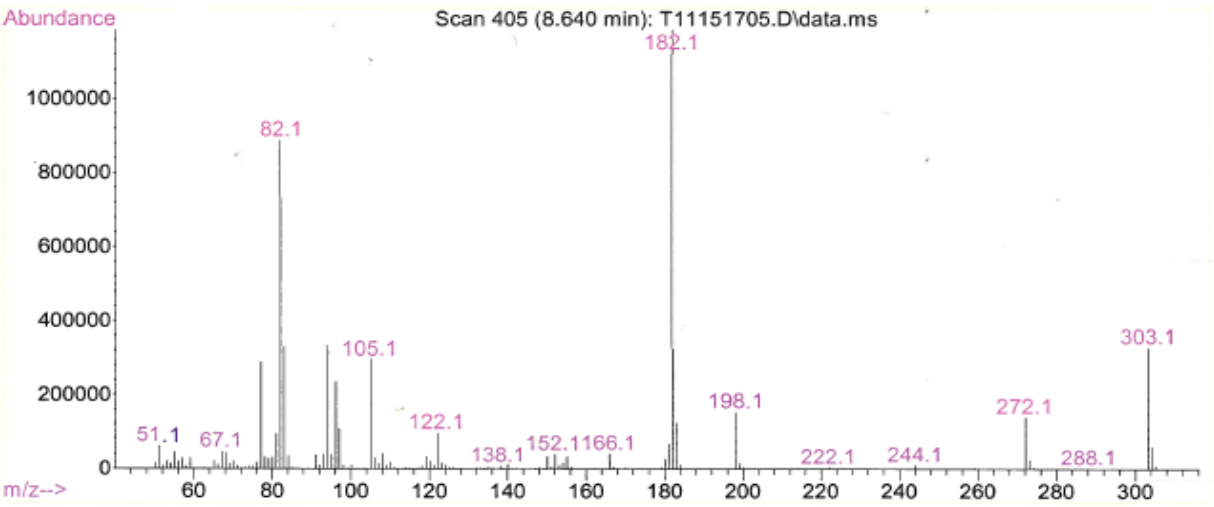
GC/MS

Compound Name	: Cocaine
Lot Number	: FE10301701
Instrument	: Agilent GCMS
Operator	: ECM(SGIUFFRE)
Date Reported	: Wed Nov 15 10:07:14 2017
Column Type	: DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	: 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.	: Cool on-column
Carrier Gas	: Helium
Flow Rate (mL\min)	: 0.80 mL/min
Transfer Line Temp.	: 280°C
Scan Range	: 50-500

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (C-004, Cocaine-D_3) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 18, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

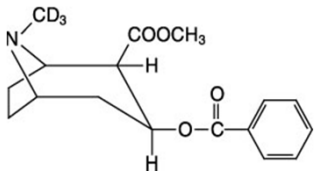
Certified Reference Material - Certificate of Analysis

Cocaine-D_3, Primary Measurement Standard

3-Benzoyloxy-8(trideuteromethyl)-8-azabicyclo[3.2.1]octane-2-carboxylic acid methyl ester

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: C-014-1ML
Lot No.: FE03022002
Description of CRM: Cocaine-D_3 in Acetonitrile (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{18}D_3NO_4$
CAS No.: 138704-14-0
Regulatory: USDEA Exempt | Canadian TK # 61-1082



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Cocaine-D_3	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

April 20, 2020
Issue Date

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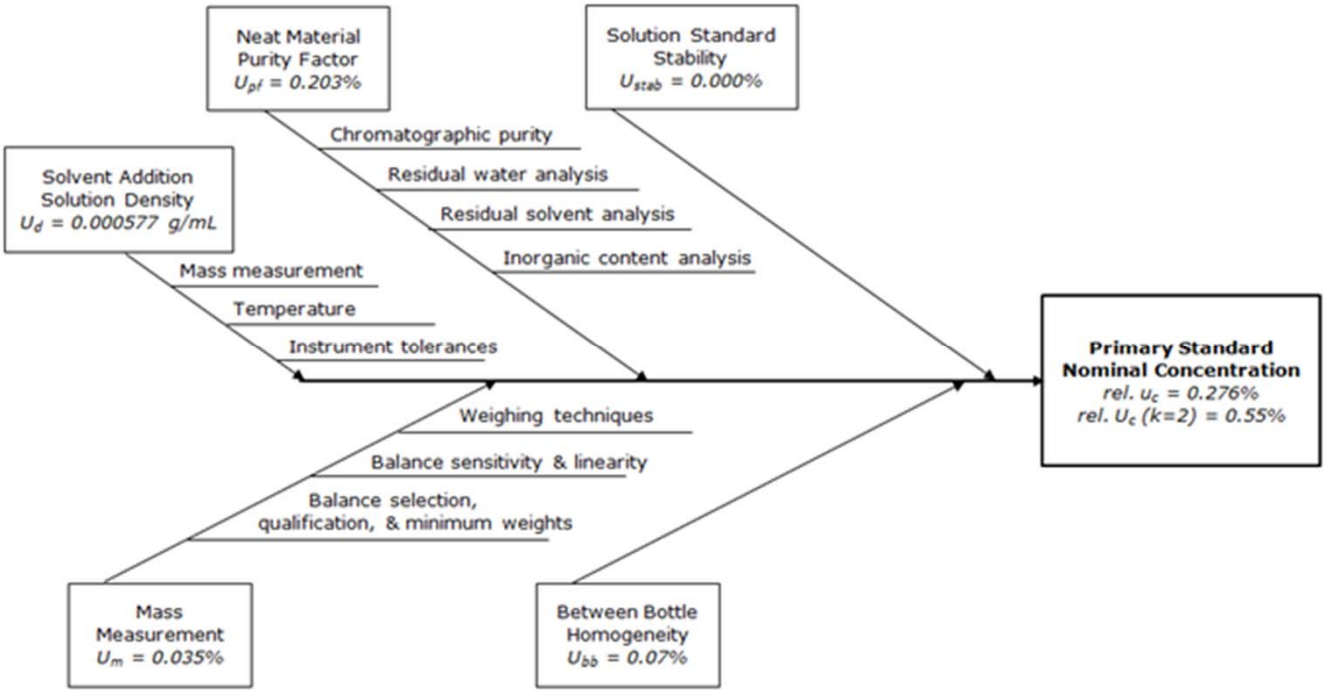
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (25:75)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	235 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03022002	1.004	0.3
Previous Lot	FE07131601	1.007	0.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Cocaine-D_3	**Chemical Formula:**	$C_{17}H_{18}D_3NO_4$
Material Lot:	FC12161903	**CAS Number:**	138704-14-0
		Molecular Weight:	306.37

Material Characterization Summary

Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.6% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	99.6%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.02% D_0 vs D_3	
		0.02% D_0	0.34% D_2
		0.01% D_1	99.64% D_3
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [2]	0.64%	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [2]	Not Detected	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		98.98%	

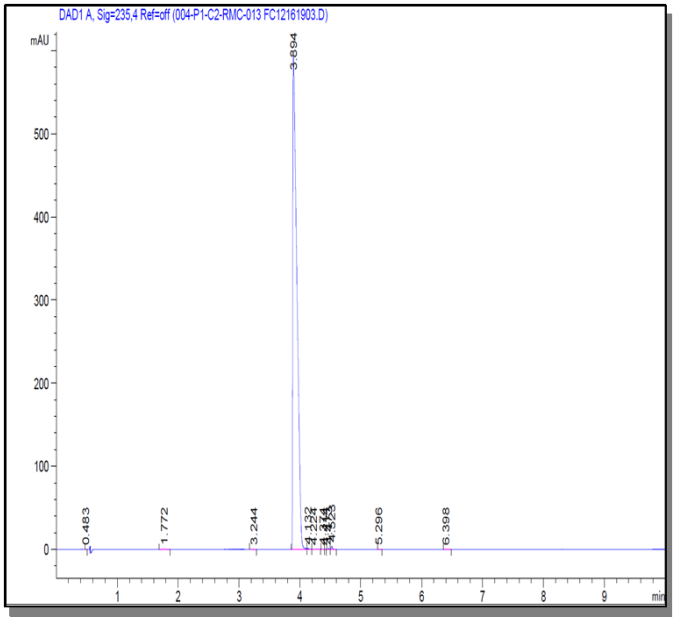
[1] 0.19% Cocaethylene and < 0.01% Benzoyecgonine detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	10	90
1.0	10	90
7.0	60	40
9.0	60	40
9.1	10	90

Flow Rate: 0.8 mL/min

Wavelength: 235 nm

Sample Name: FC12161903

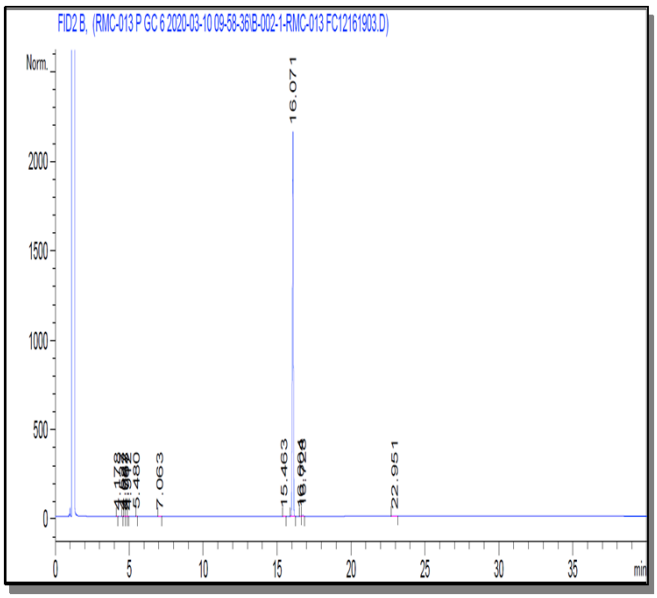
Acquired: February 20, 2020

Peak #	Ret Time	Area %
1	0.48	0.00
2	1.77	0.04
3	3.24	0.00
4	3.89	99.56
5	4.13	0.10
6	4.22	0.05
7	4.37	0.00
8	4.41	0.00
9	4.47	0.04
10	4.52	0.19
11	5.30	0.00
12	6.40	0.00

Peak 3 has been identified as Benzoylecgonine
Peak 10 has been identified as Cocaethylene

Spectral and Physical Data (cont.)

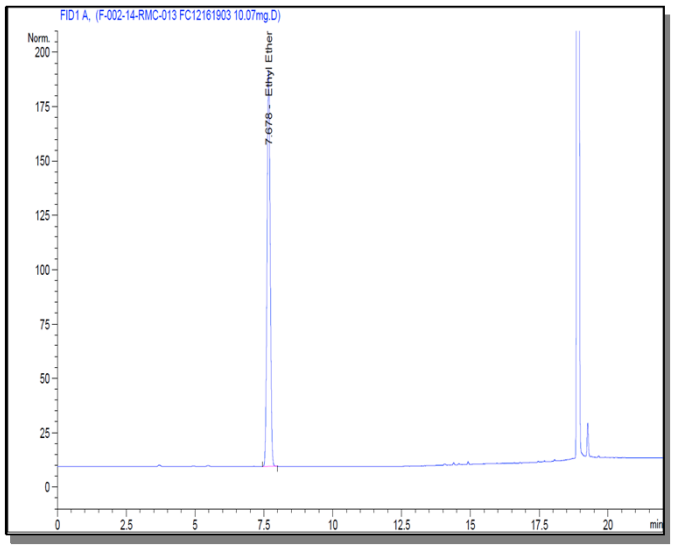
GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 300°C at 5°C/min hold 16 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC12161903
Acquired:	March 10, 2020

Peak #	Ret Time	Area %
1	4.18	0.00
2	4.53	0.00
3	4.68	0.00
4	4.77	0.03
5	4.91	0.01
6	5.48	0.04
7	7.06	0.01
8	15.46	0.03
9	16.07	99.64
10	16.60	0.02
11	16.73	0.21
12	22.95	0.02

Residual Solvent Analysis by GC/FID Headspace



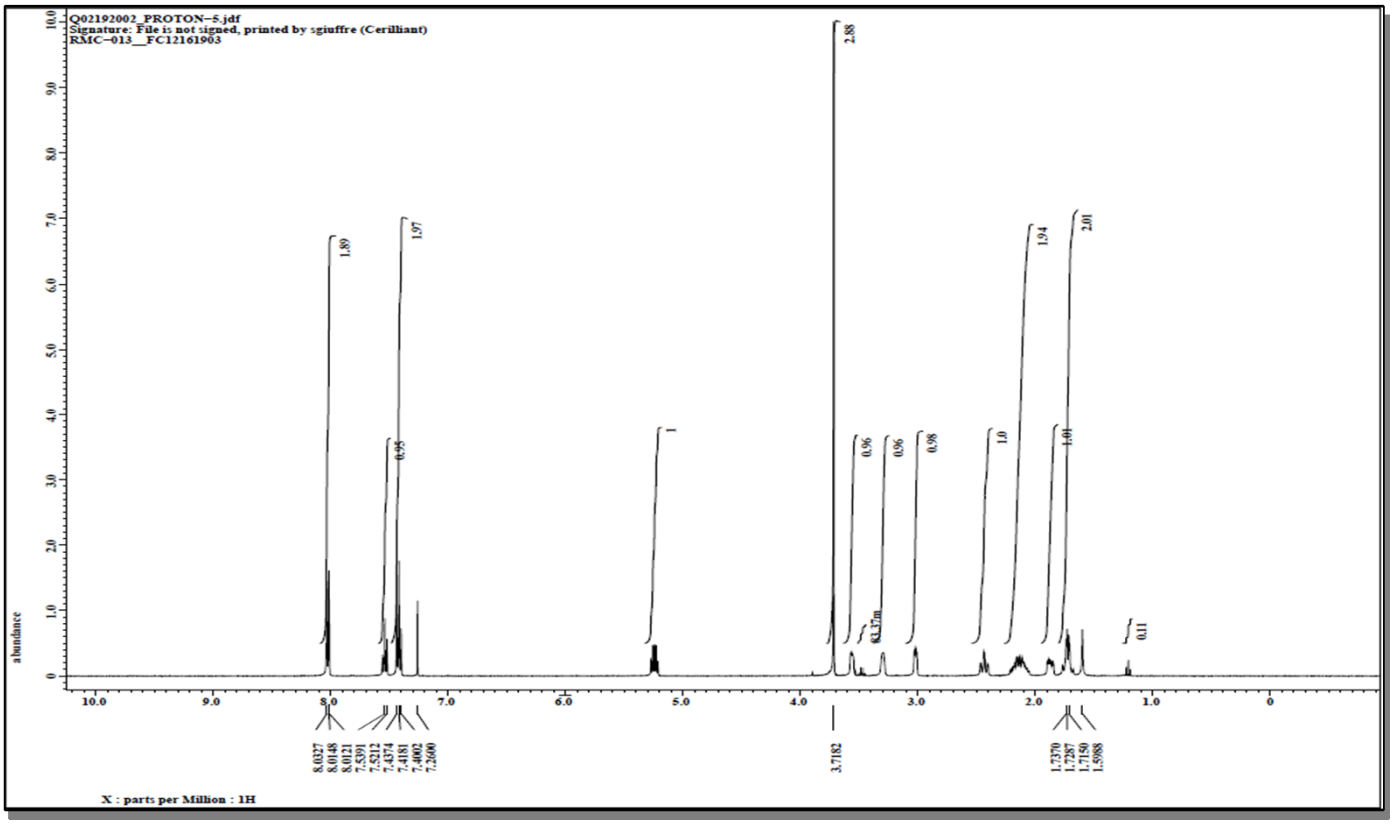
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC12161903
Acquired:	February 21, 2020

Peak	Compound	Area	Weight %
1	Ethyl ether	1474.88	0.64
2	NMP	NA	NA
Total			**0.64**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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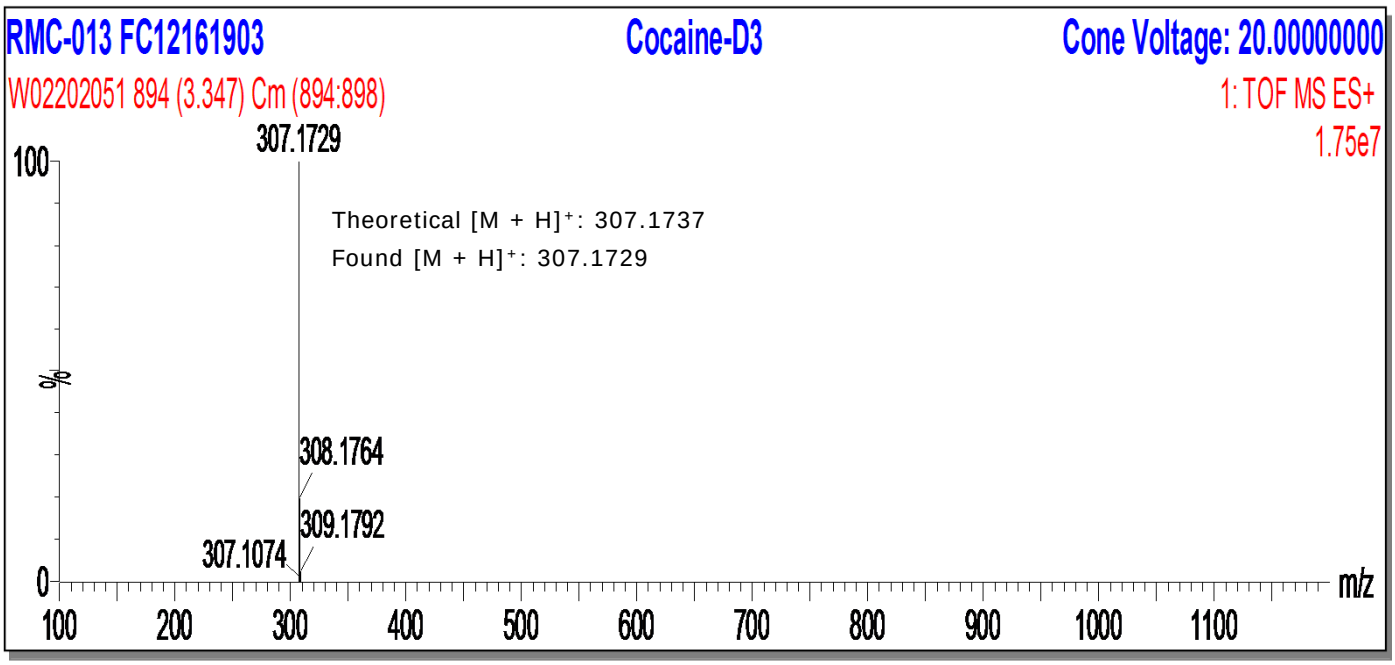
Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	February 20, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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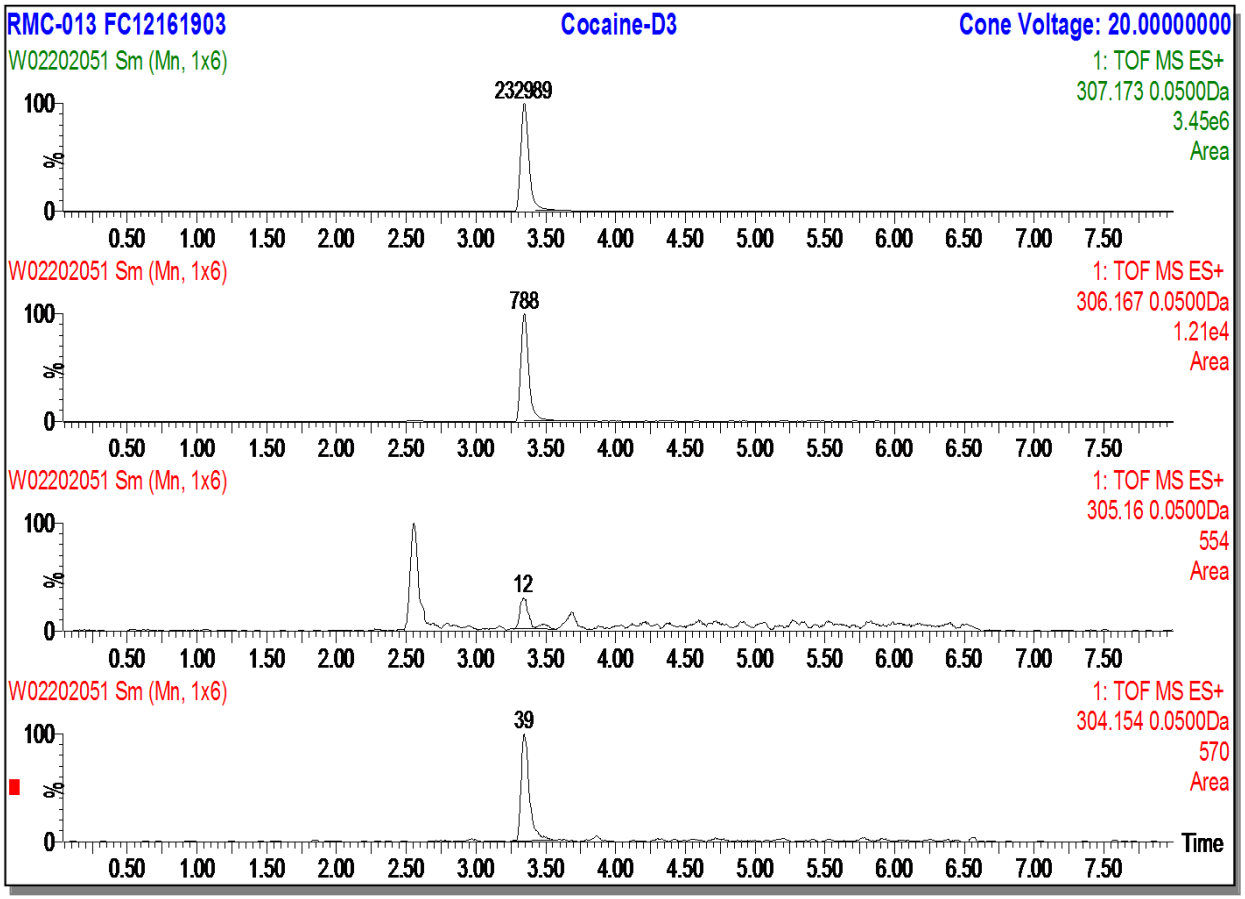
Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	304-307 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	February 20, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 20, 2020	Initial version.

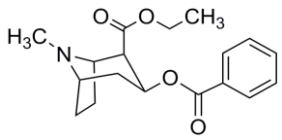
Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Certified Reference Material - Certificate of Analysis

Cocaethylene, Primary Measurement Standard

[R-(exo,exo)-3-Benzoyloxy-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid ethyl ester

Product No.: C-010-1ML
Lot No.: FE02202006
Description of CRM: Cocaethylene in Acetonitrile (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{23}NO_4$
CAS No.: 529-38-4
Regulatory: USDEA Exempt | Canadian TK # 61-1081



Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Cocaethylene	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

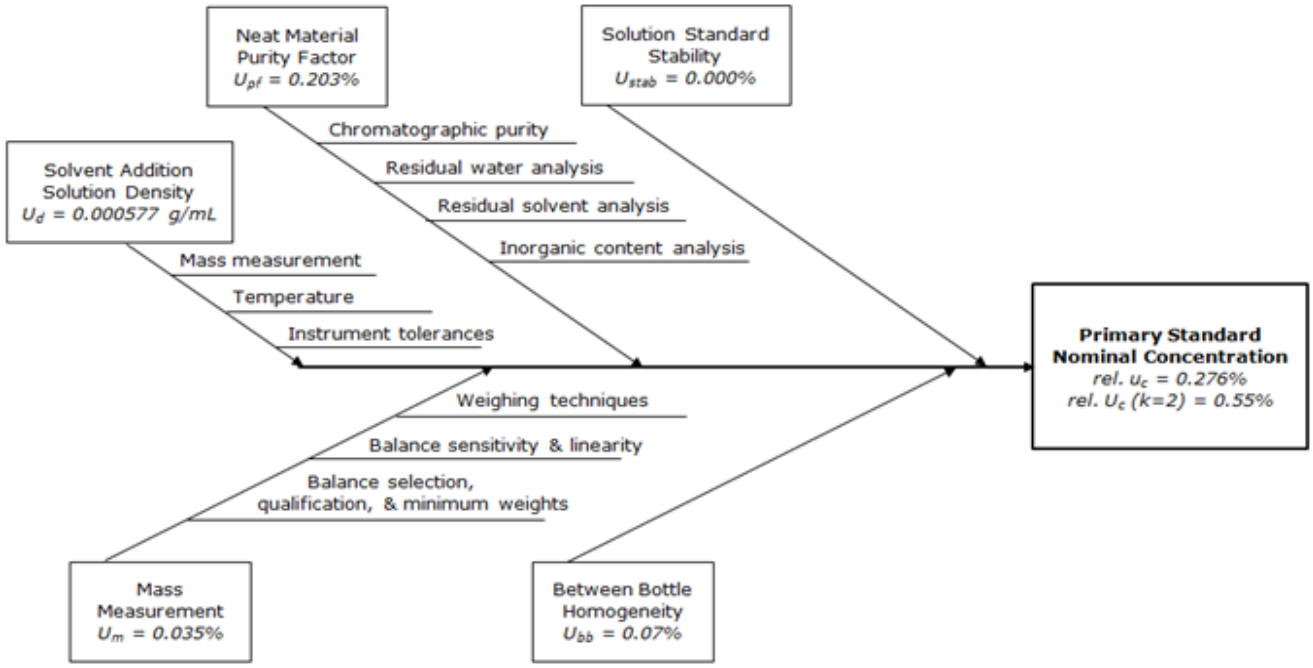
April 16, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-35ms 30 m x 0.53 mm ID, 1.0 µm film thickness	**Number of Points:**	4
Temp Program:	60°C to 280°C at 40°C/min hold 7 min	**Linearity (r) :**	1.000
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02202006	1.004	0.2
Previous Lot	FE09301903	1.001	0.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Cocaethylene	**Chemical Formula:**	$C_{18}H_{23}NO_4$
Material Lot:	FC10141905	**CAS Number:**	529-38-4
		Molecular Weight:	317.38

Material Characterization Summary

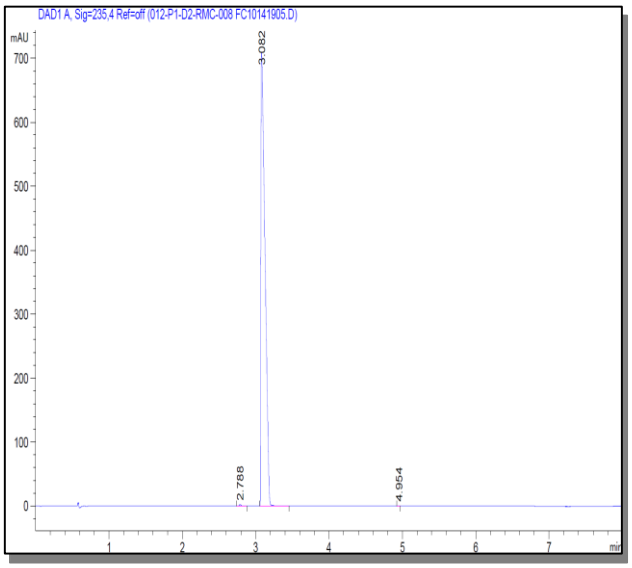
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.9% [1]
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.9% [2]
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [3]	0.37%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [3]	Not Detected
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.51%

[1] 0.12% Cocaine and no Benzoylecgonine detected by HPLC/UV analysis.
[2] 0.10% Cocaine and no Benzoylecgonine detected by GC/FID analysis.
[3] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.00	15	85
0.50	15	85
4.50	70	30
5.50	70	30
5.51	15	85

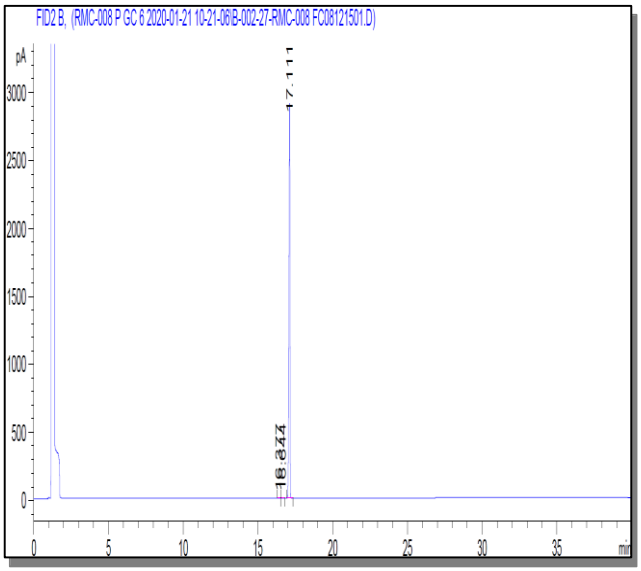
Flow Rate: 0.8 mL/min
Wavelength: 235 nm

Sample Name: FC10141905
Acquired: January 07, 2020

Peak #	Ret Time	Area %
1	2.79	0.12
2	3.08	99.88
3	4.95	0.00

Peak 1 is identified as Cocaine

GC/FID



Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness

Temp Program: 40°C to 180°C at 40°C/min
180°C to 300°C at 5°C/min
hold 12.5 min

Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC10141905
Acquired: January 21, 2020

Peak #	Ret Time	Area %
1	16.38	0.10
2	16.64	0.03
3	17.11	99.87

Peak 1 is identified as Cocaine

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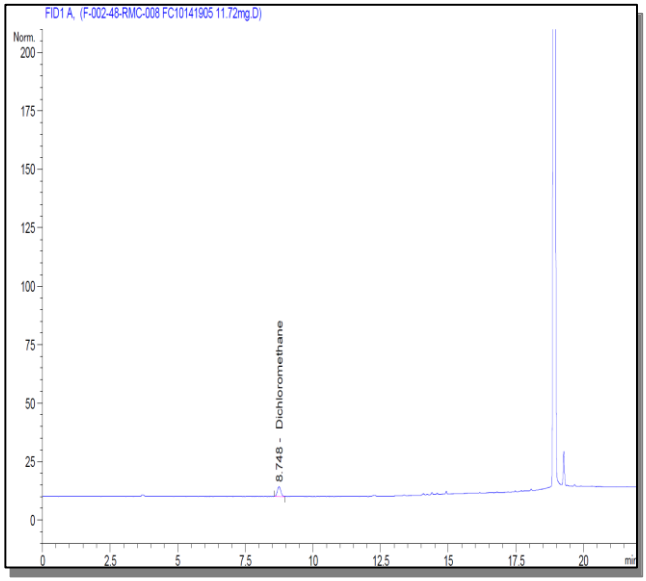
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

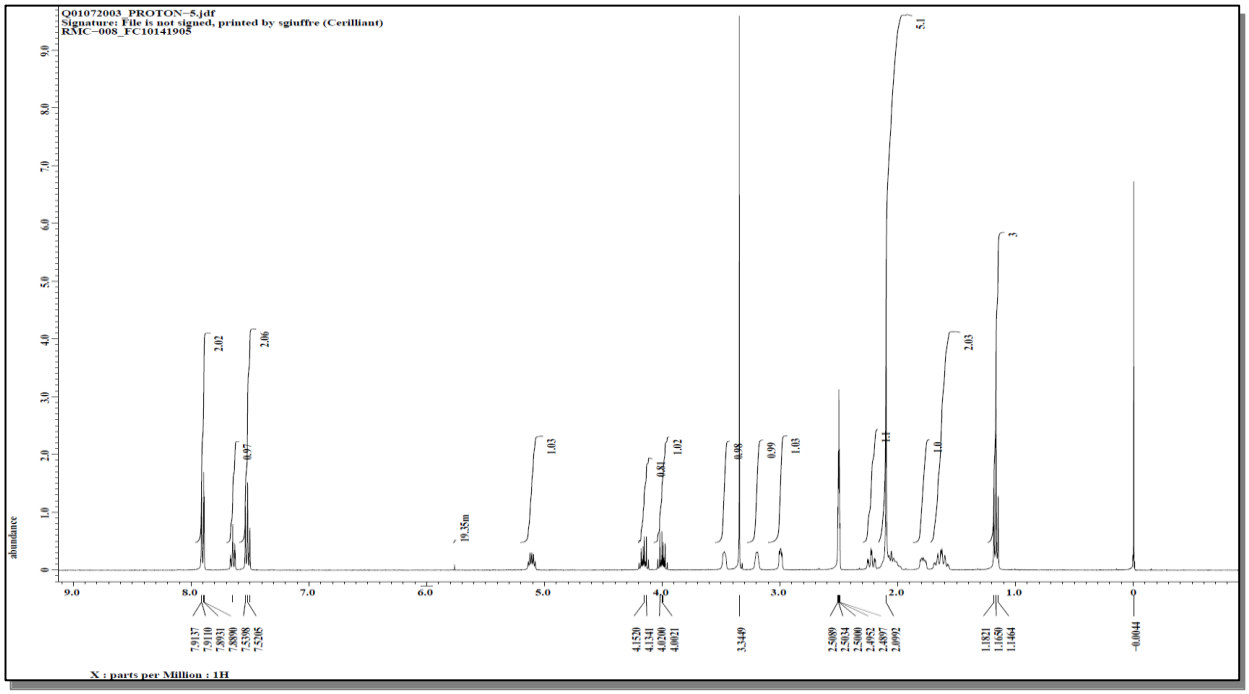


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC10141905
Acquired:	January 17, 2020

Peak	Compound	Area	Weight %
1	Dichloromethane	37.08	0.37
2	NMP	NA	NA
Total			**0.37**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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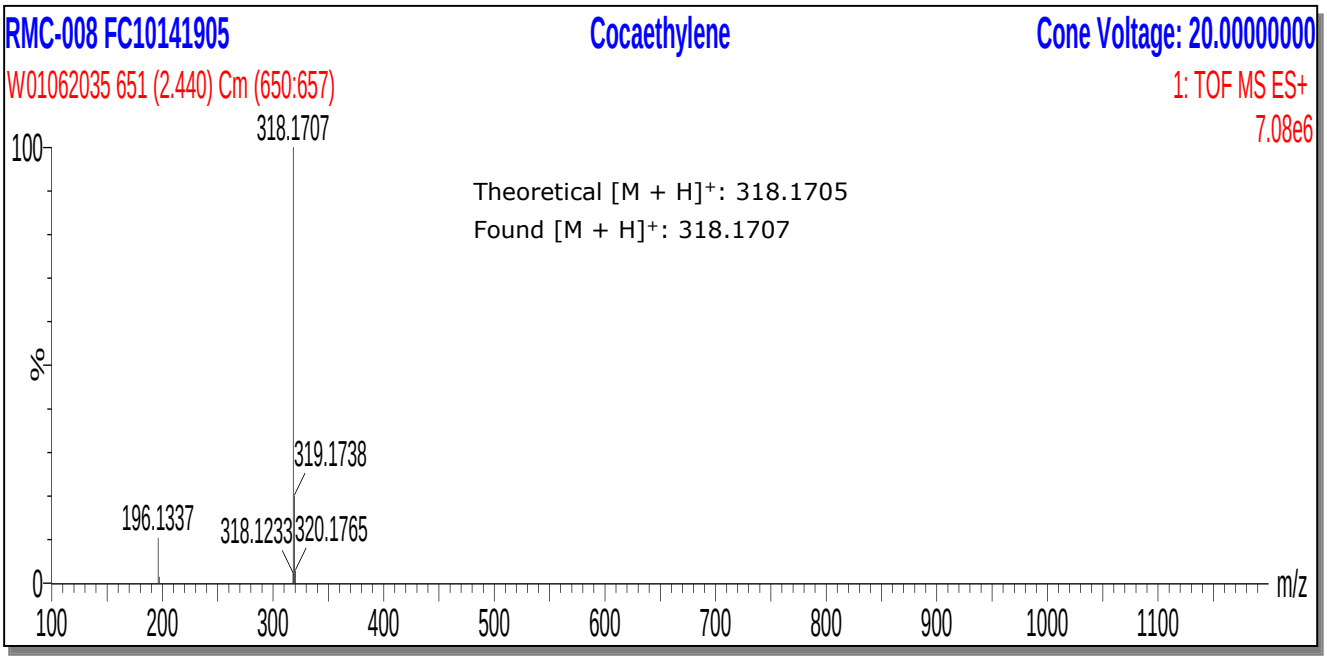
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 06, 2020

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 16, 2020	Initial version.

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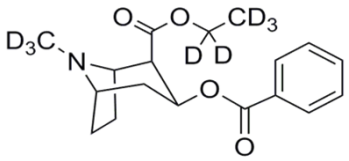
Certified Reference Material - Certificate of Analysis

Cocaethylene-D_8, Primary Measurement Standard

3-Benzoyl-8-(trideuteromethyl)-8-azabicyclo-[3.2.1]octane-2-carboxylic pentadeuteroethyl ester

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: C-025-1ML
Lot No.: FE03102005
Description of CRM: Cocaethylene-D_8 in Acetonitrile (Solution)
Retest Date: June 2021 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{15}D_8NO_4$
CAS No.: 152521-09-0
Regulatory: USDEA Exempt



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Cocaethylene-D_8	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability“ on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See “Details about certification process” on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

April 24, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

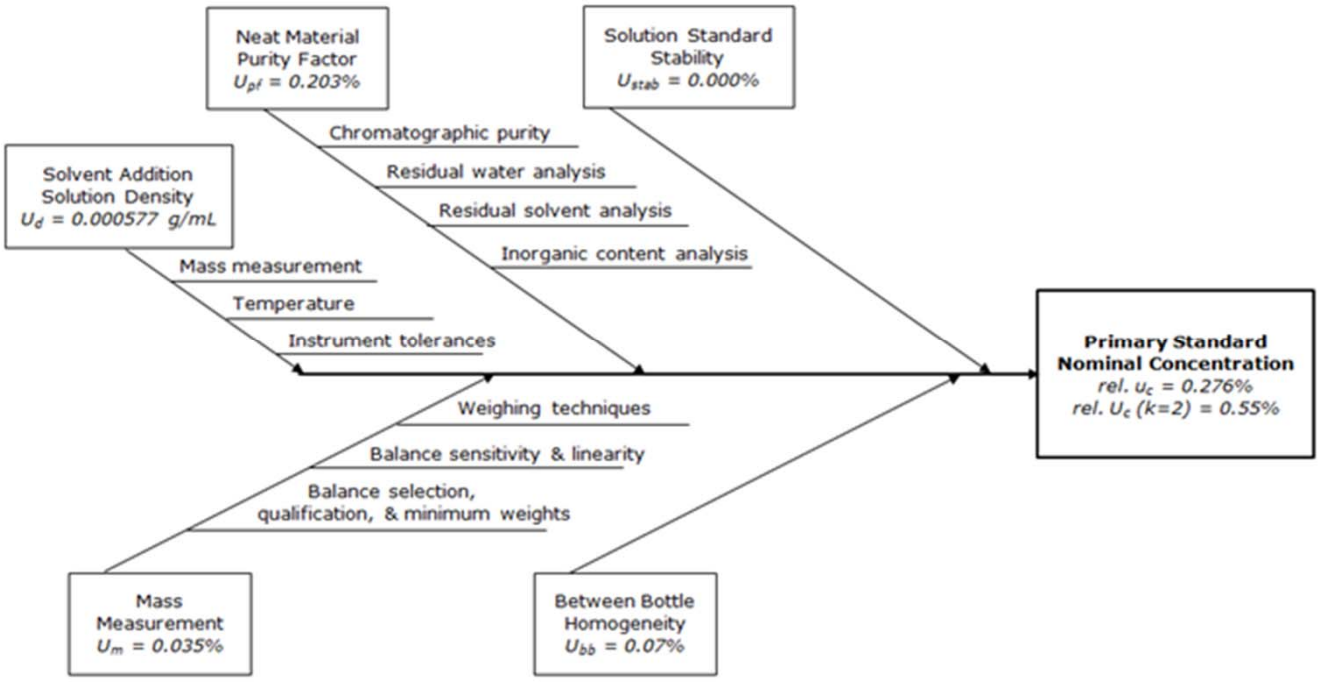
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
		Linearity (r) :	1.000
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (35:65)		
Flow Rate:	1.5 mL/min		
Wavelength:	235 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03102005	0.995	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Cocaethylene-D_8	**Chemical Formula:**	$C_{18}H_{15}D_8NO_4$
Material Lot:	FC12181901	**CAS Number:**	152521-09-0
		Molecular Weight:	325.43

Material Characterization Summary

Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.8% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	99.9%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.00% D_0 vs D_8	
		0.00% D_0 to D_1	0.02% D_5 to D_6
		0.03% D_2	1.97% D_7
		0.01% D_3	97.95% D_8
		0.00% D_4	
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [2]	0.19%	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [2]	Not Detected	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		99.60%	

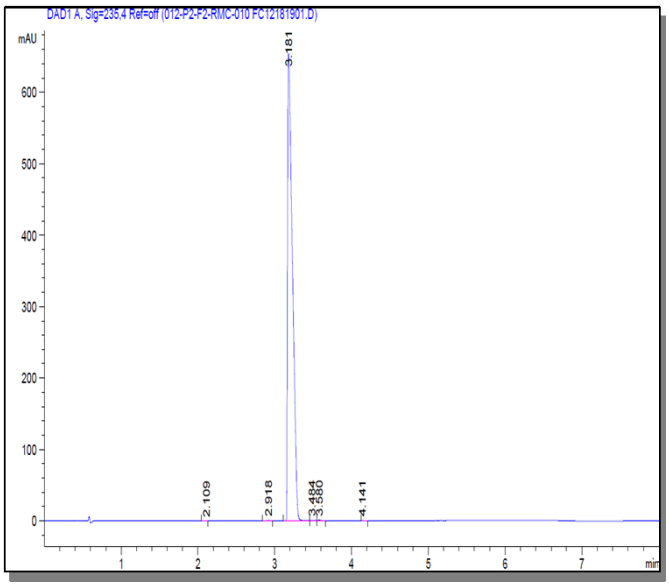
[1] < 0.01% Benzoylecgonine-D_8 and 0.03% Cocaine-D_8 detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.00	15	85
0.50	15	85
4.50	70	30
5.50	70	30
5.51	15	85

Flow Rate: 0.8 mL/min

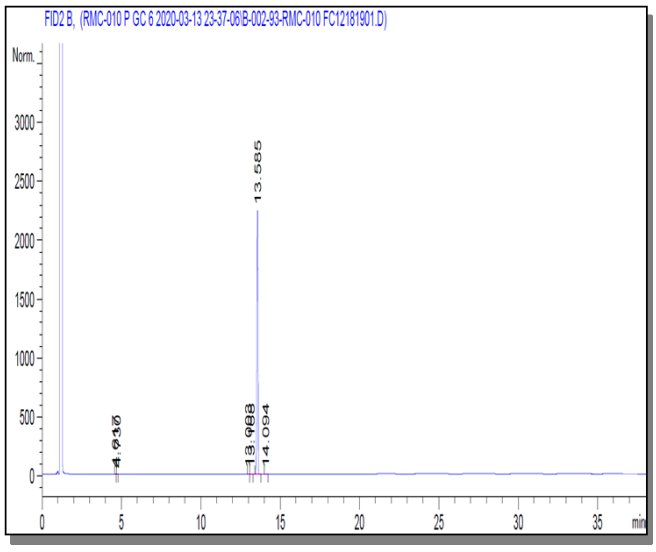
Wavelength: 235 nm

Sample Name: FC12181901

Acquired: March 04, 2020

Peak #	Ret Time	Area %	
1	2.11	0.00	Benzoylecgonine-D_8
2	2.92	0.03	Cocaine-D_8
3	3.18	99.87	
4	3.48	0.03	
5	3.58	0.06	
6	4.14	0.00	

GC / FID



Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

Sample Name: FC12181901

Acquired: March 14, 2020

Peak #	Ret Time	Area %
1	4.62	0.00
2	4.73	0.00
3	13.00	0.02
4	13.17	0.04
5	13.59	99.92
6	14.09	0.01

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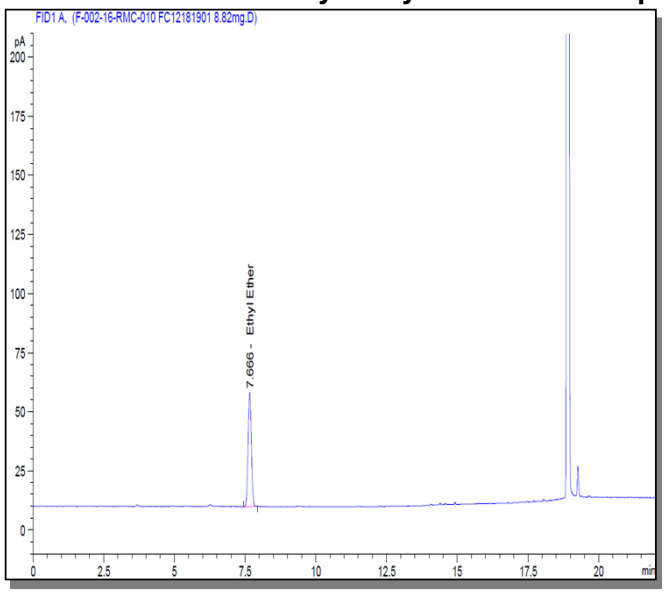
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

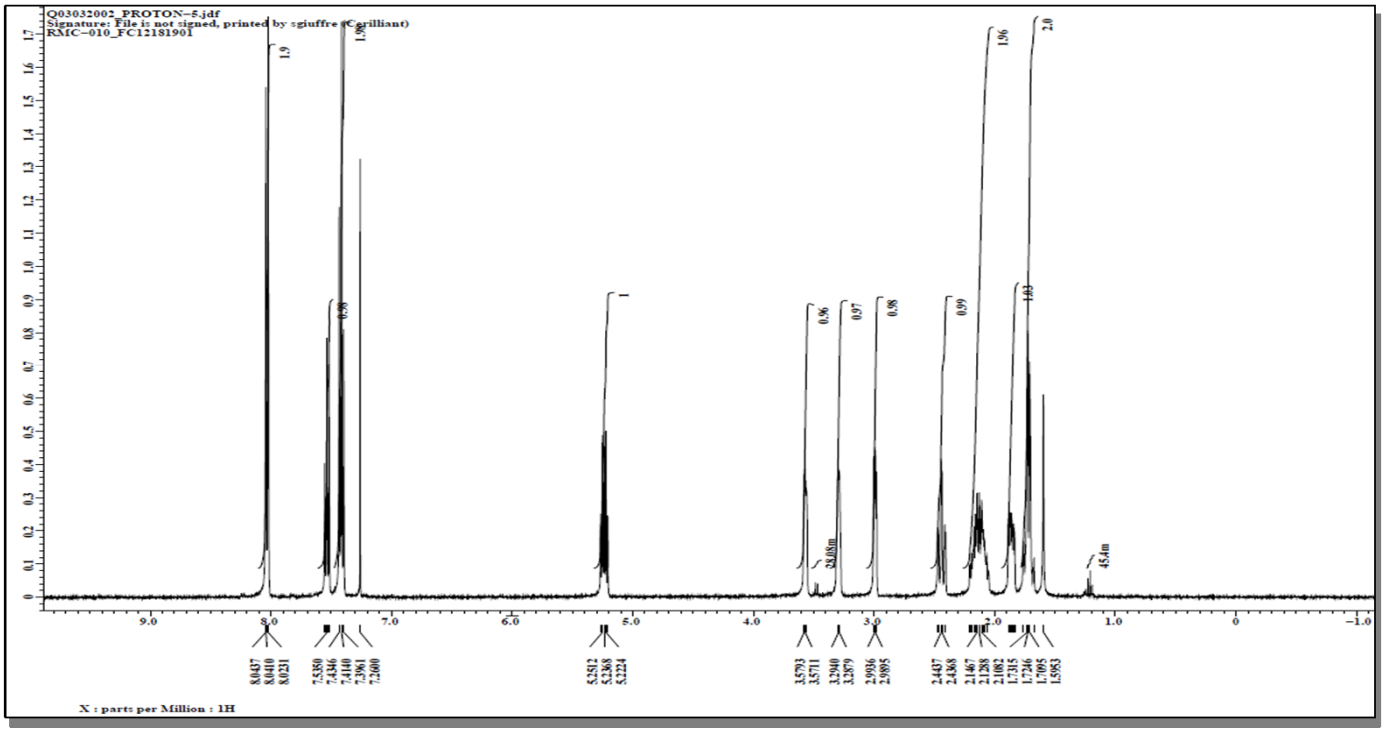


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC12181901
Acquired:	March 04, 2020

Peak	Compound	Area	Weight %
1	Ethyl Ether	389.68	0.19
2	NMP	NA	NA
Total			**0.19**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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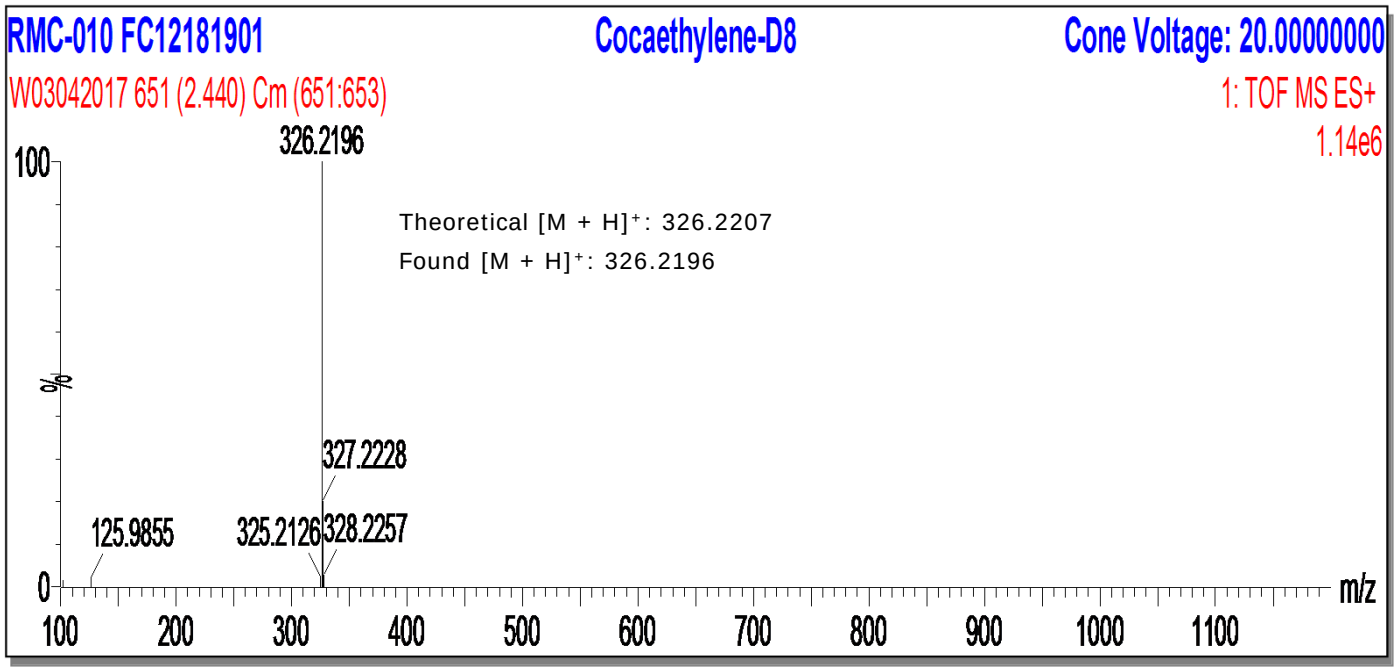
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 04, 2020

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10



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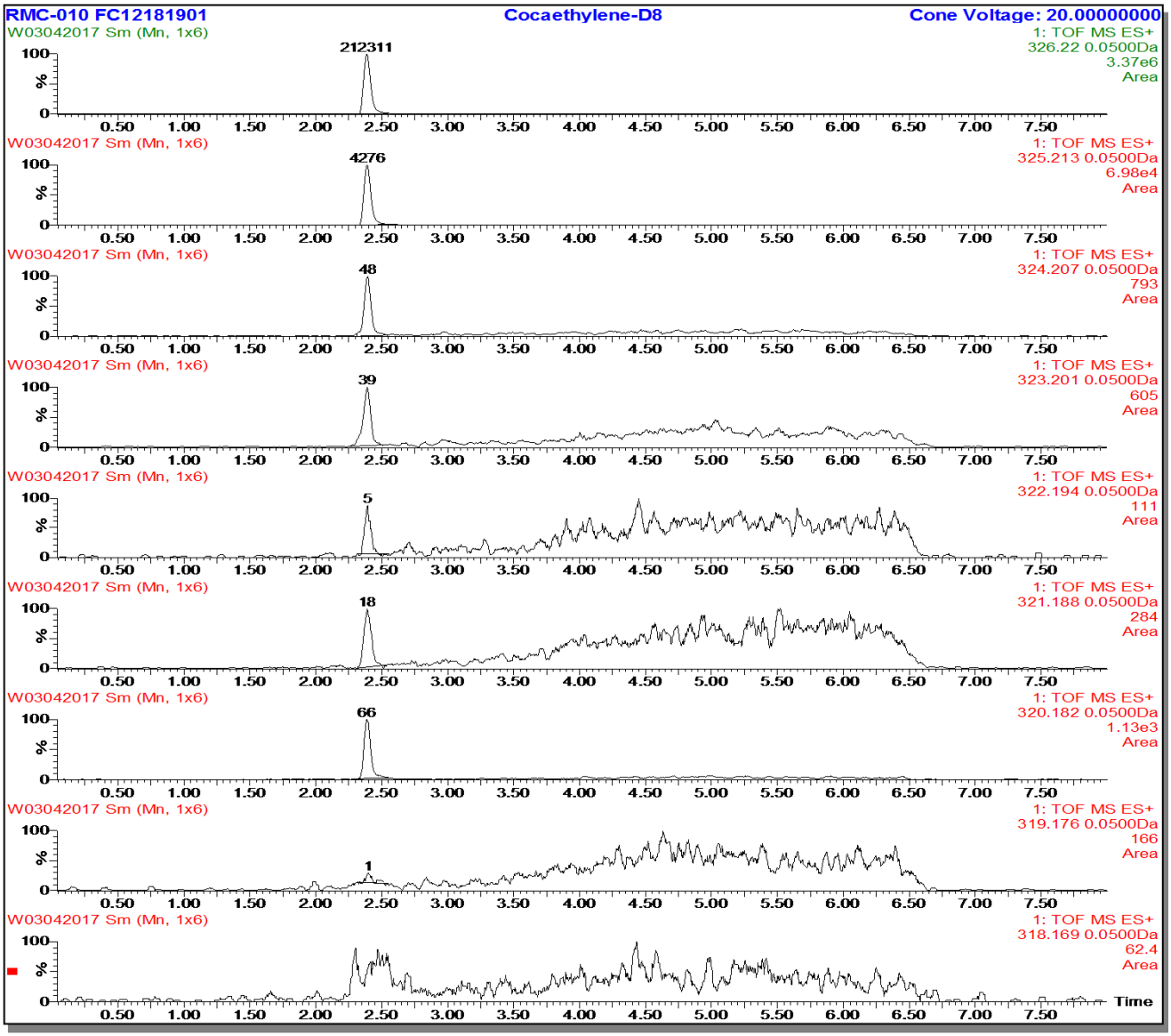
Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
		Scan Range:	318-326 amu
Mobile Phase:	A: 0.1% Formic acid in Water	**Ionization:**	Electrospray, Positive Ion
	B: Acetonitrile	**Instrument:**	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 04, 2020

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (C-010, Cocaethylene) 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 24, 2020	Initial version.

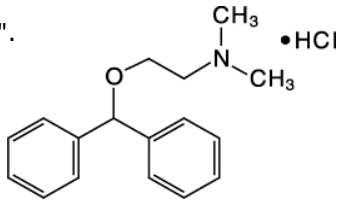
Certified Reference Material - Certificate of Analysis

Diphenhydramine, Primary Measurement Standard

2-(Diphenylmethoxy)-N,N-dimethylethylamine hydrochloride

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: D-015-1ML
Lot No.: FN02212010
Description of CRM: Diphenhydramine HCl in Methanol (Solution)
Nominal concentration is adjusted for HCl content.
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{21}NO \bullet HCl$
CAS No.: 147-24-0



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Diphenhydramine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
Nominal concentration is adjusted for HCl content. No adjustment required before use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

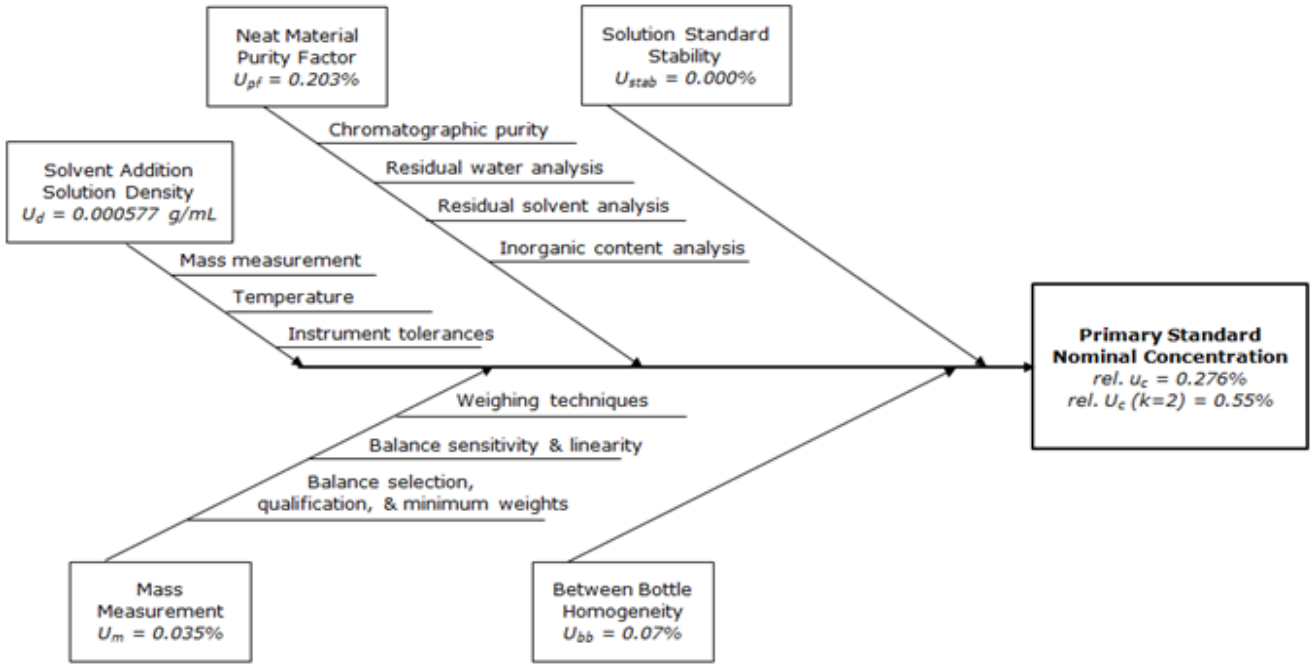
April 06, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl Hexyl, 2.7 µm, 3.0 x 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (25:75)	**Linearity (r) :**	1.000
Flow Rate:	1.2 mL/min		
Wavelength:	220 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN02212010	0.999	0.3
Previous Lot	FN11091601	0.997	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Diphenhydramine HCl	**Molecular Weight (base):**	255.35
Material Lot:	PN12191901	**Molecular Weight (salt):**	291.82
Chemical Formula:	$C_{17}H_{21}NO \bullet HCl$	**Salt Adjustment:**	1.143
CAS Number:	147-24-0		

Material Characterization Summary

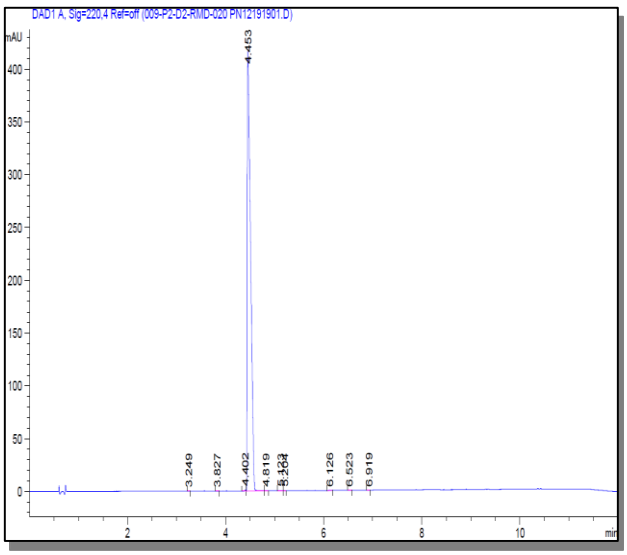
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.9%
Secondary Chromatographic Purity by GC/FID Analysis	20384346	> 99.9%
Identity by LC/MS Analysis	20384217	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.86%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	10	90
8.0	75	25
10.0	75	25
10.1	10	90

Flow Rate: 0.7 mL/min

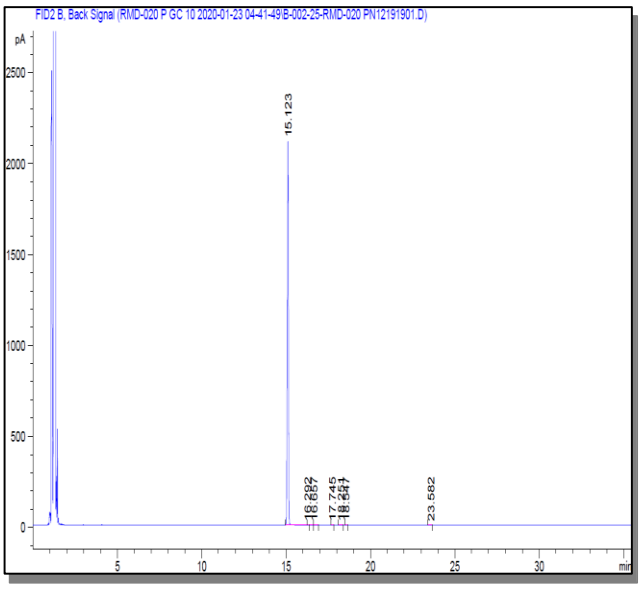
Wavelength: 220 nm

Sample Name: PN12191901

Acquired: January 23, 2020

Peak #	Ret Time	Area %
1	3.25	0.01
2	3.83	0.01
3	4.40	0.06
4	4.45	99.86
5	4.82	0.01
6	5.12	0.02
7	5.20	0.01
8	6.13	0.02
9	6.52	0.01
10	6.92	0.01

GC/FID



Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness

Temp Program: 40°C to 140°C at 40°C/min
140°C to 280°C at 5°C/min
hold 5 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

Sample Name: PN12191901

Acquired: January 23, 2020

Peak #	Ret Time	Area %
1	15.12	99.98
2	16.29	0.00
3	16.66	0.00
4	17.75	0.00
5	18.25	0.01
6	18.55	0.00
7	23.58	0.00

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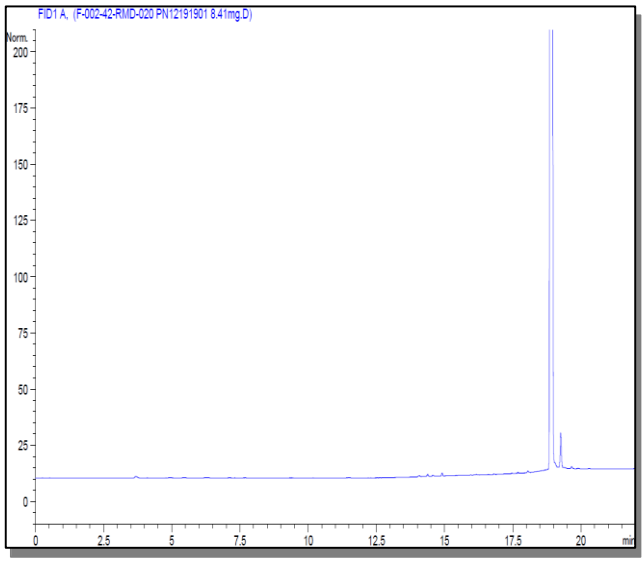
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



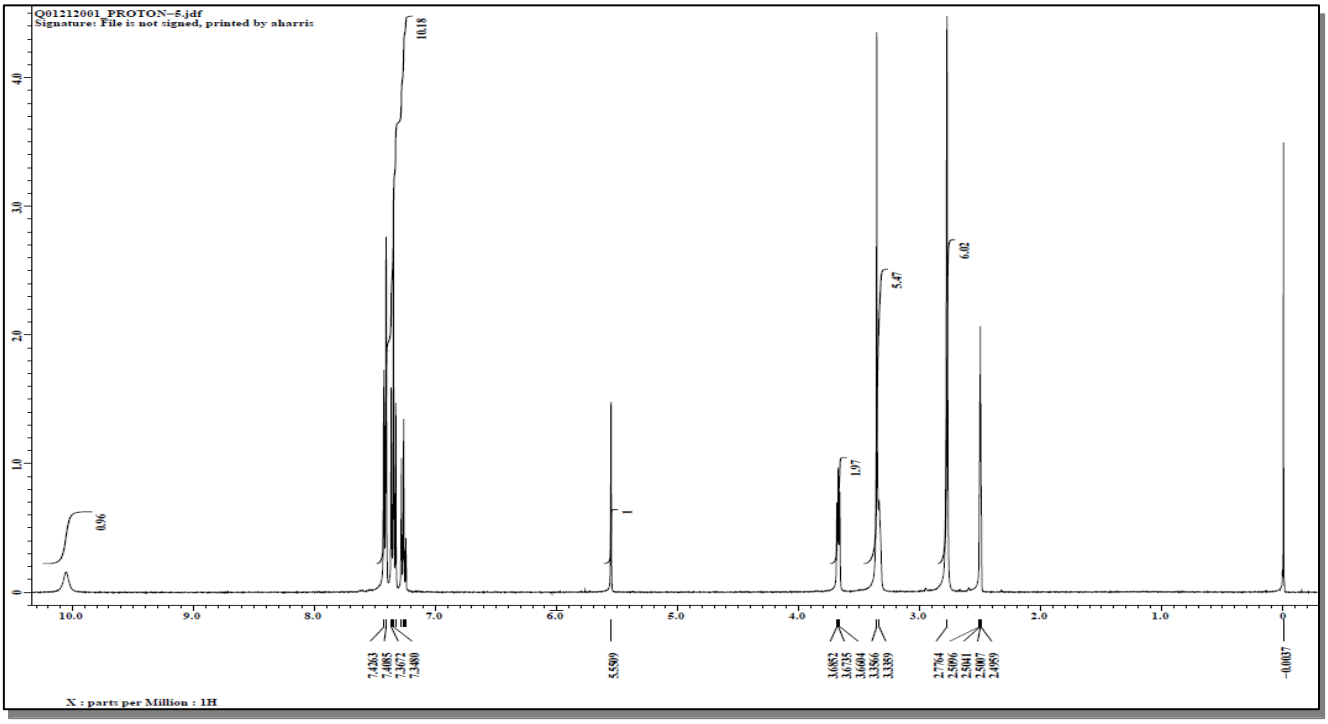
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	PN12191901
Acquired:	January 23, 2020

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

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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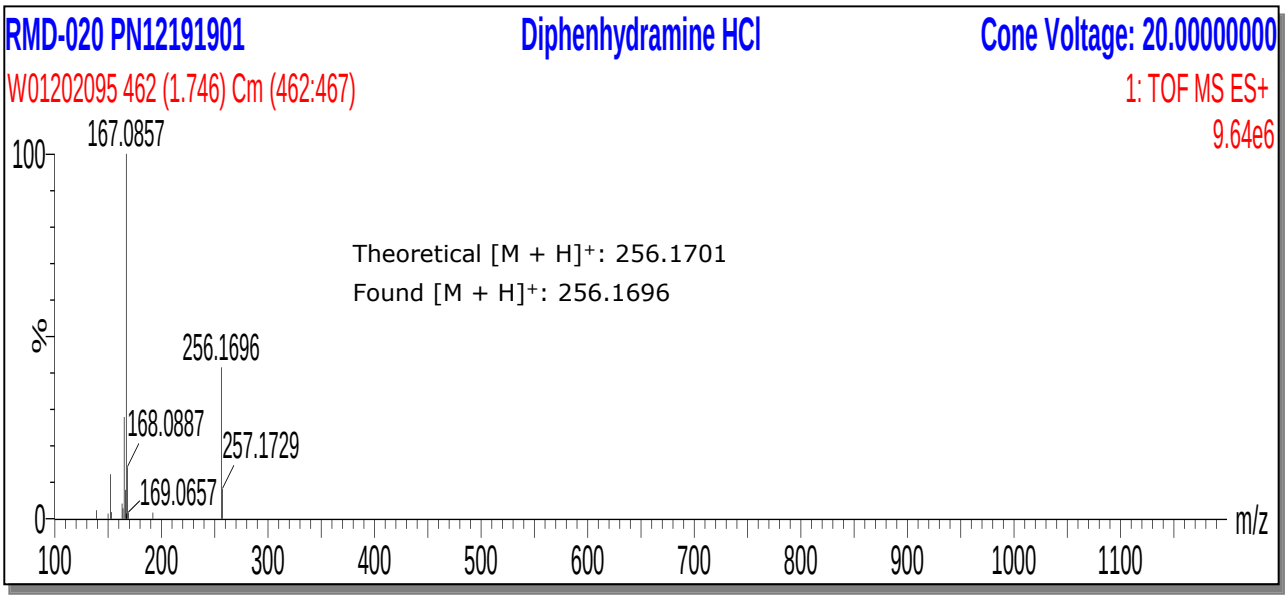
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 20, 2020

Time (min)	% A	% B
0.0	80	20
0.5	80	20
4.0	20	80
5.8	20	80
6.0	80	20
8.0	80	20



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 06, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

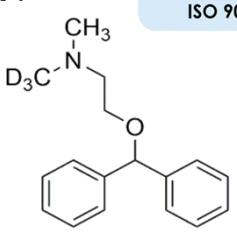
Certified Reference Material - Certificate of Analysis

Diphenhydramine-D_3, Primary Measurement Standard

2-(Diphenylmethoxy)-N-methyl-N-(trideuteromethyl)ethylamine

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: D-187-1ML
Lot No.: FN04082007
Description of CRM: Diphenhydramine-D_3 in Methanol (Solution)
Expiration Date: April 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{18}D_3NO$
CAS No.: 170082-18-5



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Diphenhydramine-D_3	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability“ on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See “Details about certification process” on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 06, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

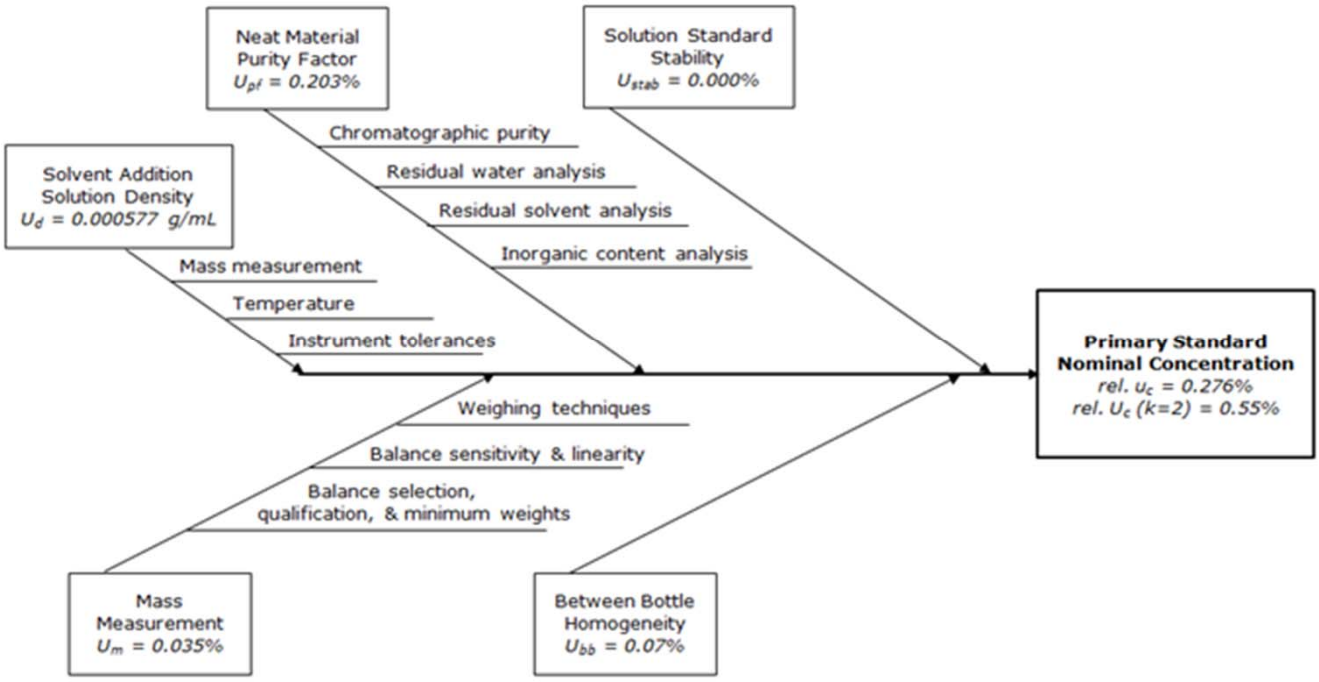
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
		Linearity (r) :	1.000
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (40:60)		
Flow Rate:	1.2 mL/min		
Wavelength:	220 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN04082007	1.000	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Diphenhydramine-D_3	**Chemical Formula:**	$C_{17}H_{18}D_3NO$
Material Lot:	FN10041909	**CAS Number:**	170082-18-5
		Molecular Weight:	258.37

Material Characterization Summary

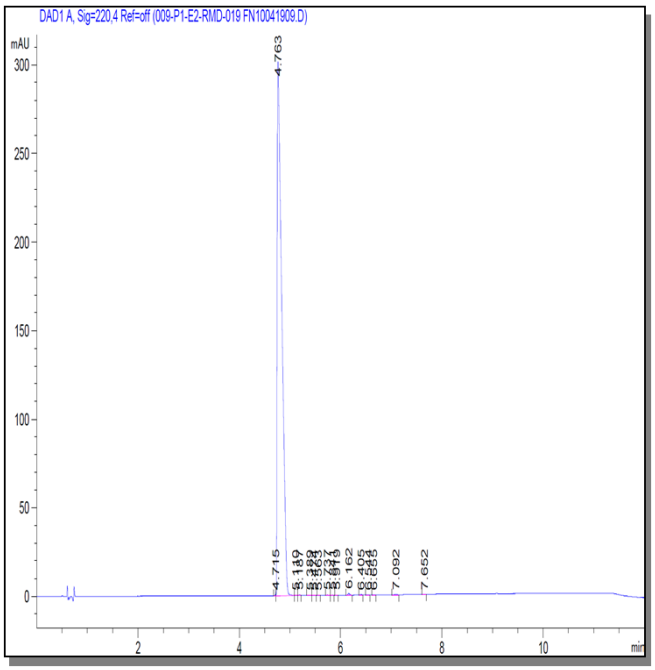
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.6%	
Secondary Chromatographic Purity by LC/MS Analysis	20384217	> 99.9%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.01% D_0 vs D_3	
		0.01% D_0	2.95% D_2
		0.04% D_1	97.01% D_3
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	Below Quantitation Limit	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	0.16%	
Mass Balance Purity Factor		99.40%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	10	90
8.0	75	25
10.0	75	25
10.1	10	90

Flow Rate: 0.7 mL/min

Wavelength: 220 nm

Sample Name: FN10041909

Acquired: March 05, 2020

Peak #	Ret Time	Area %
1	4.72	0.04
2	4.76	99.59
3	5.11	0.02
4	5.19	0.03
5	5.39	0.01
6	5.47	0.02
7	5.56	0.01
8	5.74	0.02
9	5.84	0.01
10	5.92	0.01
11	6.16	0.12
12	6.41	0.04
13	6.54	0.02
14	6.66	0.01
15	7.09	0.04
16	7.65	0.01

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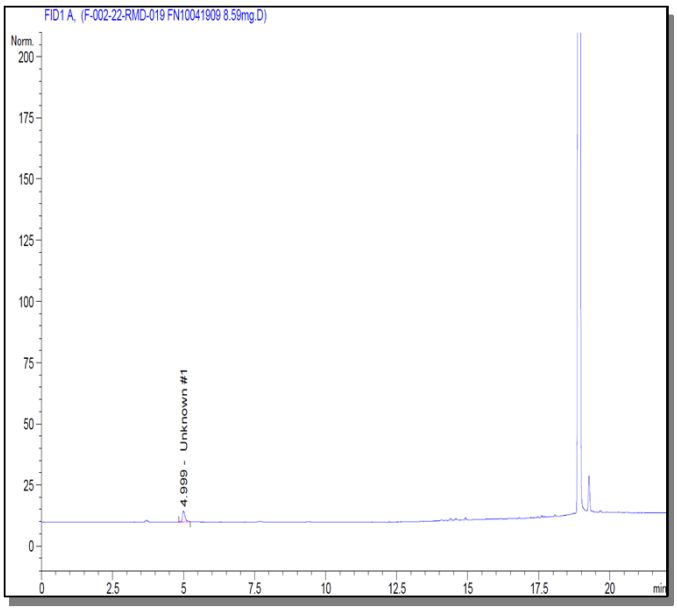
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



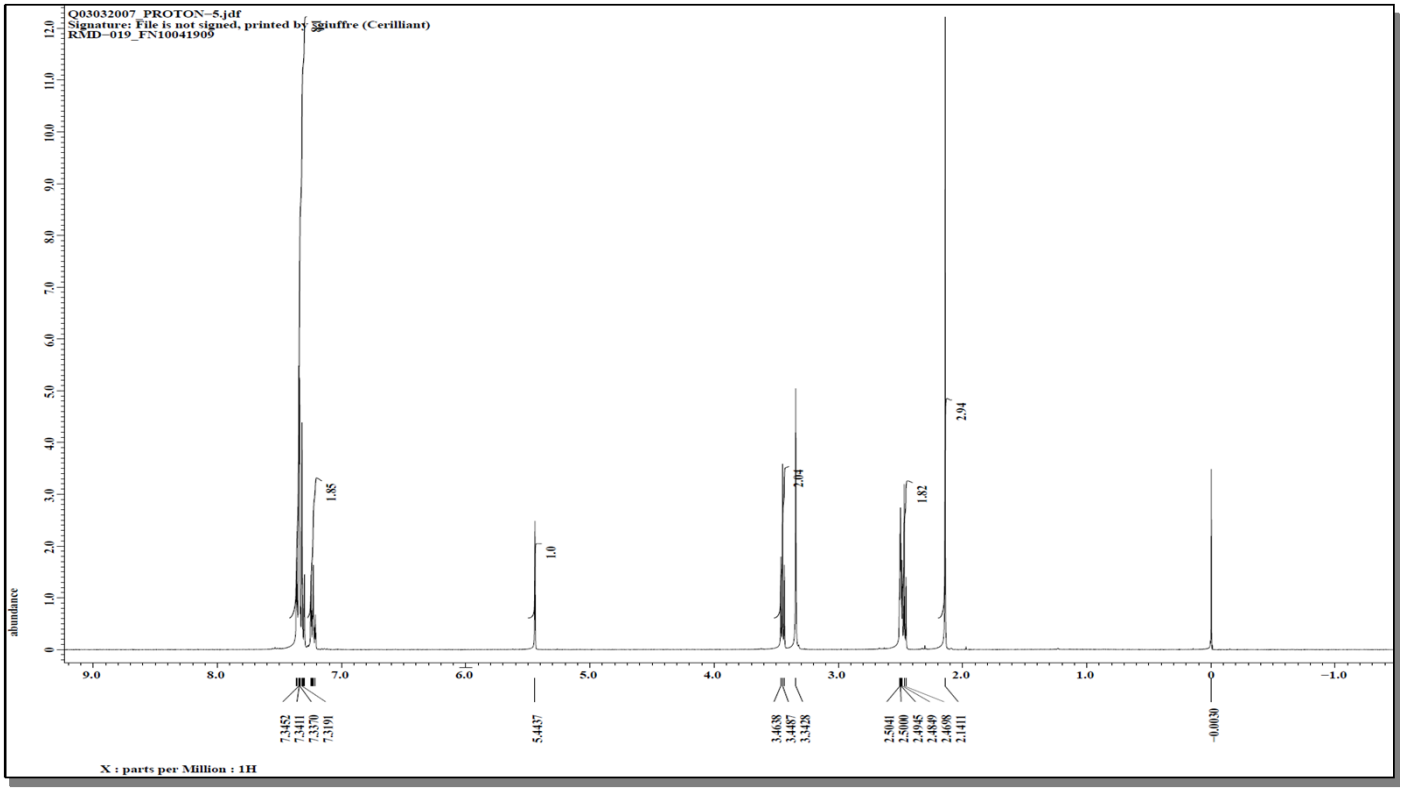
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FN10041909
Acquired:	March 04, 2020

Peak	Compound	Area	Weight %
1	Unknown #1	29.28	BQL
2	NMP	NA	NA
Total			**BQL**

BQL - Below Quantitation Limit

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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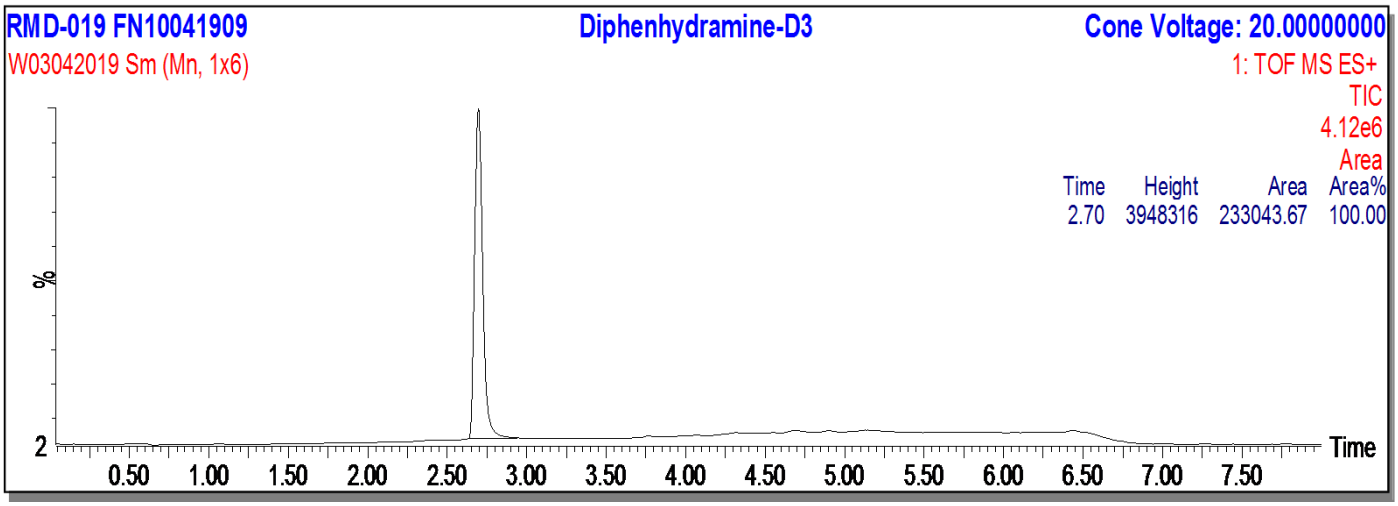
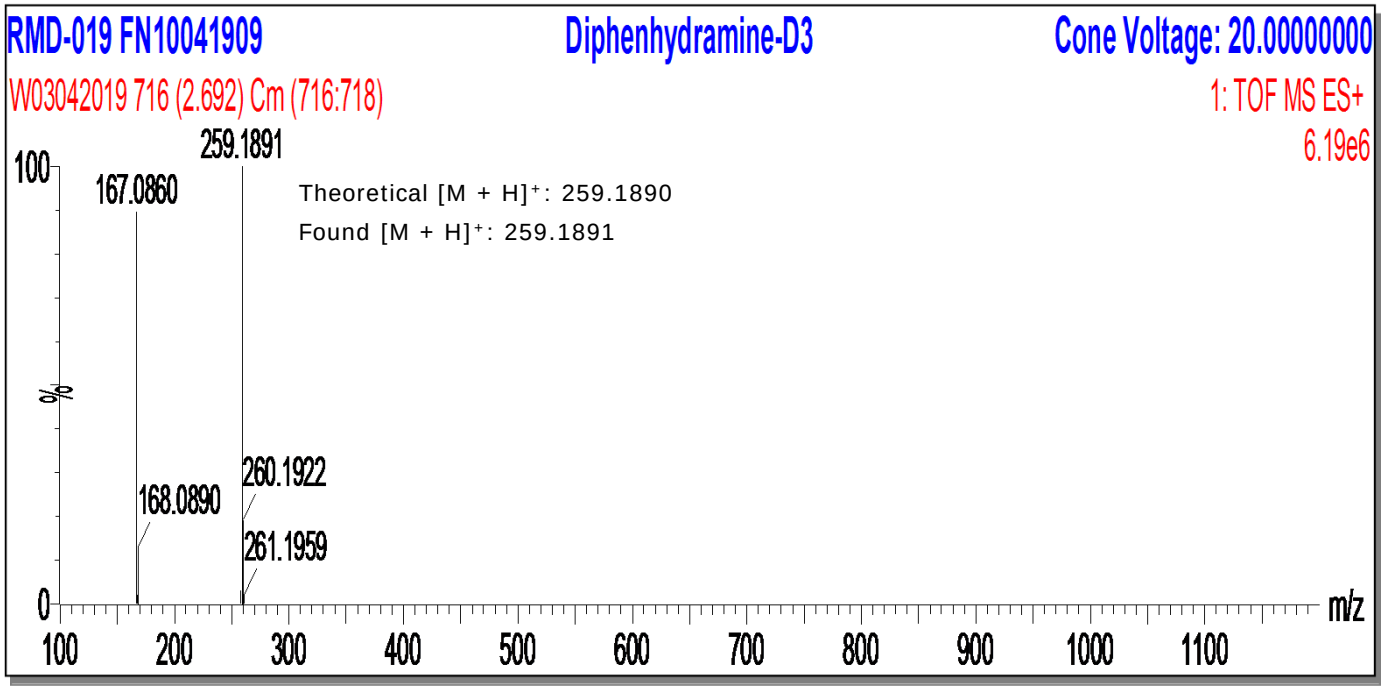
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 04, 2020

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10





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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

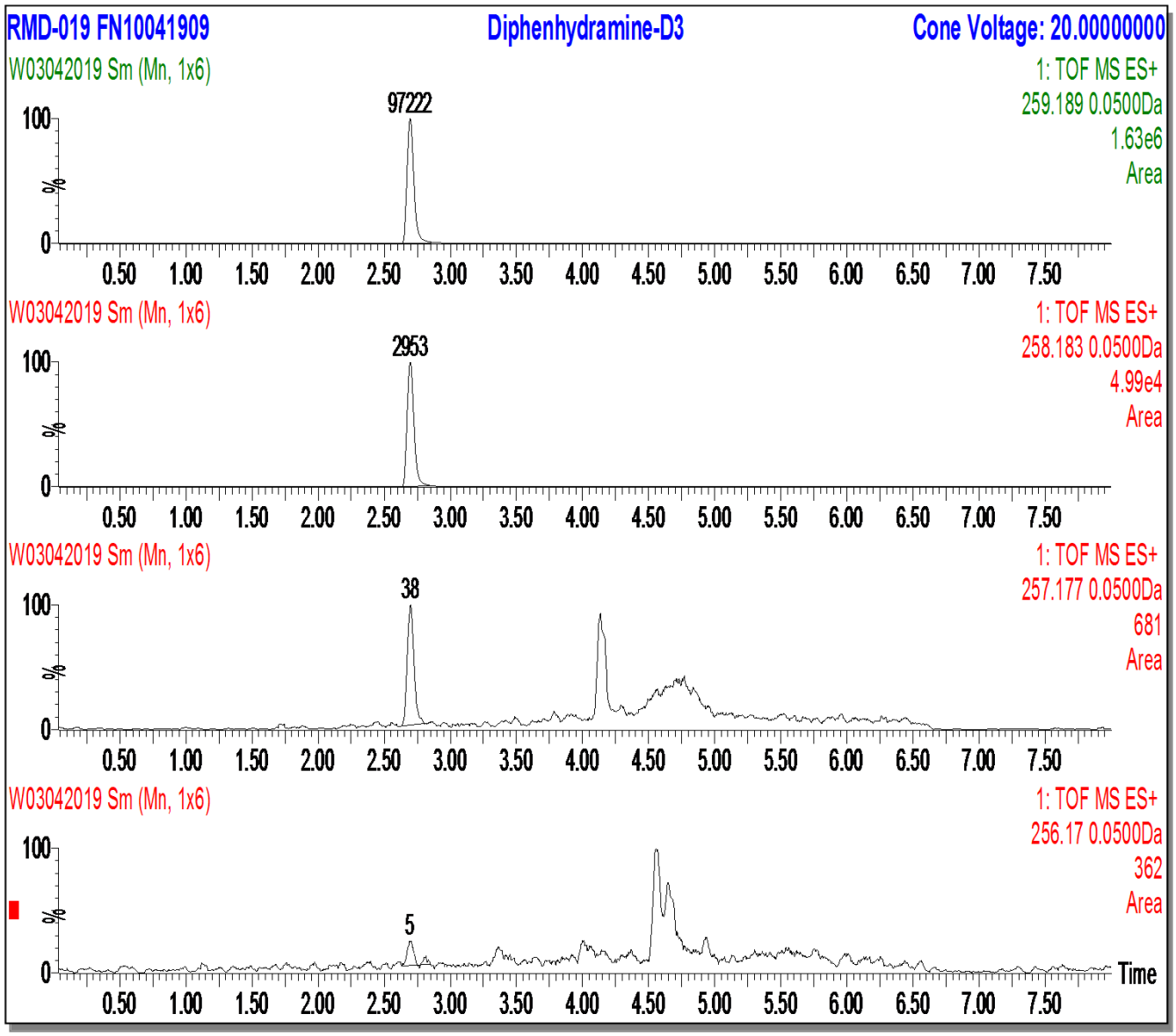
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 256-259 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: March 04, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 06, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

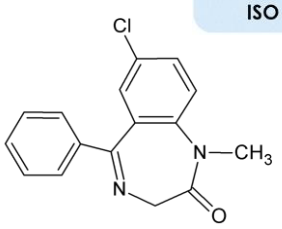
Certified Reference Material - Certificate of Analysis

Diazepam, Primary Measurement Standard

7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: D-907-1ML
Lot No.: FE02142004
Description of CRM: Diazepam in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{16}H_{13}ClN_2O$
CAS No.: 439-14-5
Regulatory: USDEA Exempt | Canadian TK # 61-1156



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Diazepam	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

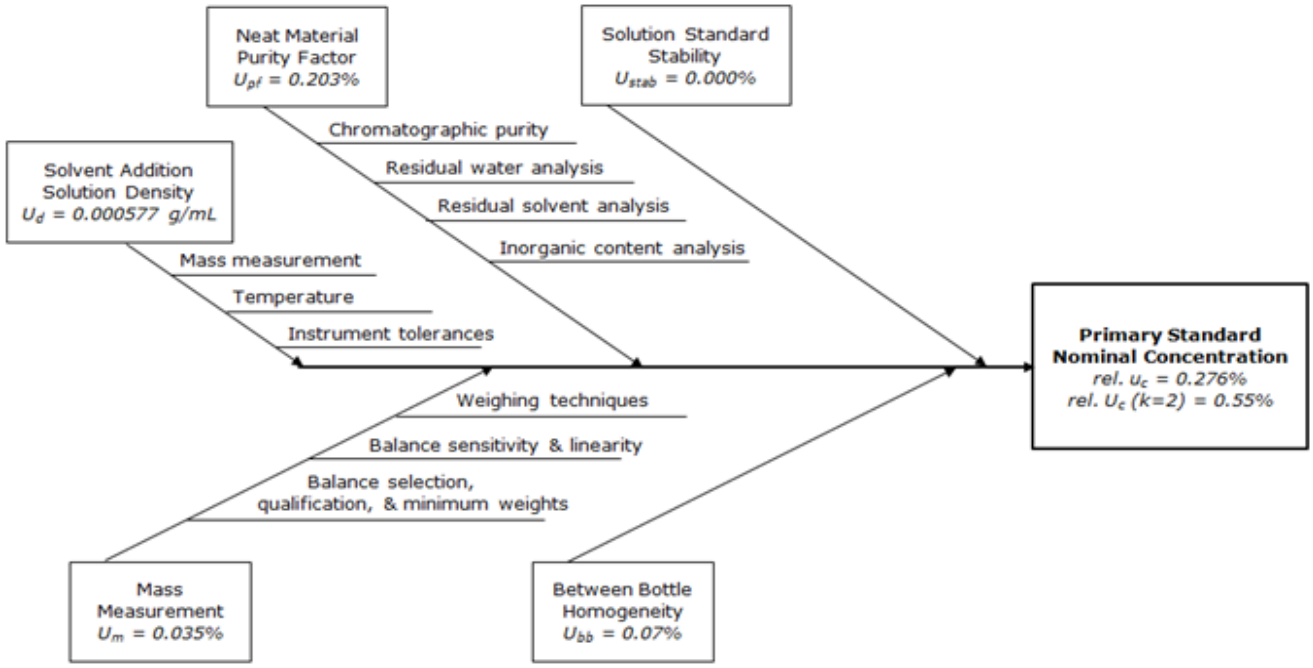
March 11, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:Water (50:50)	**Linearity (r) :**	1.000
Flow Rate:	1.0 mL/min		
Wavelength:	238 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02142004	1.004	0.7
Previous Lot	FE05201602	1.006	1.0

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Diazepam	**Chemical Formula:**	$C_{16}H_{13}ClN_2O$
Material Lot:	PC10141901	**CAS Number:**	439-14-5
		Molecular Weight:	284.74

Material Characterization Summary

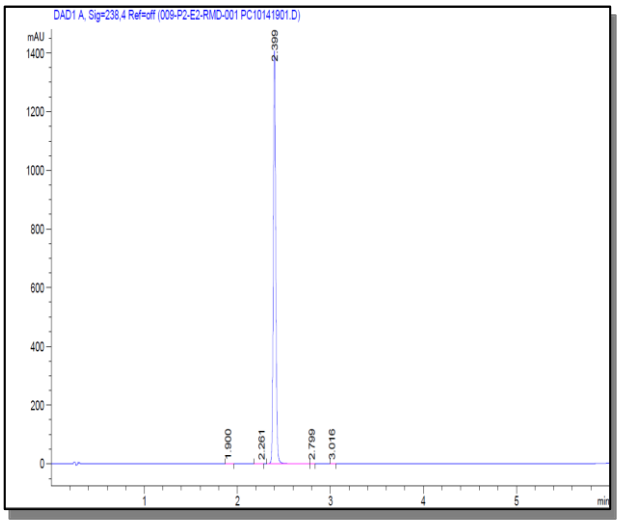
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	> 99.9%
Secondary Chromatographic Purity by GC/FID Analysis	20384346	> 99.9%
Identity by LC/MS Analysis	20384217	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Not Detected
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.99%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: Acetonitrile
B: Water
Gradient:

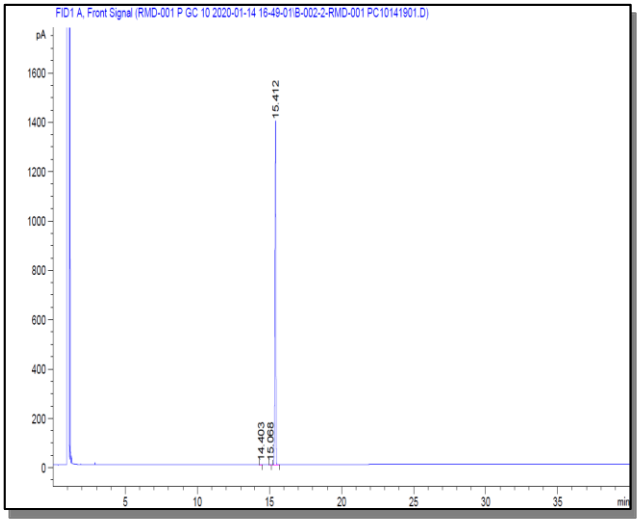
Time (min)	% A	% B
0.0	30	70
4.0	85	15
5.0	85	15
5.1	30	70

Flow Rate: 0.8 mL/min
Wavelength: 238 nm

Sample Name: PC10141901
Acquired: January 07, 2020

Peak #	Ret Time	Area %
1	1.90	0.00
2	2.26	0.00
3	2.40	99.99
4	2.80	0.00
5	3.02	0.00

GC/FID



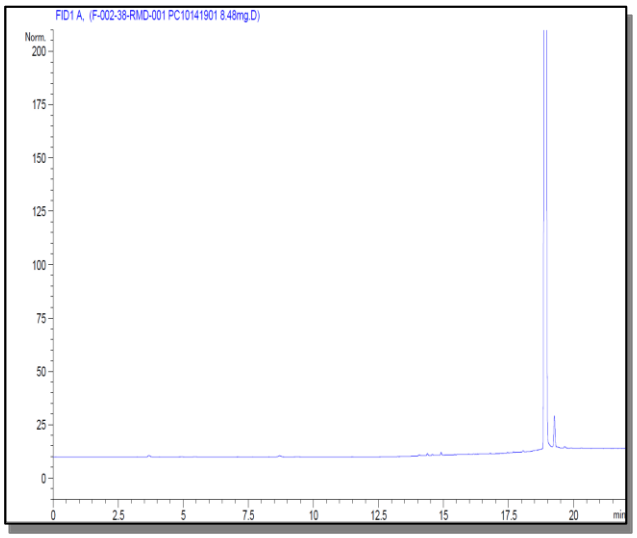
Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 300°C at 5°C/min
hold 16 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: PC10141901
Acquired: January 14, 2020

Peak #	Ret Time	Area %
1	14.40	0.01
2	15.07	0.01
3	15.41	99.98

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



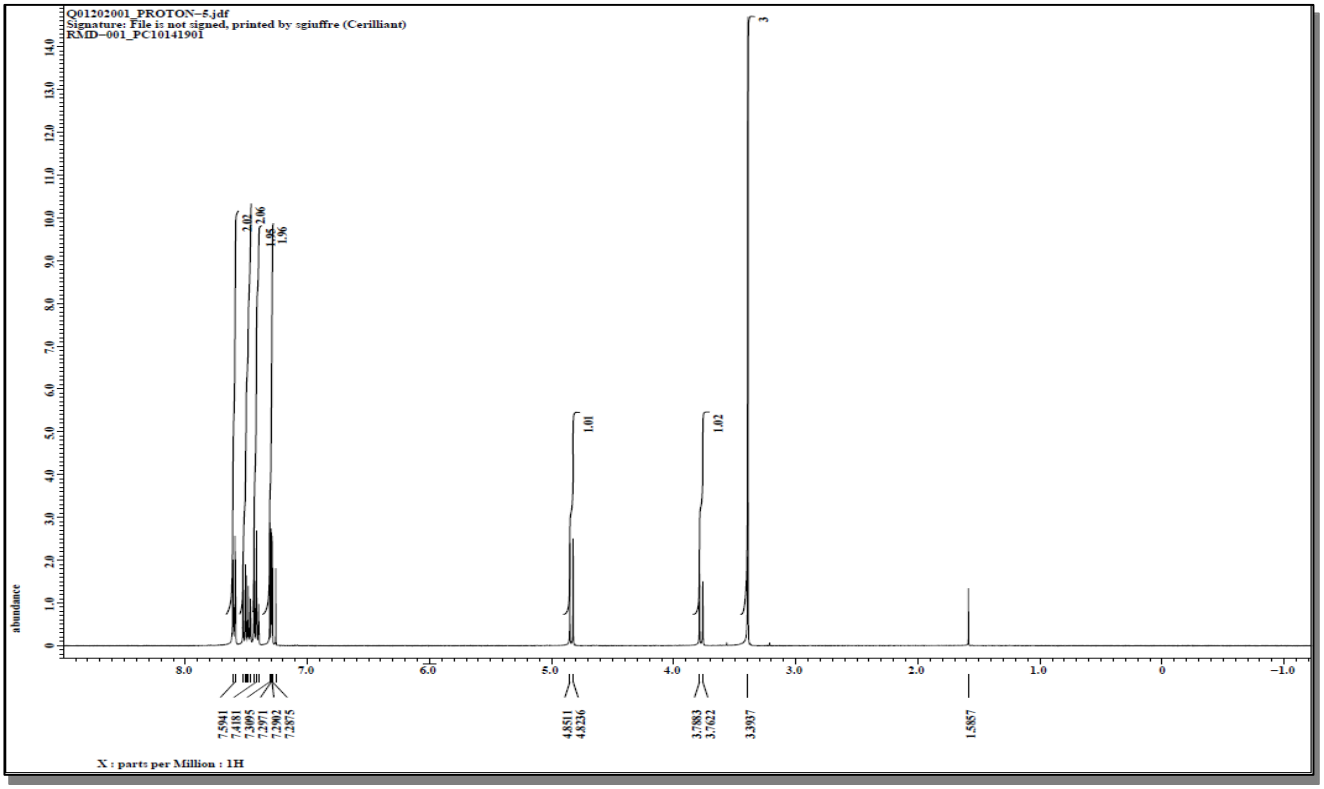
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	PC10141901
Acquired:	January 07, 2020

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

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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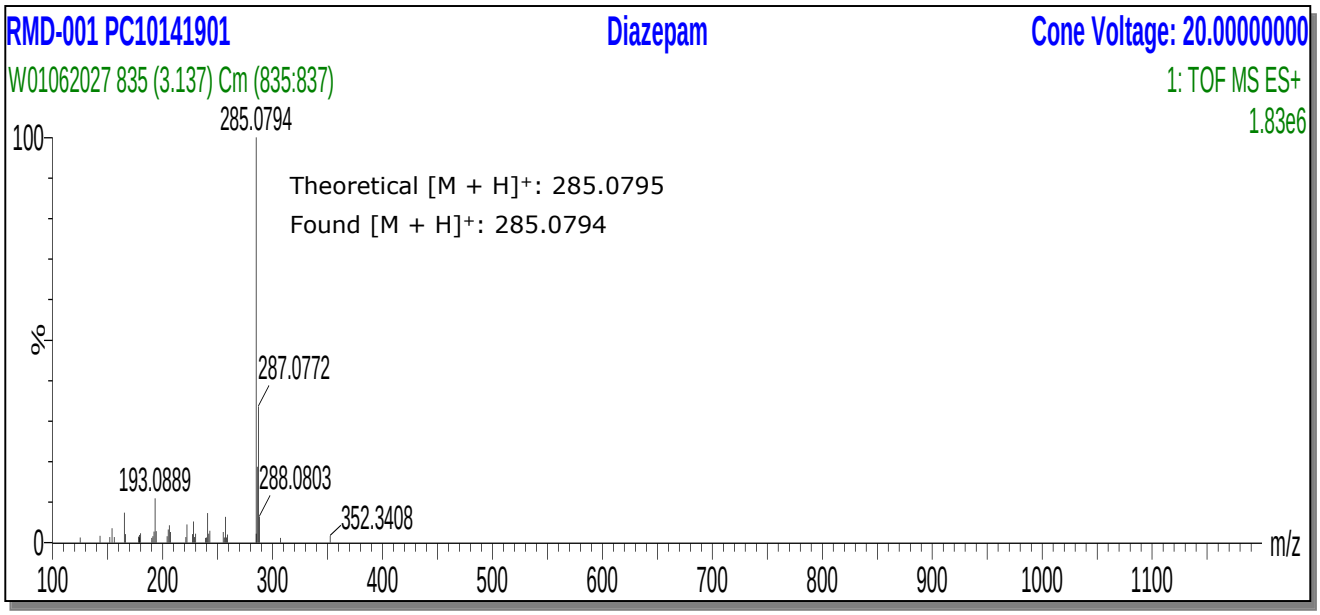
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 06, 2020

Time (min)	% A	% B
0.0	80	2
0.5	80	2
4.0	20	30
5.8	20	30
6.0	80	2
8.0	80	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (D-902, Diazepam-D_5) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 11, 2020	Initial version.

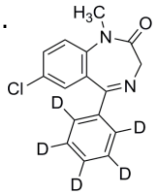
Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Certified Reference Material - Certificate of Analysis

Diazepam-D_5, Primary Measurement Standard

7-Chloro-1,3-dihydro-1-methyl-5-(pentyl-2,3,4,5,6-d $_5$)-2H-1,4-benzodiazepin-2-one

Product No.: D-910-1ML
Lot No.: FE01142012
Description of CRM: Diazepam-D_5 in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{16}H_8D_5ClN_2O$
CAS No.: 65854-76-4
Regulatory: USDEA Exempt | Canadian TK # 61-1157



Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Diazepam-D_5	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

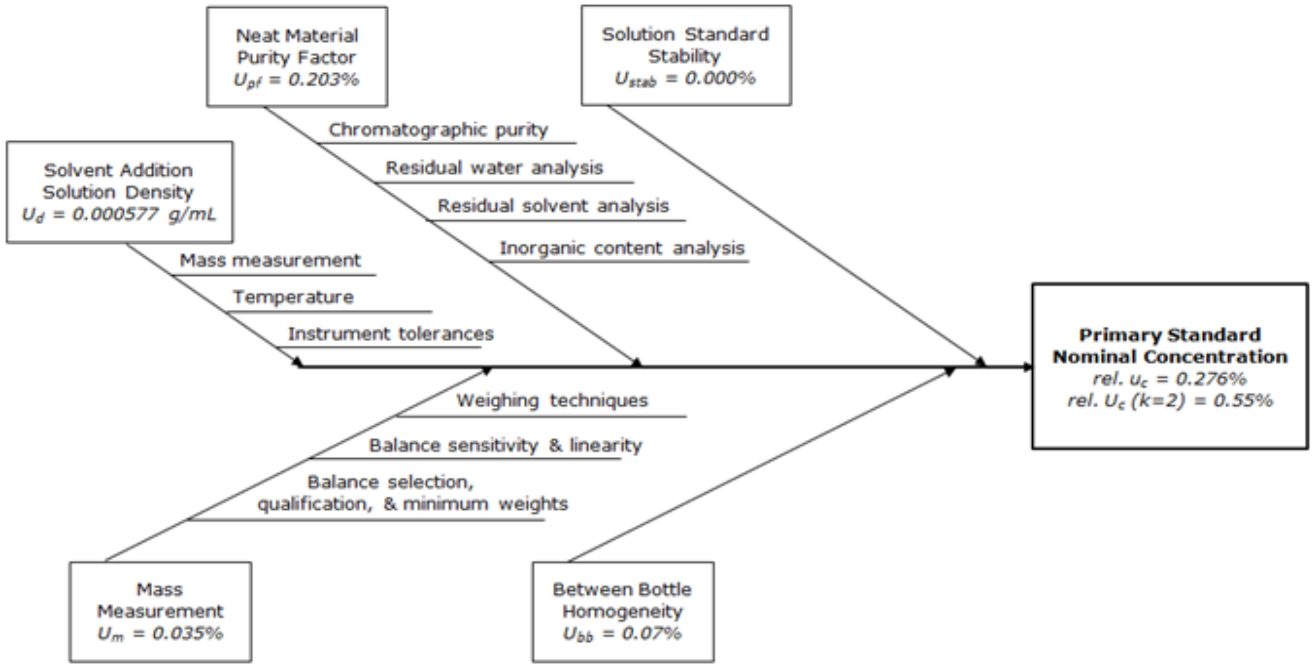
February 25, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters

Analysis Method: HPLC/UV

Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

Mobile Phase: A: Acetonitrile
B: Water

Gradient:

Time (min)	% A	% B
0.00	30	70
4.50	70	30
5.50	70	30
5.51	30	70
8.00	30	70

Flow Rate: 0.8 mL/min

Wavelength: 238 nm

Calibration Curve

Calibration Curve: Linear Regression

Number of Points: 4

Linearity (r) : 1.000

		Verified Concentration (mg/mL)	%RSD - Homogeneity
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01142012	0.998	2.0
Previous Lot	FE08011803	1.009	2.1

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Diazepam-D_5	**Chemical Formula:**	$C_{16}H_8D_5ClN_2O$
Material Lot:	FC02201702	**CAS Number:**	65854-76-4
		Molecular Weight:	289.77

Material Characterization Summary

Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.6% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%	
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_6	
		0.00% D_0 to D_2	95.75% D_5
		0.01% D_3	0.40% D_6
		1.57% D_4	2.28% D_7
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	0.40%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Not Detected	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.18%	

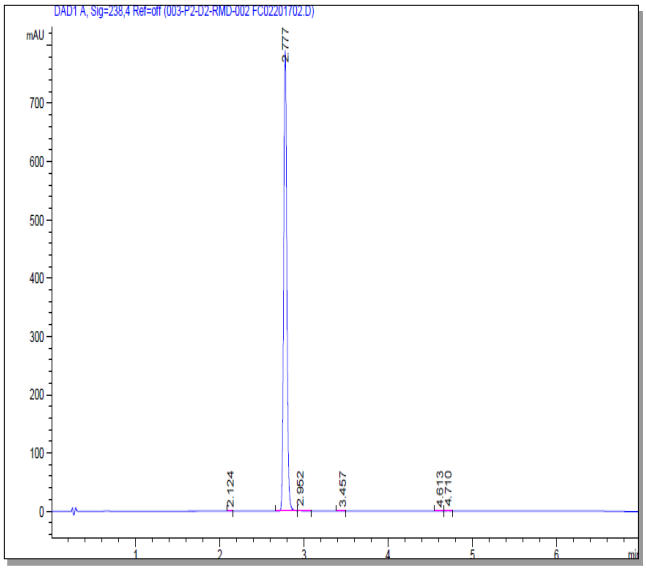
[1] 0.01% Nordiazepam-D5 detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: Acetonitrile
B: Water
Gradient:

Time (min)	% A	% B
0.00	30	70
4.50	70	30
5.50	70	30
5.51	30	70

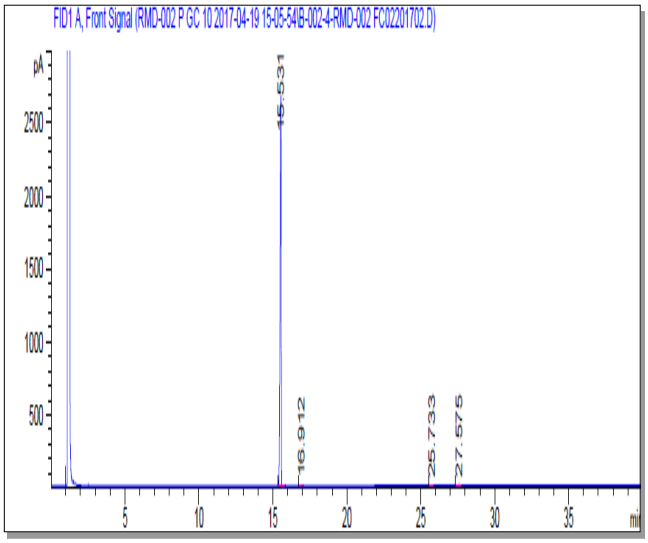
Flow Rate: 0.8 mL/min
Wavelength: 238 nm

Sample Name: FC02201702
Acquired: May 01, 2017

Peak #	Ret Time	Area %
1	2.12	0.01
2	2.78	99.68
3	2.95	0.17
4	3.46	0.01
5	4.61	0.06
6	4.71	0.08

Peak 1 identified as Nordiazepam-D_5

GC/FID



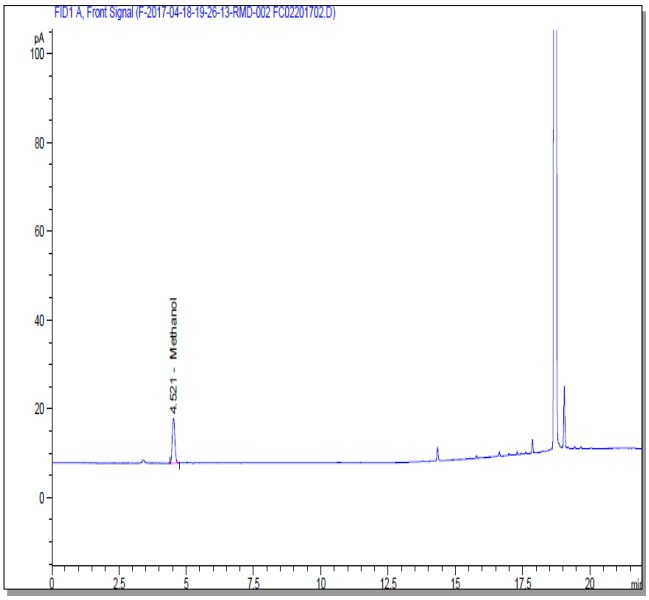
Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 300°C at 5°C/min
hold 16 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC02201702
Acquired: April 19, 2017

Peak #	Ret Time	Area %
1	15.53	99.78
2	16.91	0.08
3	25.73	0.05
4	27.58	0.09

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

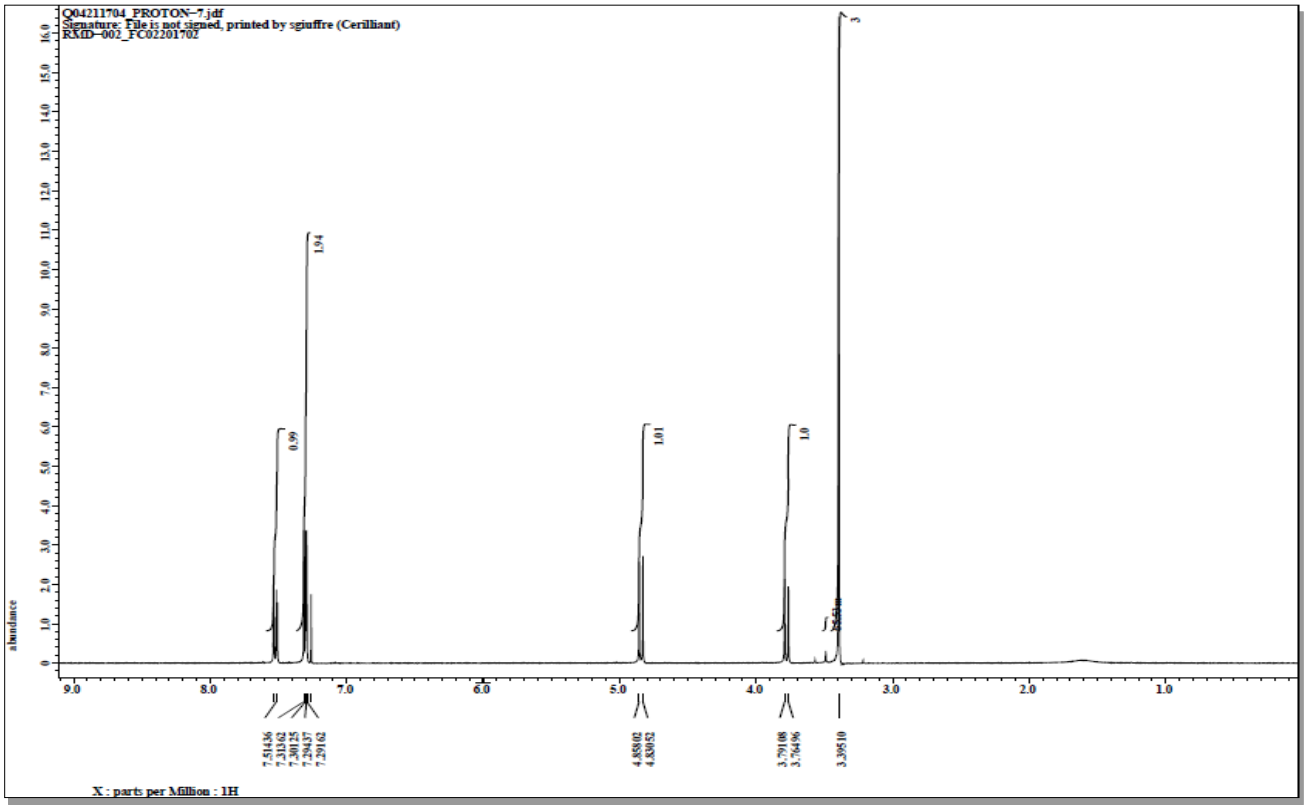


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC02201702
Acquired:	April 18, 2017

Peak	Compound	Area	Weight %
1	Methanol	67.92	0.40
2	NMP	NA	NA
Total			**0.40**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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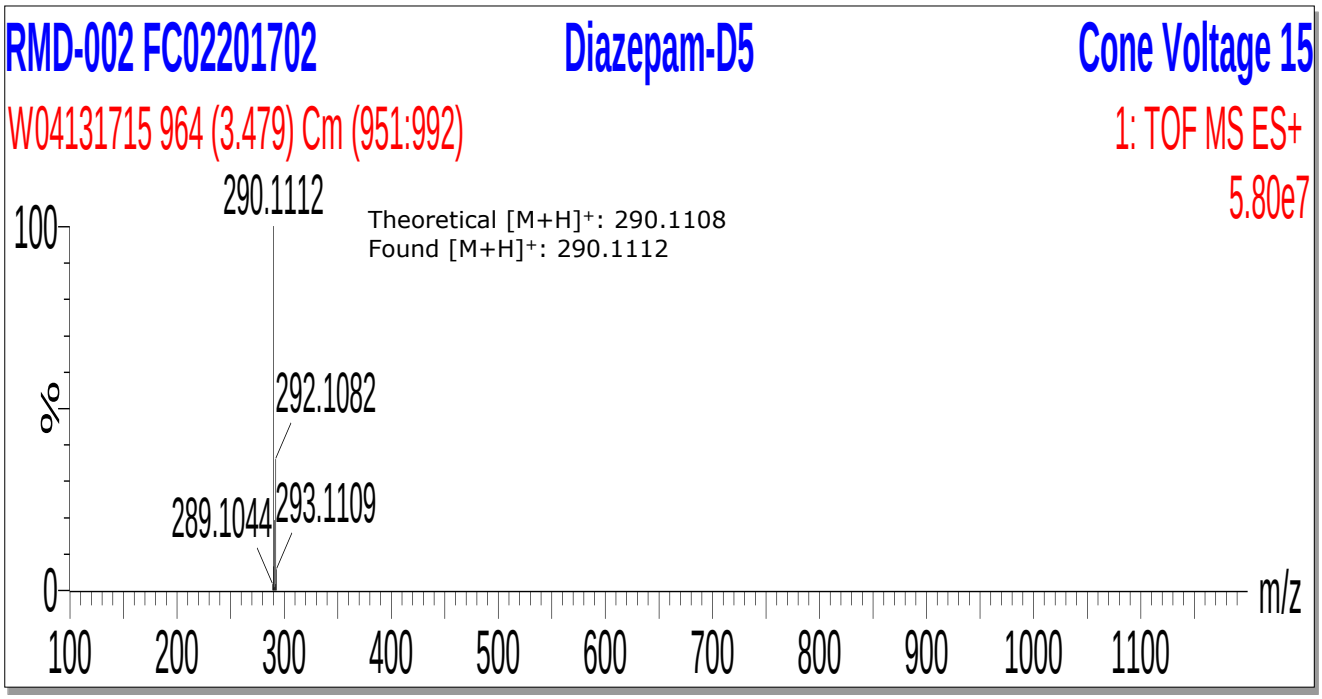
Spectral and Physical Data (cont.)

LC/MS

Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: 0.1% Formic acid in Water
B: Acetonitrile

0.0	70	30
5.0	40	60
6.0	40	60
6.1	70	30
8.0	70	30

Flow Rate: 0.4 mL/min
Scan Range: 100 - 1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: April 13, 2017



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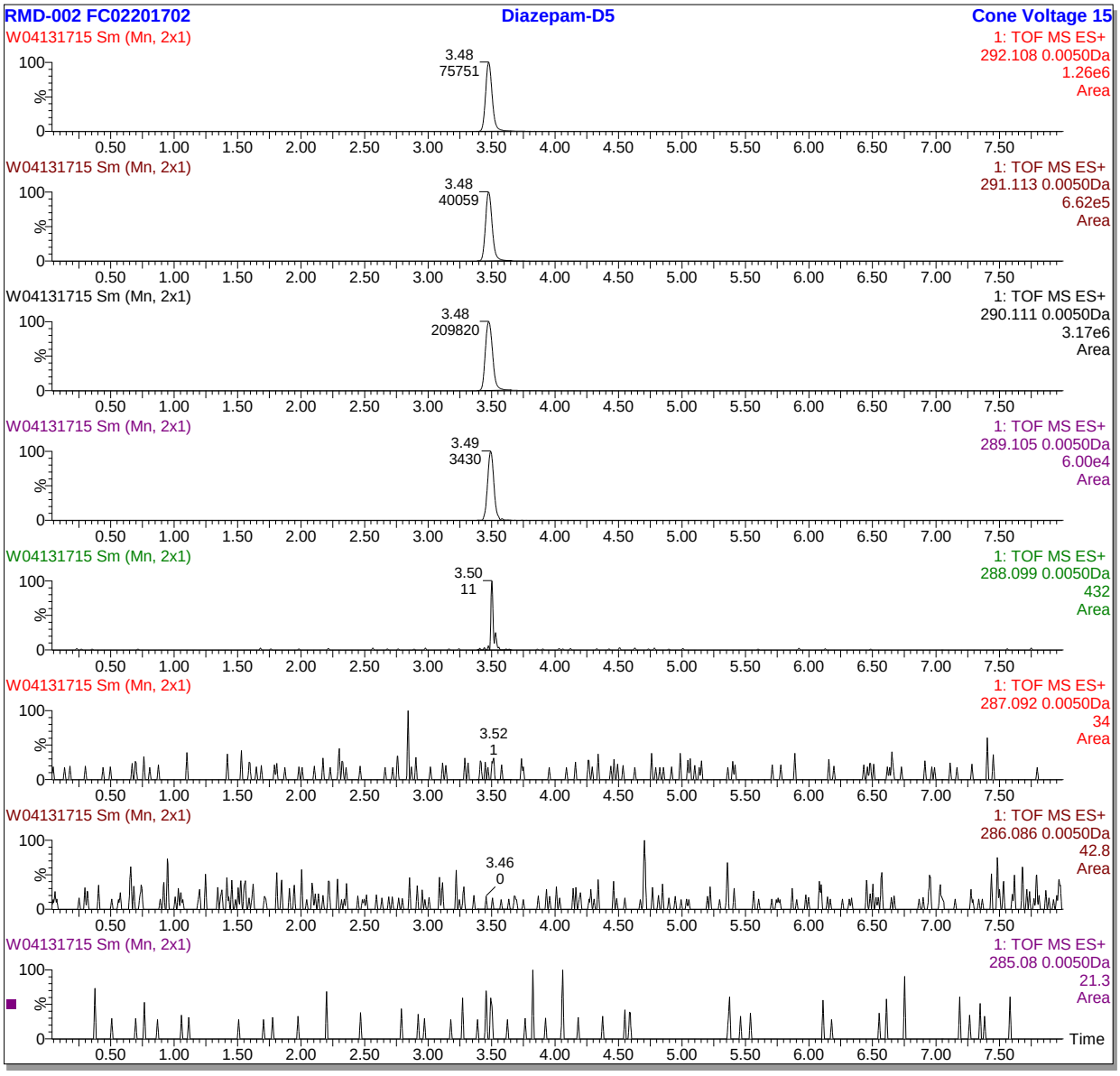
Spectral and Physical Data (cont.)

Isotopic Purity and Distribution by LC/MS

Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: 0.1% Formic acid in Water
B: Acetonitrile

0.0	70	30
5.0	40	60
6.0	40	60
6.1	70	30
8.0	70	30

Flow Rate: 0.4 mL/min
Scan Range: 285 - 292 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: April 13, 2017



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 25, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

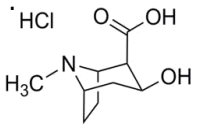
Certified Reference Material - Certificate of Analysis

Ecgonine, Primary Measurement Standard

[1R-(exo,exo)]-3-hydroxy-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid hydrochloride

Product No.: E-004-1ML
Lot No.: FE03232001
Description of CRM: Ecgonine HCl in Methanol (Solution)
Nominal concentration is adjusted for HCl content.
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_9H_{15}NO_3 \bullet HCl$
CAS No.: 5796-31-6
Regulatory: USDEA Exempt | Canadian TK # 61-1165

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Ecgonine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
Nominal concentration is adjusted for HCl content. No adjustment required before use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darren Ellsworth, Quality Assurance Manager

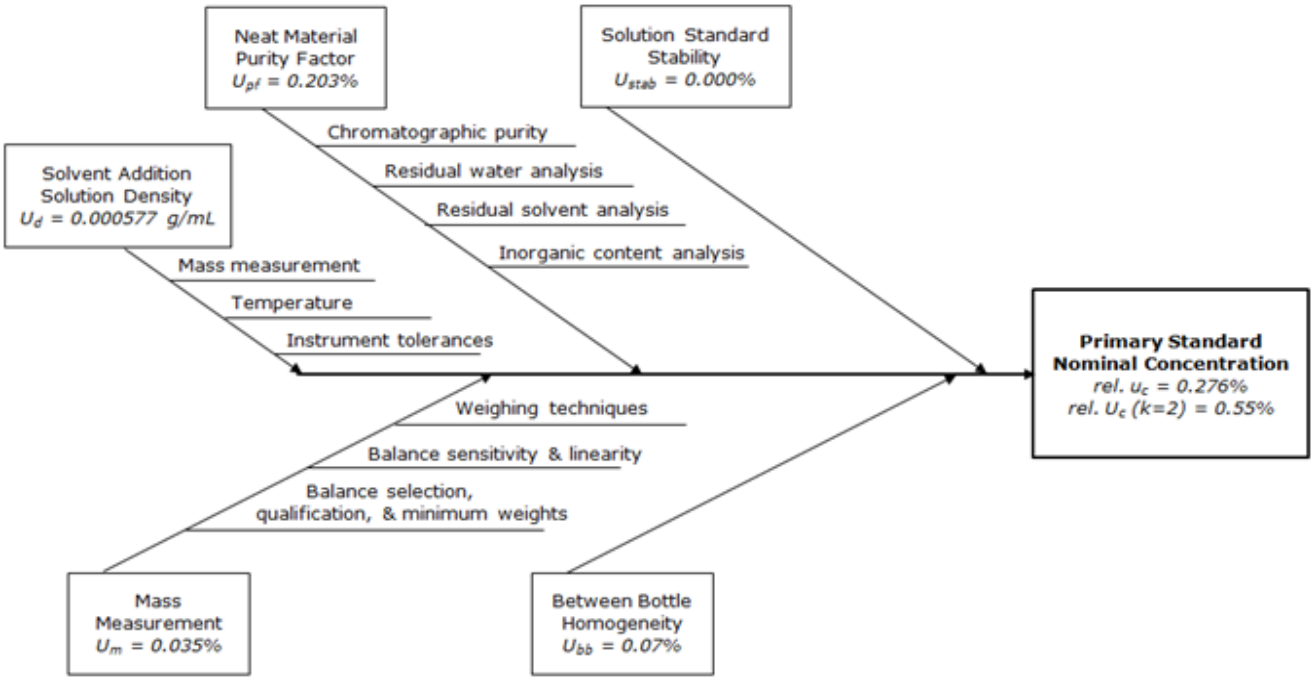
May 06, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	LC/MS	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express F5, 3 µm, 2.7 x 100 mm	**Number of Points:**	4
Mobile Phase:	0.1% Formic acid in Water:Acetonitrile (99:1)	**Linearity (r) :**	0.998
Flow Rate:	0.4 mL/min		
Polarity:	MRM, Positive Ion		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03232001	0.985	0.5
Previous Lot	FE01221901	0.998	1.4

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Ecgonine HCl	**Molecular Weight (base):**	185.22
Material Lot:	FC10141904	**Molecular Weight (salt):**	221.68
Chemical Formula:	$C_9H_{15}NO_3$ • HCl	**Salt Adjustment:**	1.197
CAS Number:	5796-31-6		

Material Characterization Summary

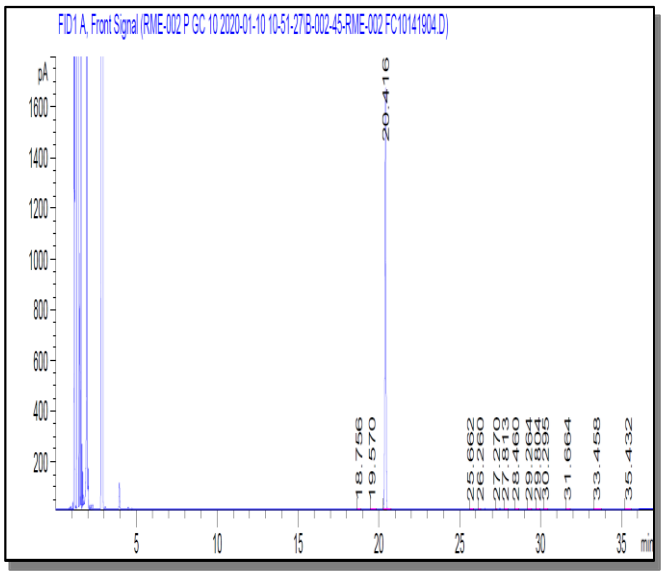
Analytical Test	Method	Results
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%
Secondary Chromatographic Purity by LC/MS Analysis	SP10-0107	> 99.9%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Level
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.76%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

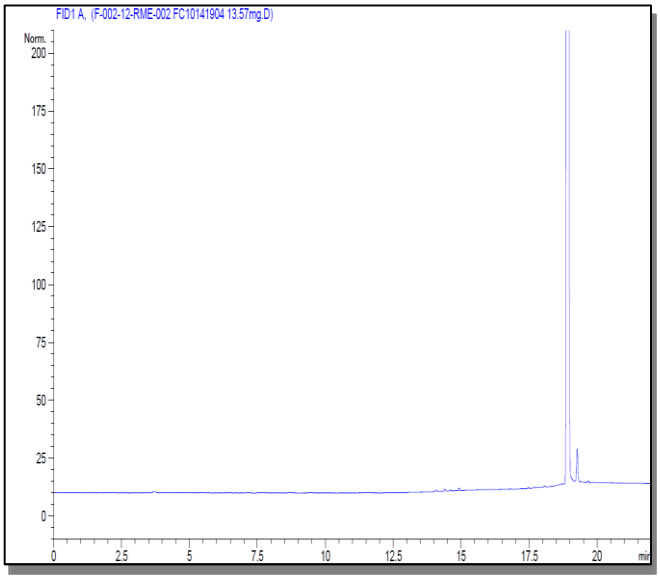
GC/FID



Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 180°C at 40°C/min 180°C to 280°C at 5°C/min hold 5 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC10141904
Acquired:	January 10, 2020

Peak #	Ret Time	Area %
1	18.76	0.02
2	19.57	0.03
3	20.42	99.78
4	25.66	0.03
5	26.26	0.01
6	27.27	0.01
7	27.81	0.02
8	28.46	0.01
9	29.26	0.01
10	29.80	0.02
11	30.30	0.01
12	31.66	0.01
13	33.46	0.02
14	35.43	0.02

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FC10141904
Acquired:	January 16, 2020

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

ND - None Detected

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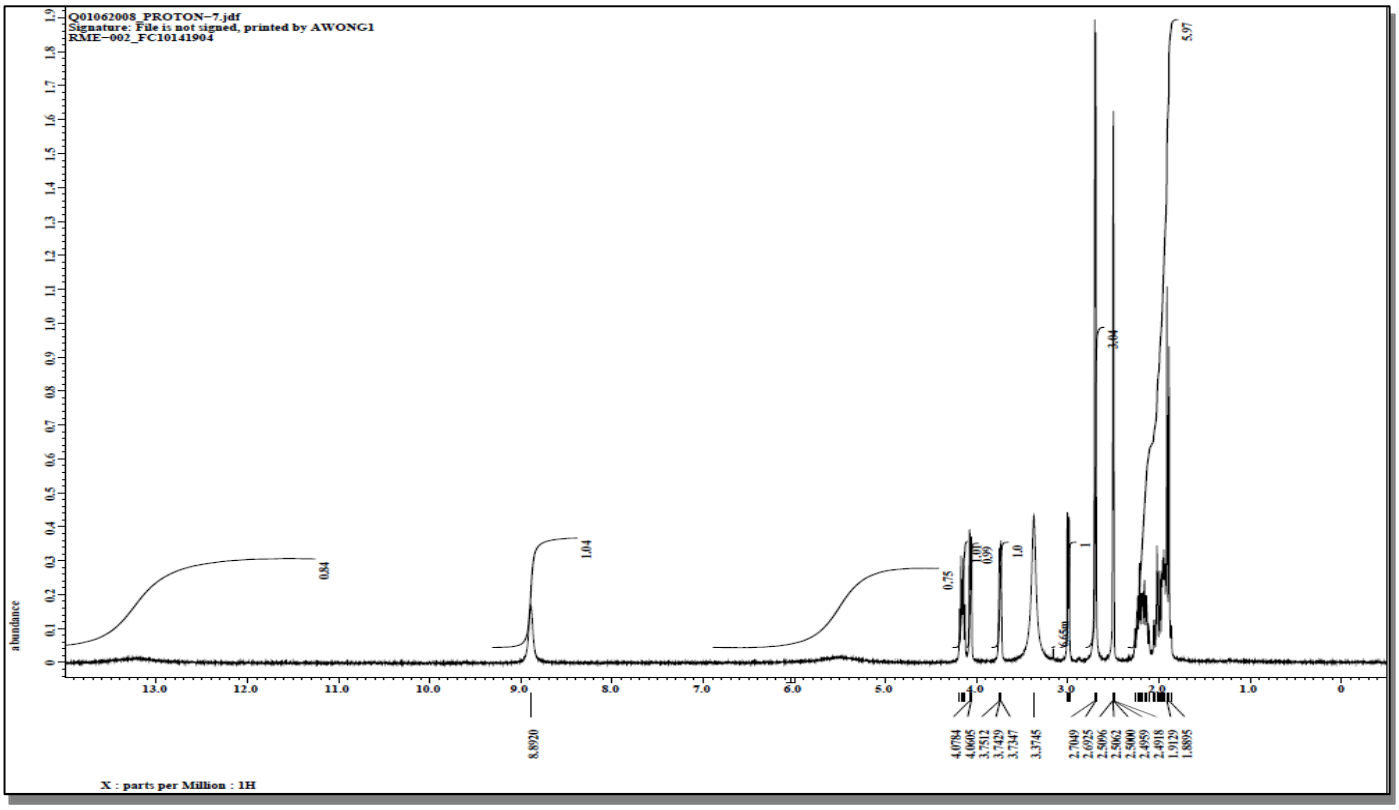
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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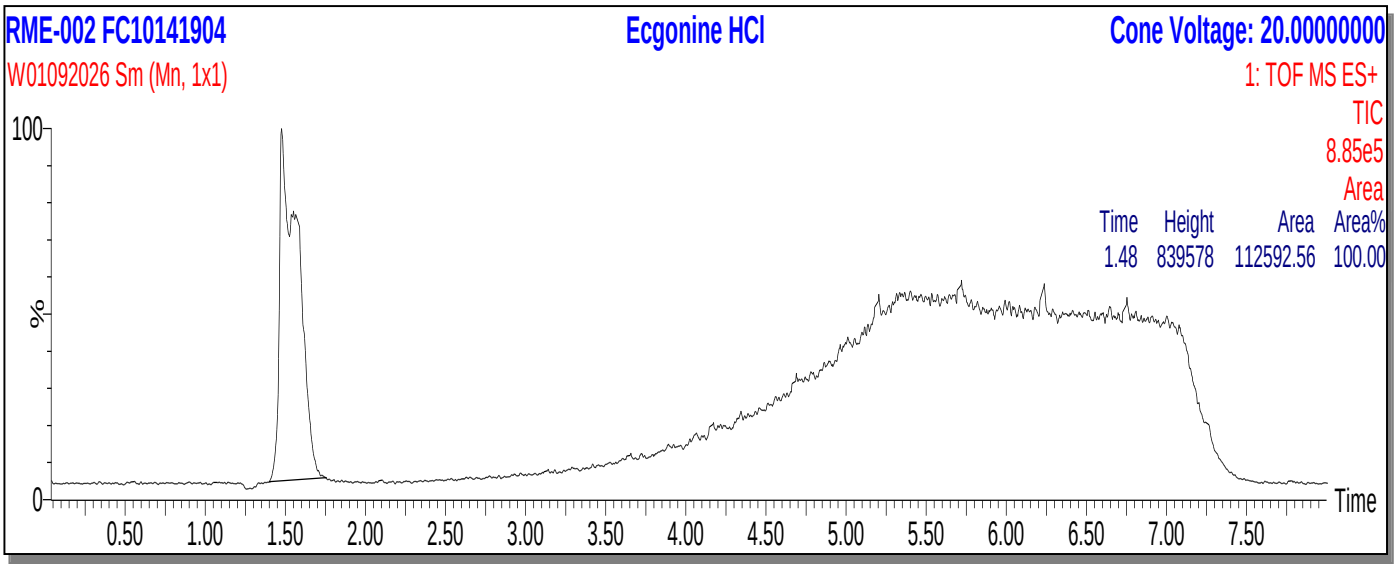
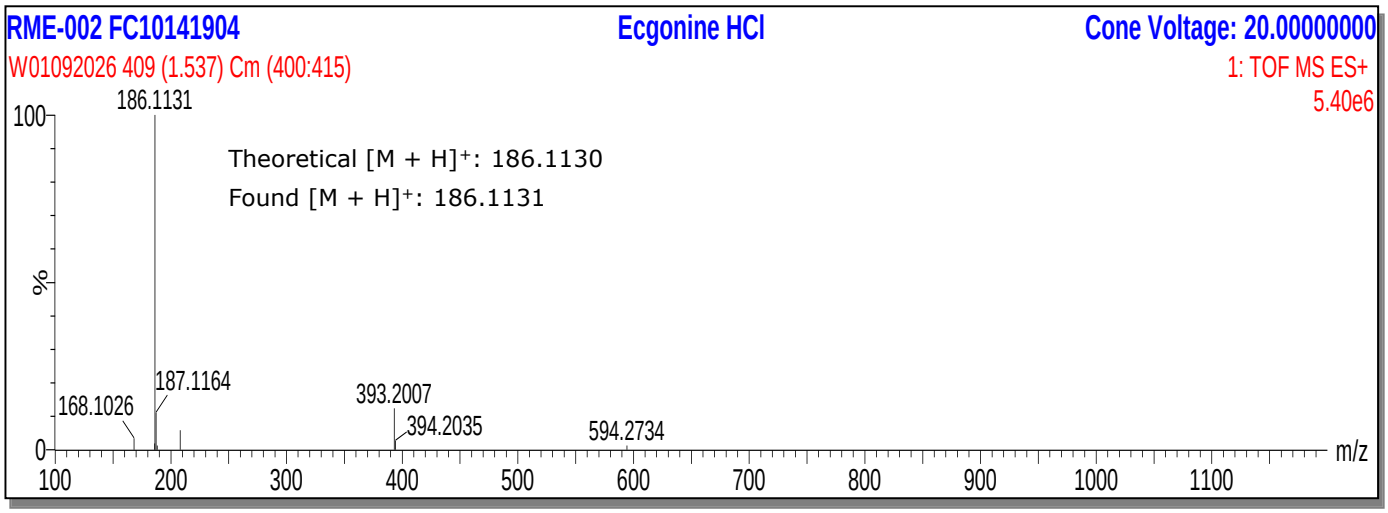
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express F5, 2.7 µm, 3.0 x 100 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 09, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2





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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (E-003, Ecgonine-D_3 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 06, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

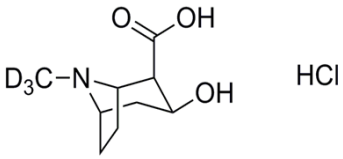
Certified Reference Material - Certificate of Analysis

Ecgonine-D_3, Primary Measurement Standard

[1R-(exo,exo)]-3hydroxy-8-(trideuteromethyl)-8-azabicyclo[3.2.1]octane-2-carboxylic acid hydrochloride

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: E-010-1ML
Lot No.: FE03192003
Description of CRM: Ecgonine-D_3 HCl in Methanol (Solution)
Nominal concentration is adjusted for HCl content.
Retest Date: July 2021 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_9H_{12}D_3NO_3 \bullet HCl$
CAS No.: 115144-41-7
Regulatory: USDEA Exempt



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Ecgonine-D_3	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Nominal concentration is adjusted for HCl content. No adjustment required before use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

June 05, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

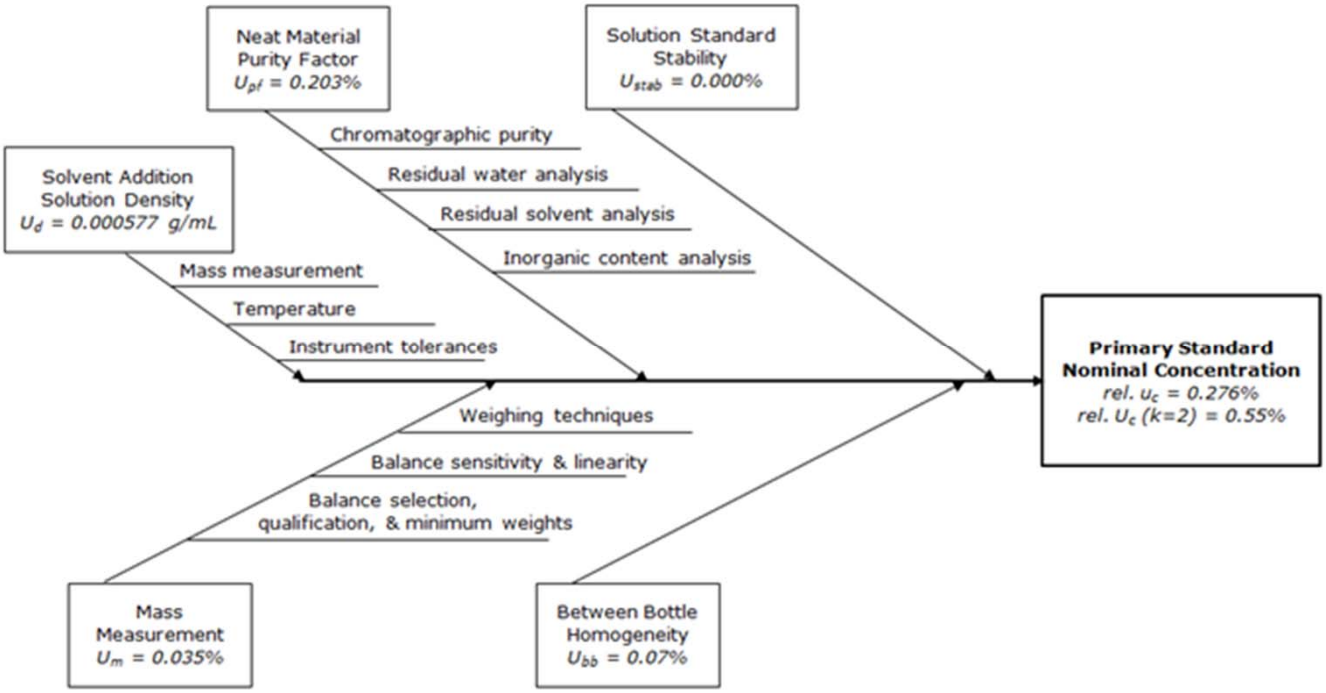
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	LC/MS	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	0.1% Formic acid in Water:Acetonitrile (99:1)	**Linearity (r) :**	1.000
Flow Rate:	0.4 mL/min		
Polarity:	MRM, Positive Ion		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03192003	0.995	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Ecgonine-D_3 HCl	**Molecular Weight (base):**	188.24
Material Lot:	FC12161904	**Molecular Weight (salt):**	224.70
Chemical Formula:	$C_9H_{12}D_3NO_3$ • HCl	**Salt Adjustment:**	1.194
CAS Number:	115144-41-7		

Material Characterization Summary

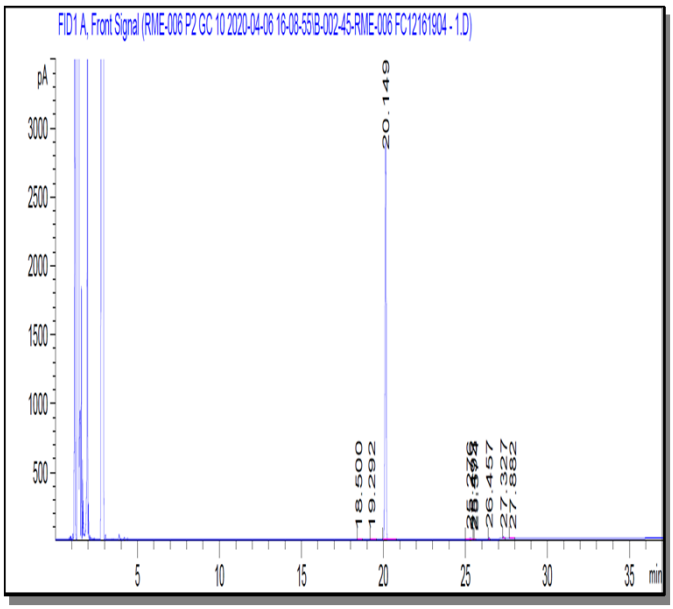
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.4%	
Secondary Chromatographic Purity by LC/MS Analysis	SP10-0107	> 99.9%	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.02% D_0 vs D_3	
		0.02% D_0	0.28% D_2
		0.01% D_1	99.68% D_3
Identity by ^{1}H-NMR Analysis	SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.40%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

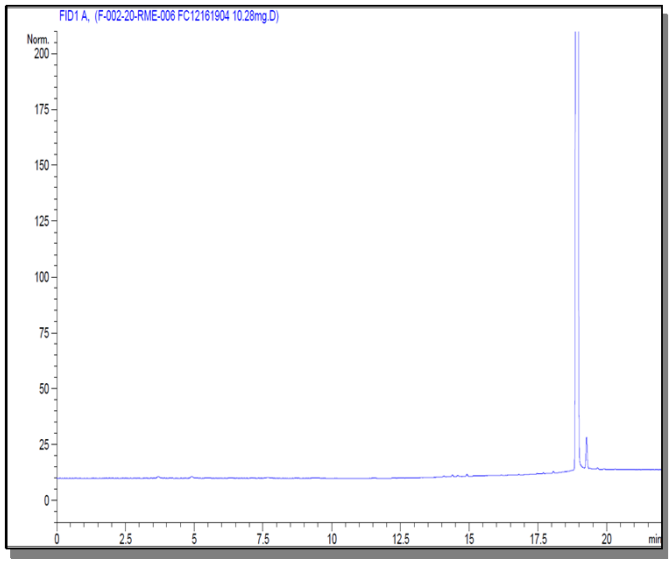
GC/FID



Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 80°C at 40°C/min 80°C to 200°C at 5°C/min 200°C to 280°C at 40°C/min hold 10 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC12161904
Acquired:	April 06, 2020

Peak #	Ret Time	Area %
1	18.50	0.02
2	19.29	0.08
3	20.15	99.17
4	25.28	0.37
5	25.49	0.03
6	25.57	0.01
7	26.46	0.15
8	27.33	0.13
9	27.88	0.03

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FC12161904
Acquired:	March 04, 2020

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

ND- None Detected

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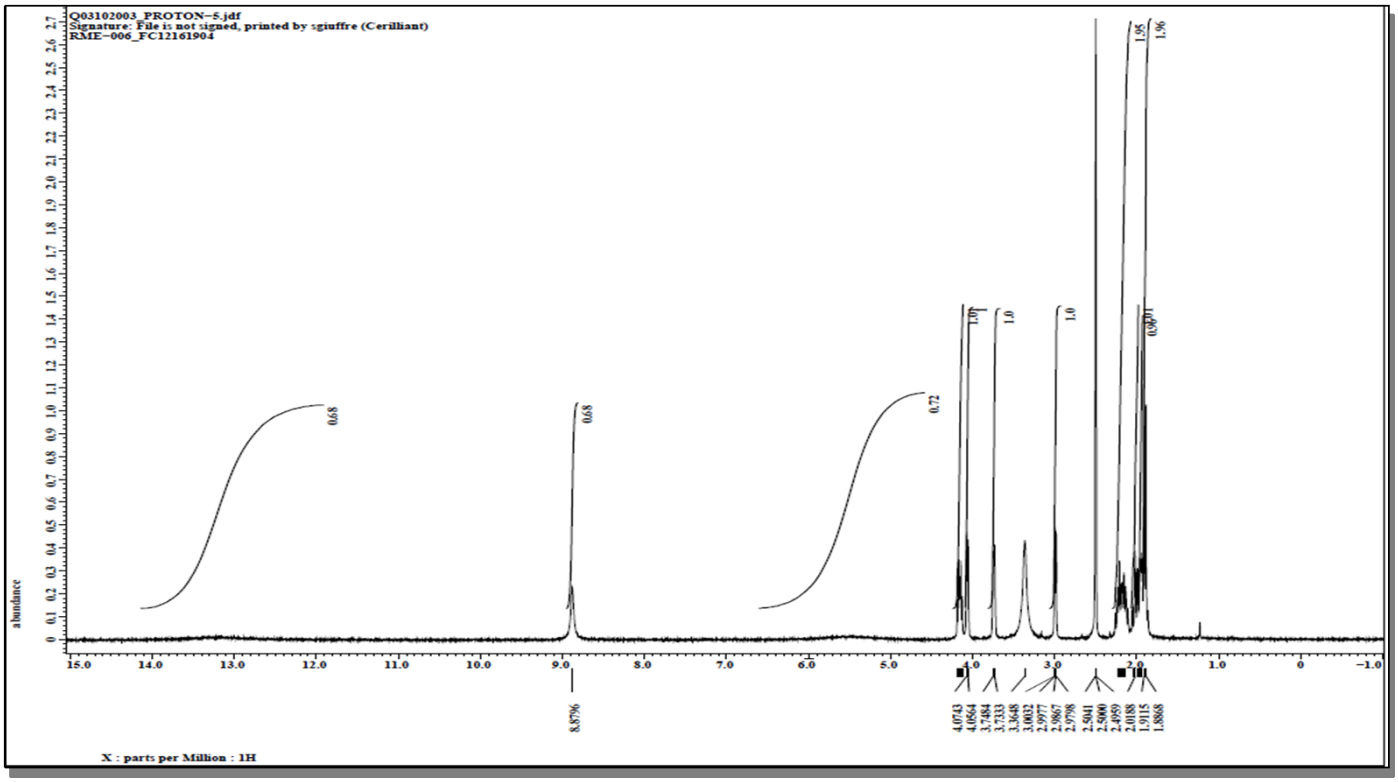
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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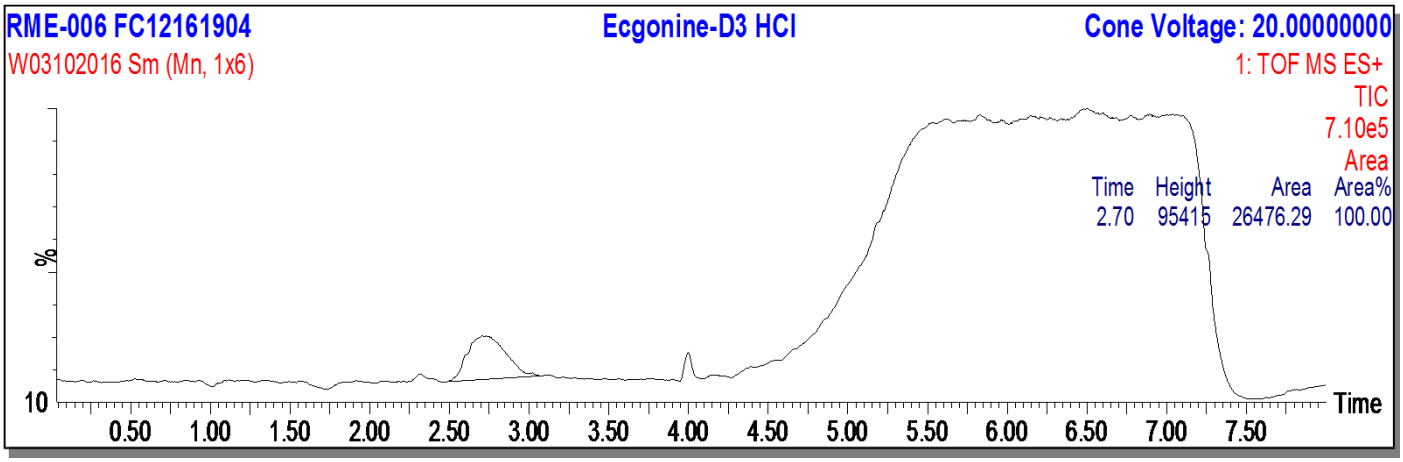
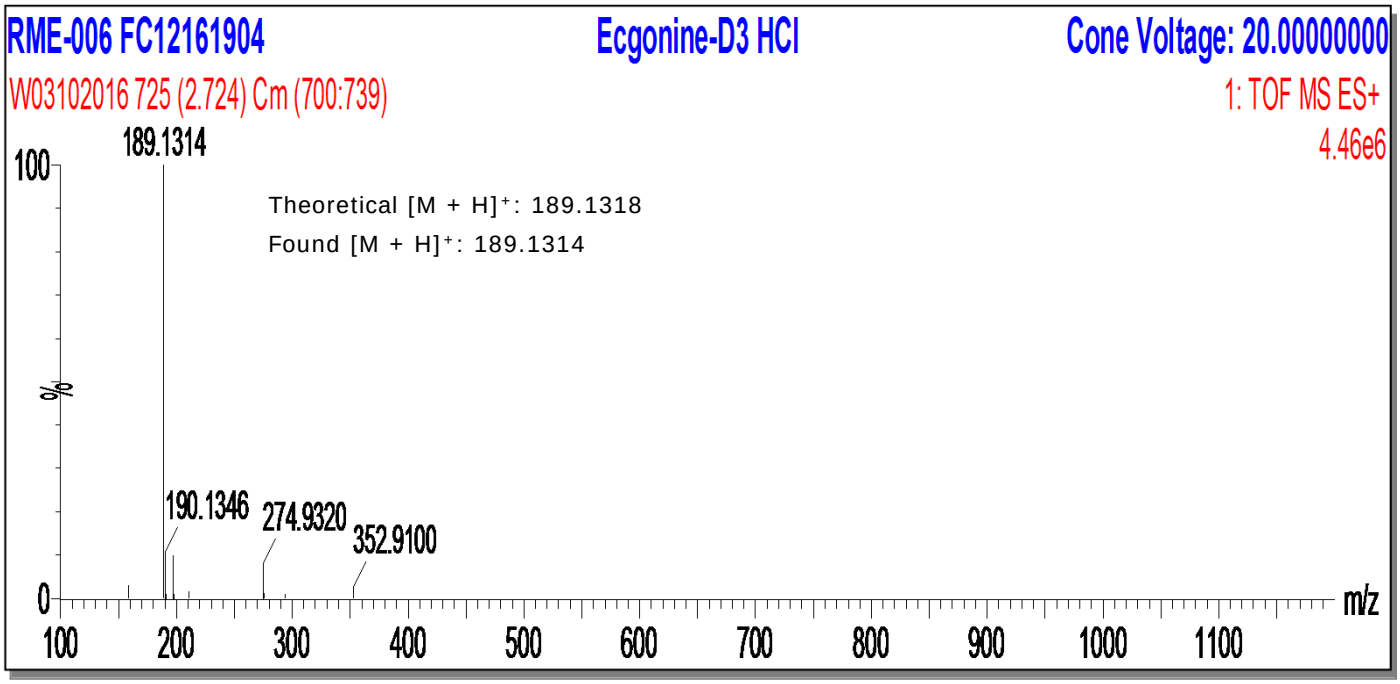
Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Ammonium acetate in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 10, 2020

Time (min)	% A	% B
0.0	100	0
2.0	100	0
4.0	80	20
5.8	80	20
6.0	100	0
8.0	100	0





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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

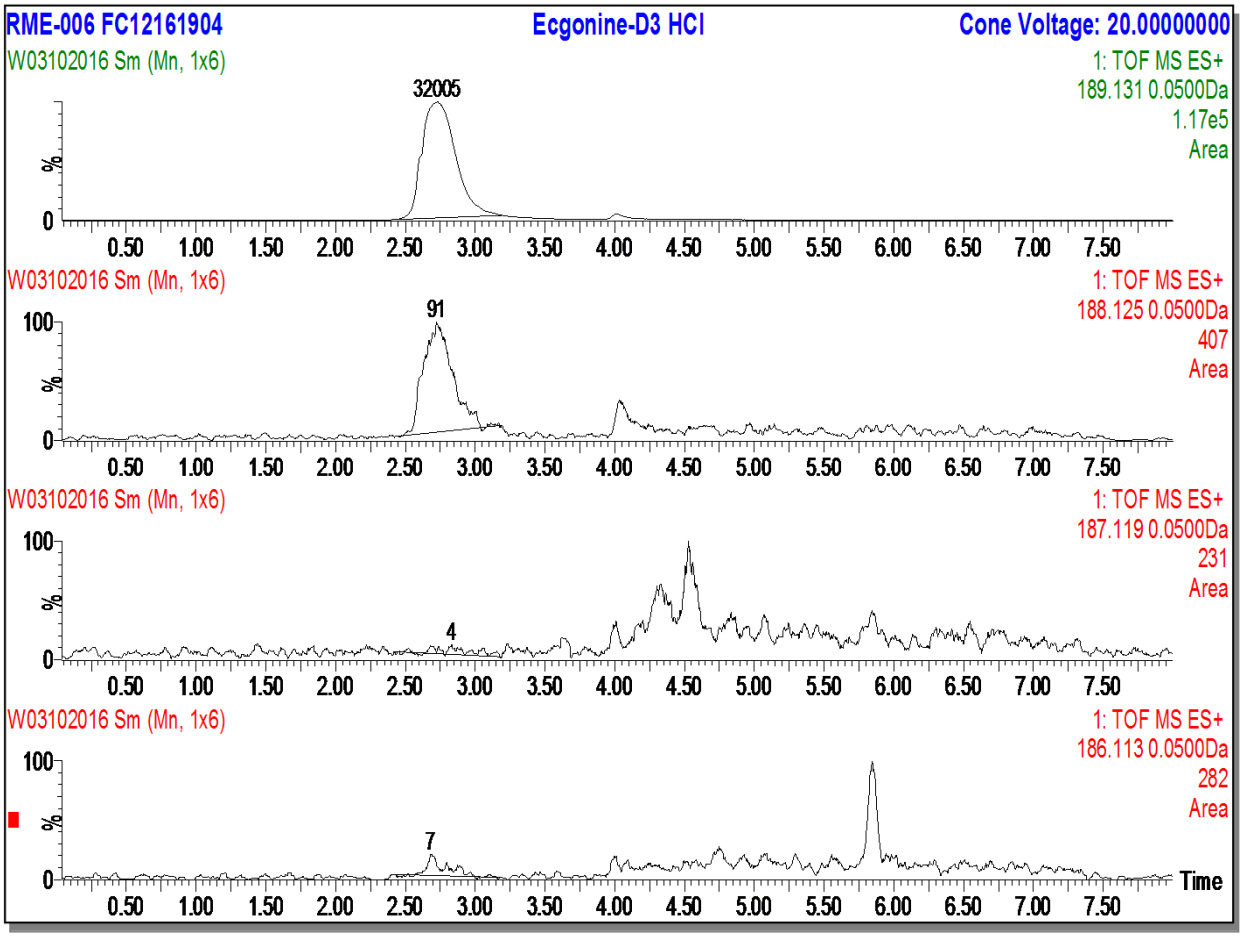
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

Mobile Phase: A: 0.1% Ammonium acetate in Water
B: Acetonitrile

Gradient:

Time (min)	% A	% B
0.0	100	0
2.0	100	0
4.0	80	20
5.8	80	20
6.0	100	0
8.0	100	0

Flow Rate: 0.4 mL/min
Scan Range: 186-189 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: March 10, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	June 05, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

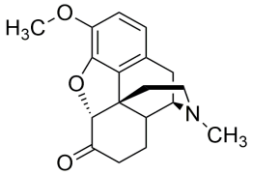
Certified Reference Material - Certificate of Analysis

Hydrocodone, Primary Measurement Standard

4,5-α-Epoxy-3-methoxy-17-methylmorphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: H-003-1ML
Lot No.: FE01082011
Description of CRM: Hydrocodone in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{21}NO_3$
CAS No.: 125-29-1
Regulatory: USDEA Exempt | Canadian TK # 61-1213



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Hydrocodone	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

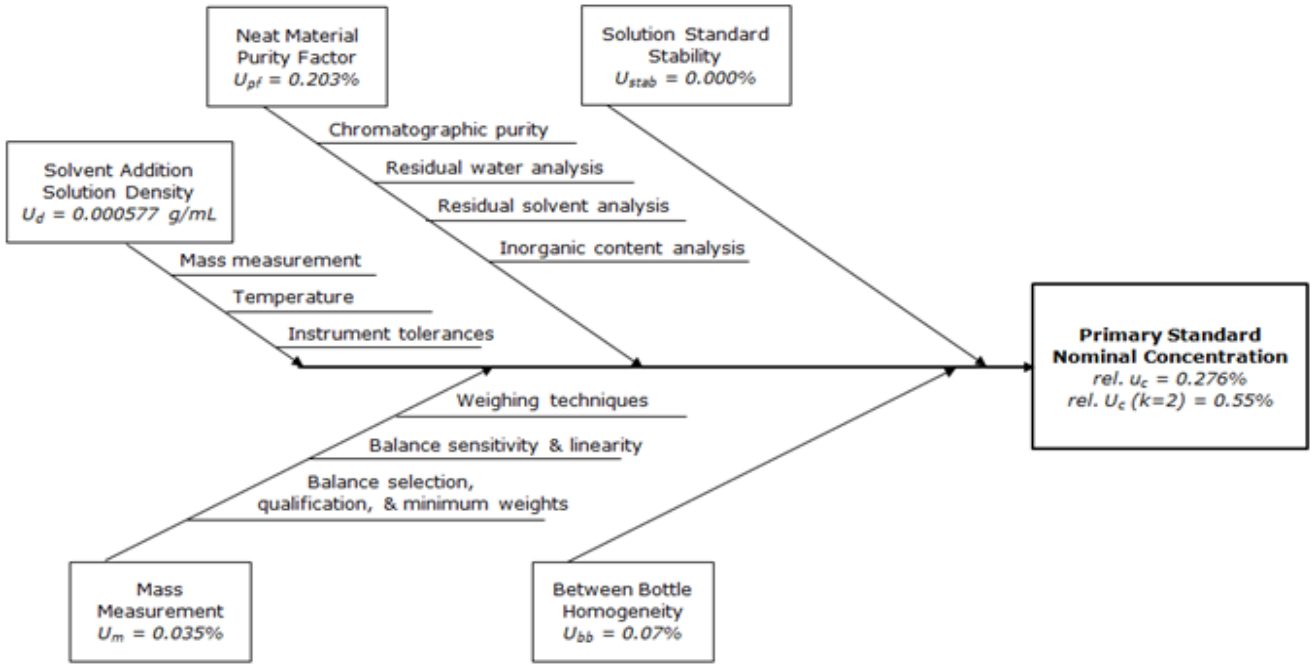
February 19, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (12:88)	**Linearity (r) :**	1.000
Flow Rate:	1.8 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082011	1.004	0.2
Previous Lot	FE04241902	1.000	0.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Hydrocodone	**Chemical Formula:**	$C_{18}H_{21}NO_3$
Material Lot:	FC08241802	**CAS Number:**	125-29-1
		Molecular Weight:	299.36

Material Characterization Summary

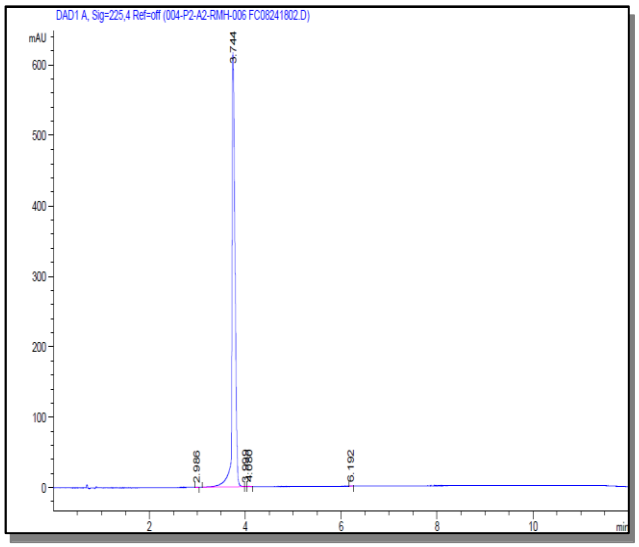
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8%
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.5%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.27%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Not Detected
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.53%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
8.0	60	40
10.0	60	40
10.1	2	98

Flow Rate: 0.6 mL/min

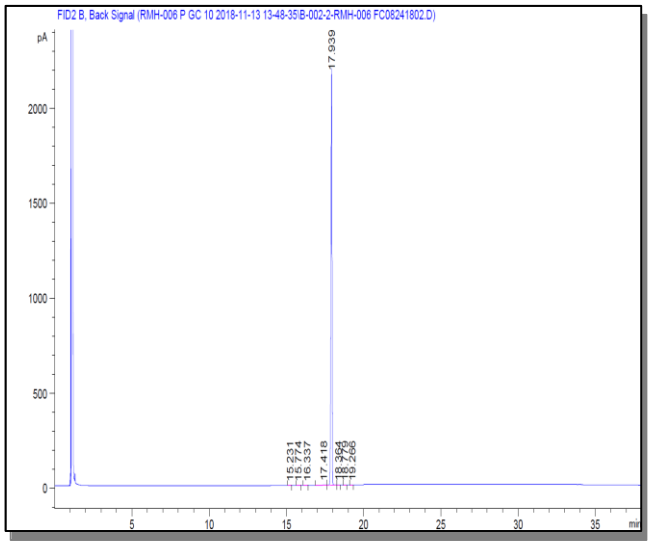
Wavelength: 225 nm

Sample Name: FC08241802

Acquired: November 08, 2018

Peak #	Ret Time	Area %
1	2.99	0.02
2	3.74	99.80
3	4.00	0.06
4	4.08	0.09
5	6.19	0.03

GC/FID



Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

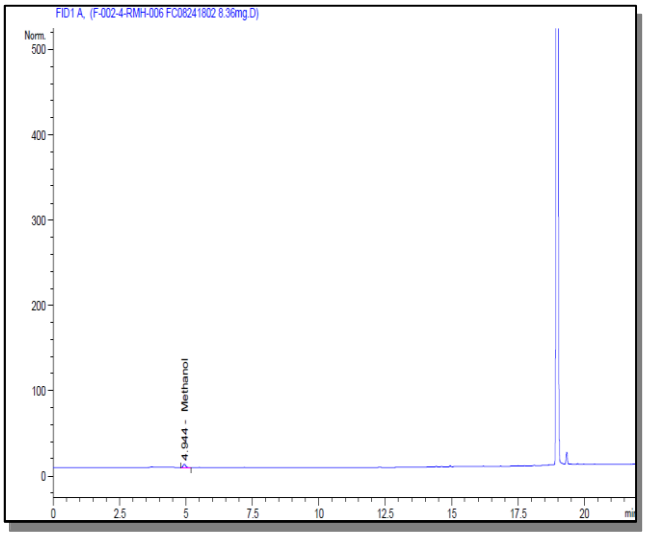
Sample Name: FC08241802

Acquired: November 13, 2018

Peak #	Ret Time	Area %
1	15.23	0.01
2	15.77	0.02
3	16.34	0.01
4	17.42	0.35
5	17.94	99.51
6	18.36	0.02
7	18.78	0.04
8	19.27	0.03

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

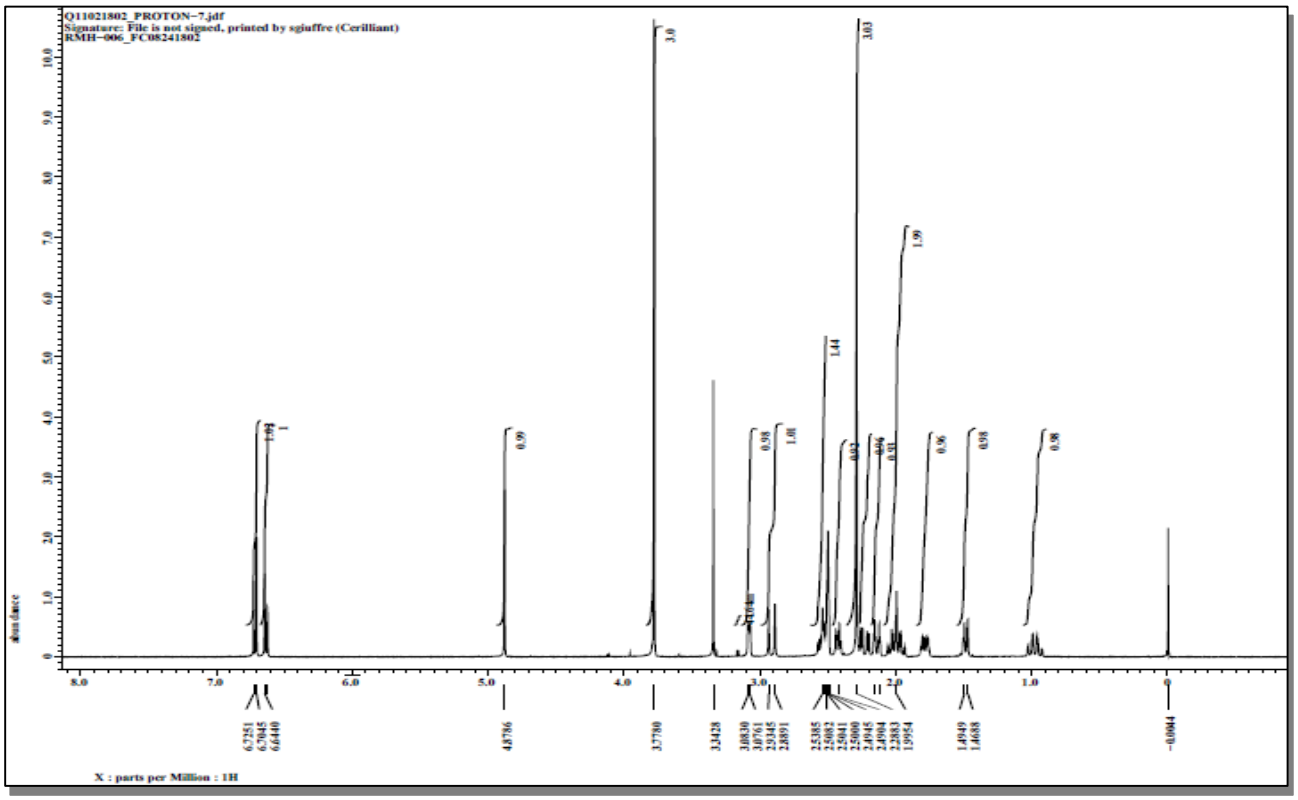


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC08241802
Acquired:	November 02, 2018

Peak	Compound	Area	Weight %
1	Methanol	25.28	0.27
2	NMP	NA	NA
Total			**0.27**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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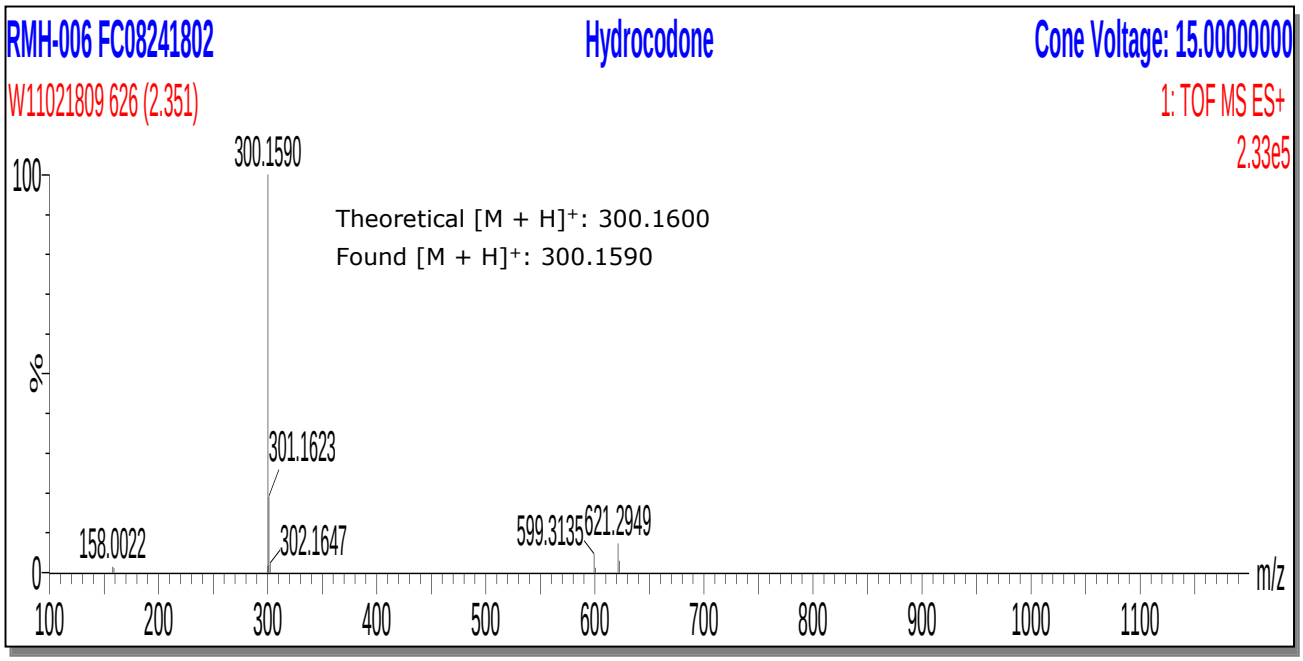
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	November 02, 2018

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	60	40
5.8	60	40
6.0	98	2
8.0	98	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 19, 2020	Initial version.

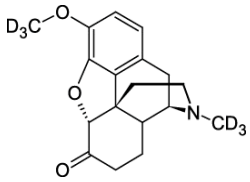
Certified Reference Material - Certificate of Analysis

Hydrocodone-D_6, Primary Measurement Standard

(5α)-4,5-Epoxy-3-trideuteromethoxy-17-trideuteromethylmorphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: H-048-1ML
Lot No.: FE01142004
Description of CRM: Hydrocodone-D_6 in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{15}D_6NO_3$
CAS No.: 1007844-38-3
Regulatory: USDEA Exempt | Canadian TK # 61-1228



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Hydrocodone-D_6	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

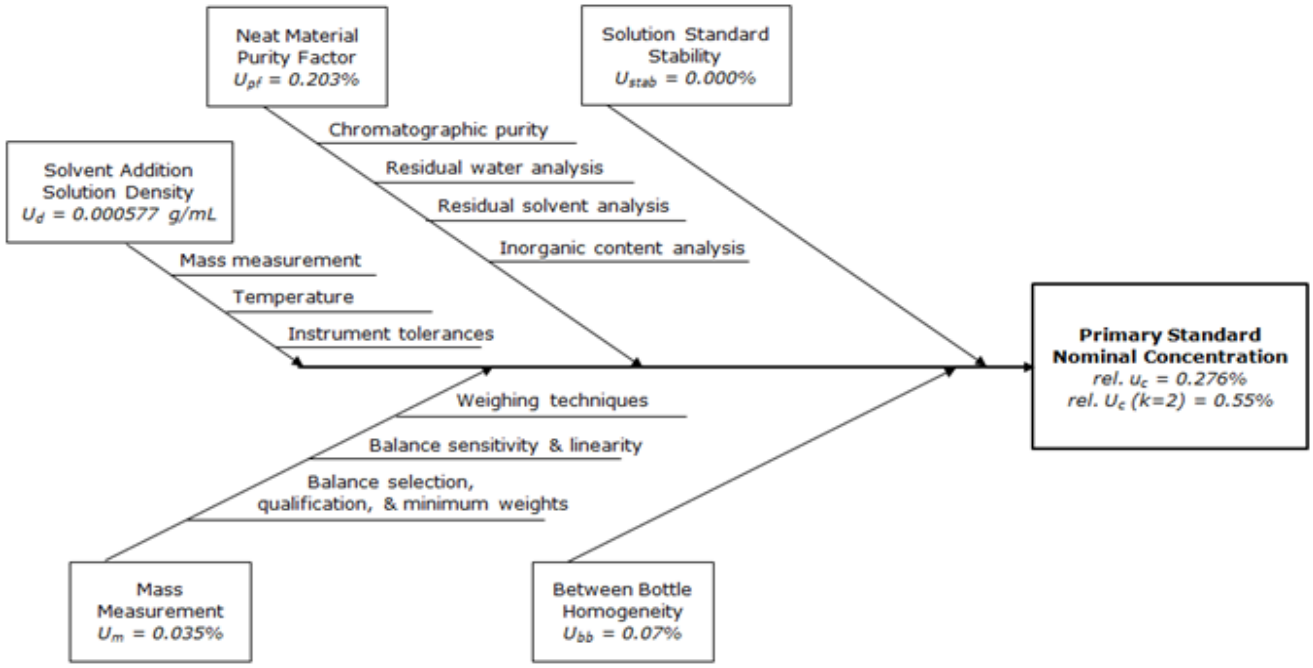
March 02, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (15:85)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01142004	1.001	1.2
Previous Lot	FE02081801	1.002	1.5

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Hydrocodone-D_6	**Chemical Formula:**	$C_{18}H_{15}D_6NO_3$
Material Lot:	FC11301601	**CAS Number:**	1007844-38-3
		Molecular Weight:	305.40

Material Characterization Summary

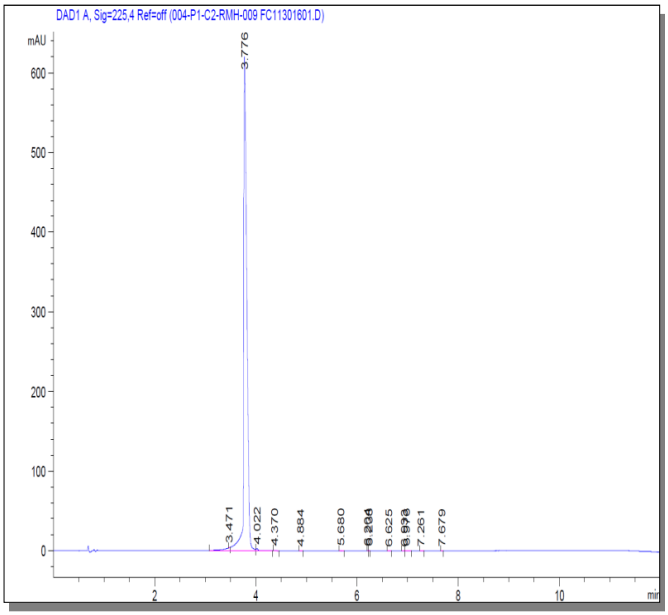
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.7%	
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.7%	
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure	
Isotopic Purity and Distribution by GC/MS SIM Analysis	SP10-0105	0.01% D_0 vs D_6	
		0.01% D_0 to D_1	1.23% D_4
		0.07% D_2	12.61% D_5
		0.17% D_3	85.90% D_6
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.41%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.28%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

Mobile Phase: A: Acetonitrile
B: 0.1% Phosphoric acid

Gradient:

Time (min)	% A	% B
0.0	2	98
8.0	60	40
10.0	60	40
10.1	2	98

Flow Rate: 0.6 mL/min

Wavelength: 225 nm

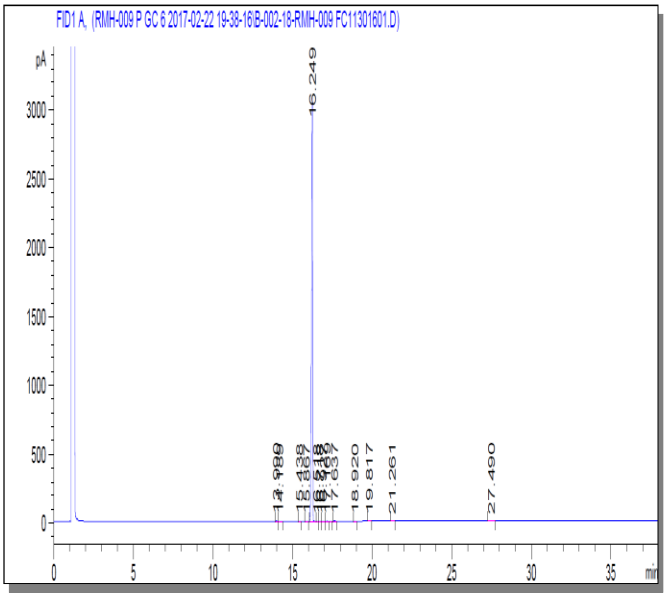
Sample Name: FC11301601

Acquired: March 13, 2017

Peak #	Ret Time	Area %
1	3.47	0.01
2	3.78	99.58
3	4.02	0.31
4	4.37	0.01
5	4.88	0.01
6	5.68	0.01
7	6.20	0.01
8	6.24	0.01
9	6.63	0.01
10	6.93	0.01
11	6.98	0.02
12	7.26	0.01
13	7.68	0.00

Spectral and Physical Data (cont.)

GC/FID

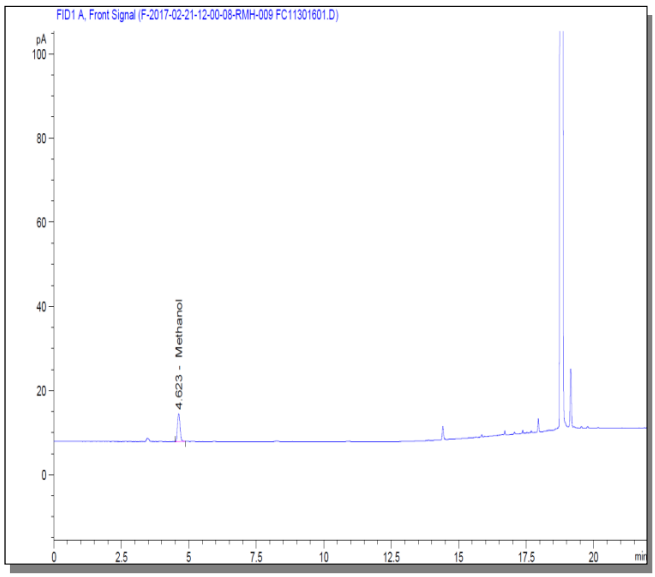


Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 280°C at 5°C/min hold 18 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC11301601
Acquired:	February 22, 2017

Peak #	Ret Time	Area %
1	13.99	0.08
2	14.19	0.01
3	15.44	0.00
4	15.87	0.00
5	16.25	99.68
6	16.52	0.01
7	16.72	0.00
8	16.93	0.02
9	17.17	0.02
10	17.64	0.11
11	18.92	0.00
12	19.82	0.01
13	21.26	0.03
14	27.49	0.02

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

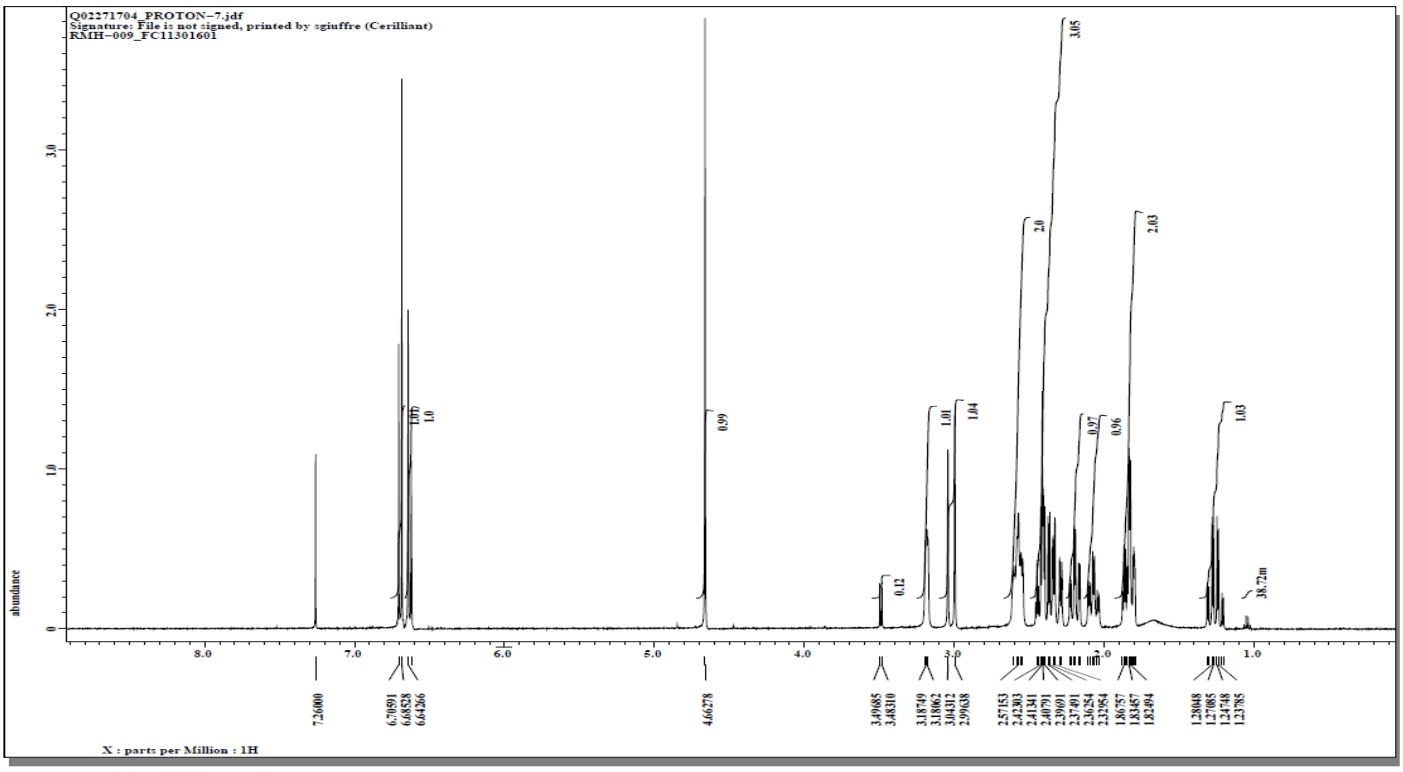


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC11301601
Acquired:	February 21, 2017

Peak	Compound	Area	Weight %
1	Methanol	45.43	0.41
2	NMP	NA	NA
Total			**0.41**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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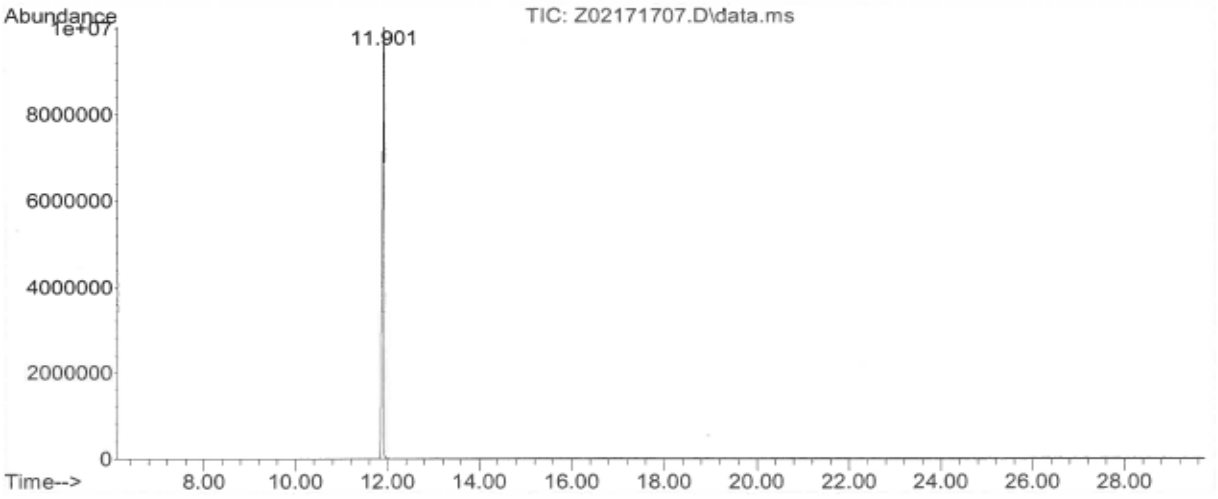
Spectral and Physical Data (cont.)

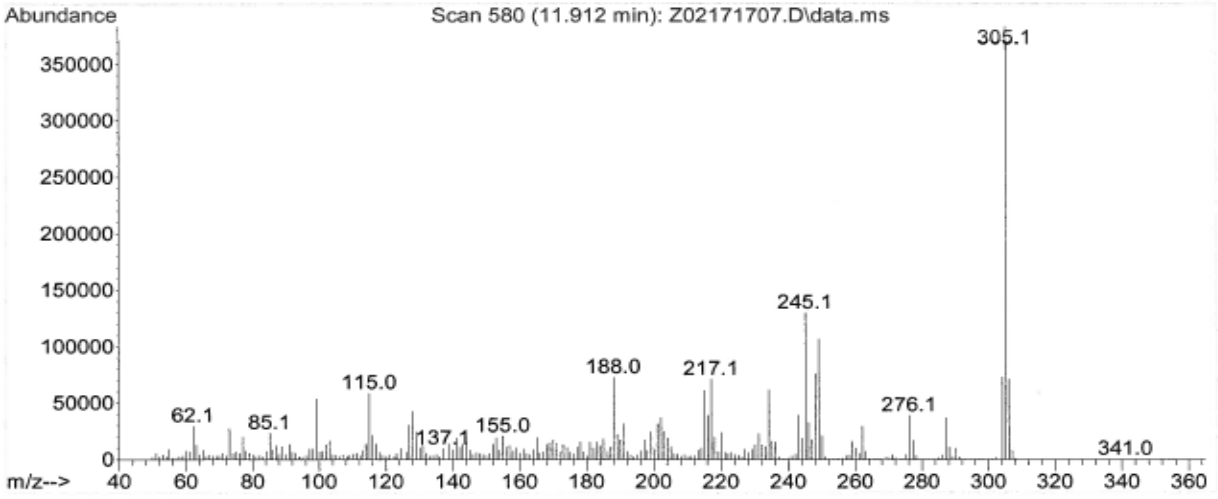
GC/MS

```
Compound Name        : Hydrocodone-D6
Lot Number           : FC11301601
Instrument           : Agilent GCMS
Operator             : ECM(SGIUFFRE)
Date Reported        : Fri Feb 17 14:52:49 2017
Column Type          : DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program        : 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.       : Cool on-column
Carrier Gas          : Helium
Flow Rate (mL\min)   : 0.80 mL/min
Transfer Line Temp.  : 280°C
Scan Range           : 50-500
```

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (H-008, Hydrocodone-D_3) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 02, 2020	Initial version.

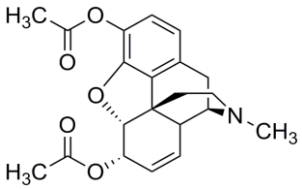
Certified Reference Material - Certificate of Analysis

Heroin, Primary Measurement Standard

Morphinan-3,6-diol-7,8-didehydro-4,5-epoxy,17, methyl-(5 α, 6 α)-3,6-diacetate

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: H-038-1ML
Lot No.: FE01082016
Description of CRM: Heroin in Acetonitrile (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{21}H_{23}NO_5$
CAS No.: 561-27-3
Regulatory: USDEA Exempt | Canadian TK # 61-1225



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Heroin	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

February 24, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

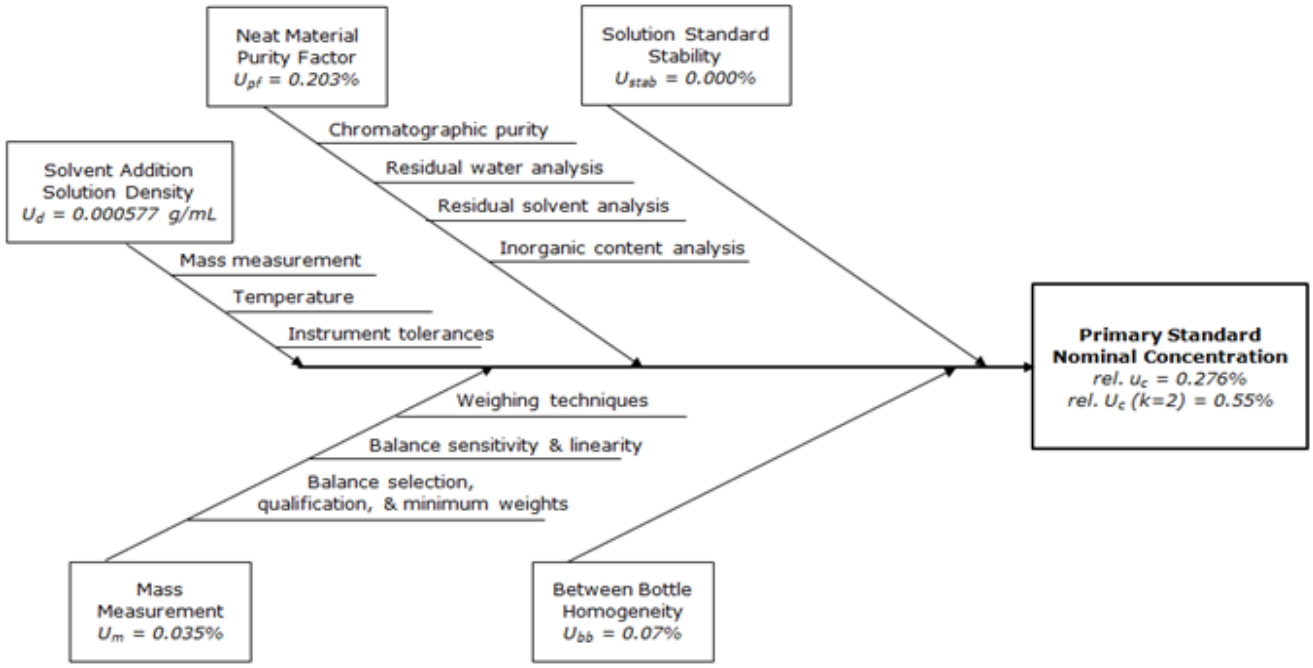
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (20:80)	**Linearity (r) :**	1.000
Flow Rate:	1.2 mL/min		
Wavelength:	235 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082016	0.994	0.2
Previous Lot	FE06151603	1.000	0.4

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Heroin	**Chemical Formula:**	$C_{21}H_{23}NO_5$
Material Lot:	FC11111601	**CAS Number:**	561-27-3
		Molecular Weight:	369.41

Material Characterization Summary

Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8% [1]
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	0.47%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Not Detected
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.37%

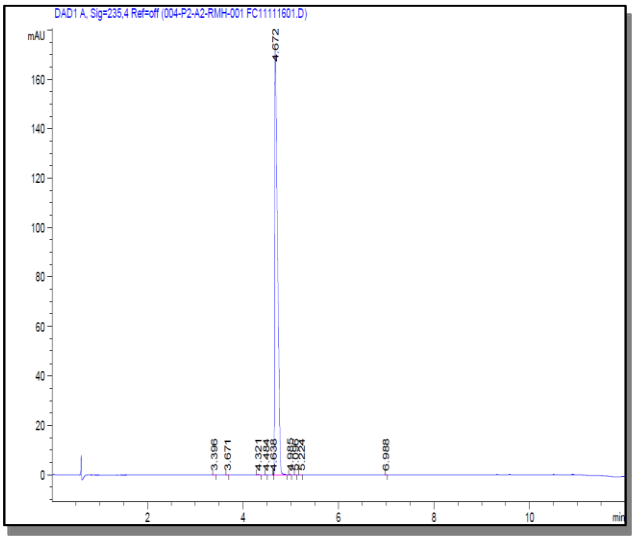
[1] No 6-Acetylmorphine or Morphine were detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
8.0	50	50
10.0	50	50
10.1	2	98

Flow Rate: 0.8 mL/min

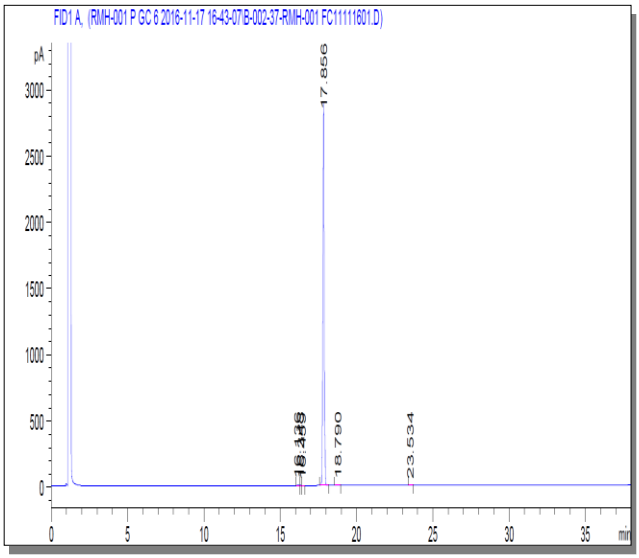
Wavelength: 235 nm

Sample Name: FC11111601

Acquired: October 18, 2019

Peak #	Ret Time	Area %
1	3.40	0.02
2	3.67	0.01
3	4.32	0.06
4	4.48	0.01
5	4.64	0.01
6	4.67	99.83
7	4.99	0.02
8	5.10	0.01
9	5.22	0.01
10	6.99	0.01

GC/FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

Sample Name: FC11111601

Acquired: November 17, 2016

Peak #	Ret Time	Area %
1	16.14	0.09
2	16.34	0.02
3	16.46	0.01
4	17.86	99.84
5	18.79	0.03
6	23.53	0.01

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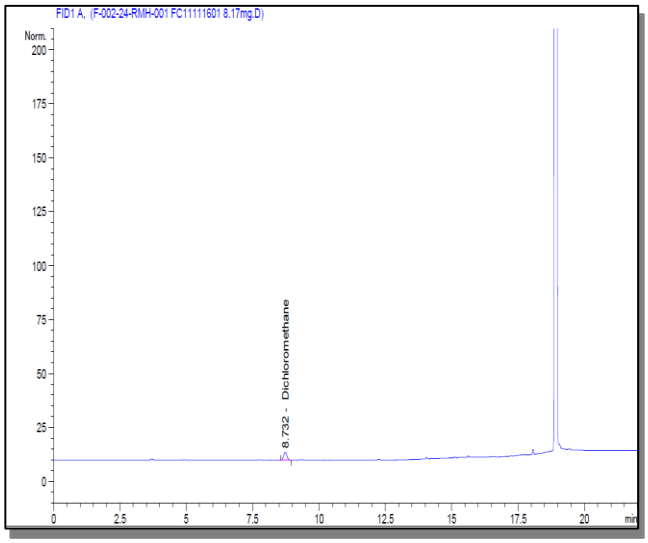
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

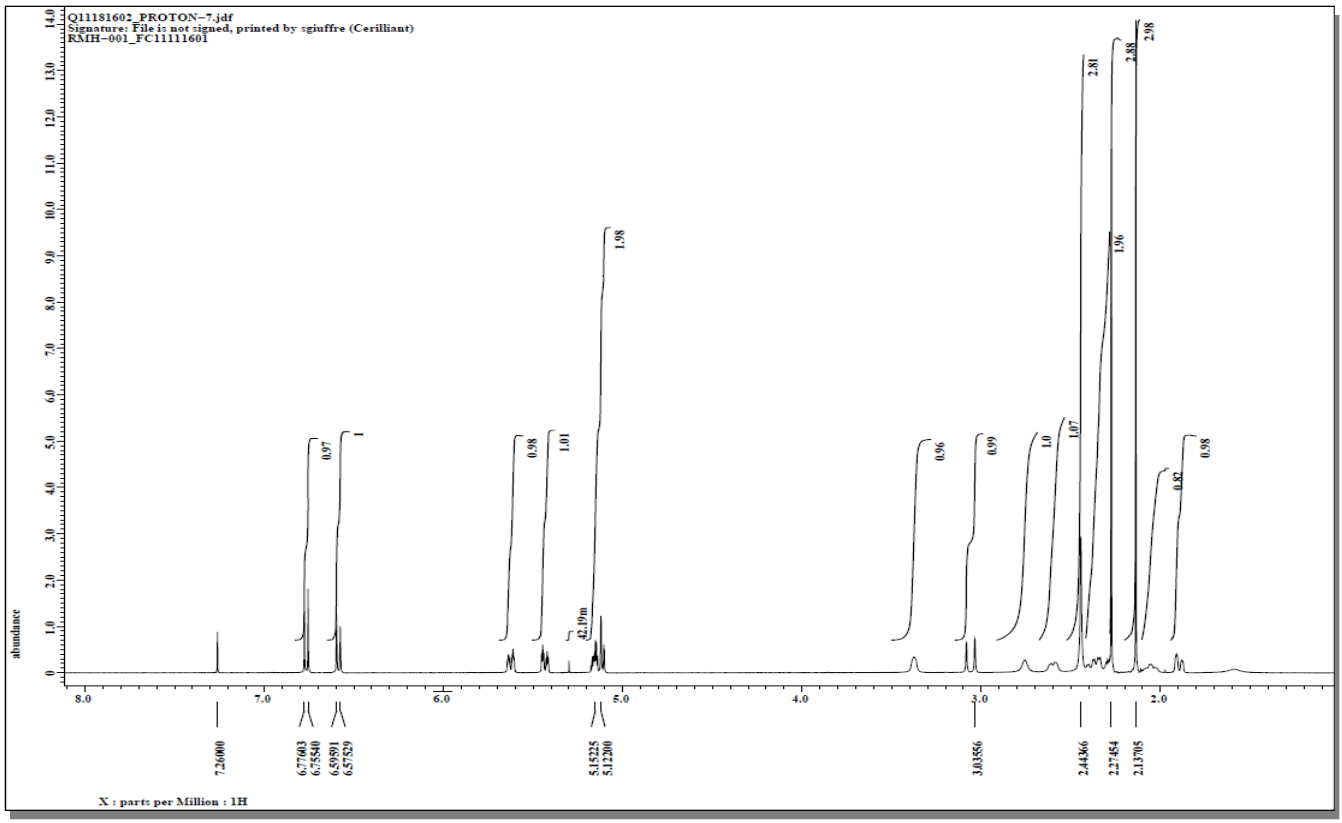


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC11111601
Acquired:	October 21, 2019

Peak	Compound	Area	Weight %
1	Dichloromethane	32.63	0.47
2	NMP	NA	NA
Total			**0.47**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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Spectral and Physical Data (cont.)

LC/MS

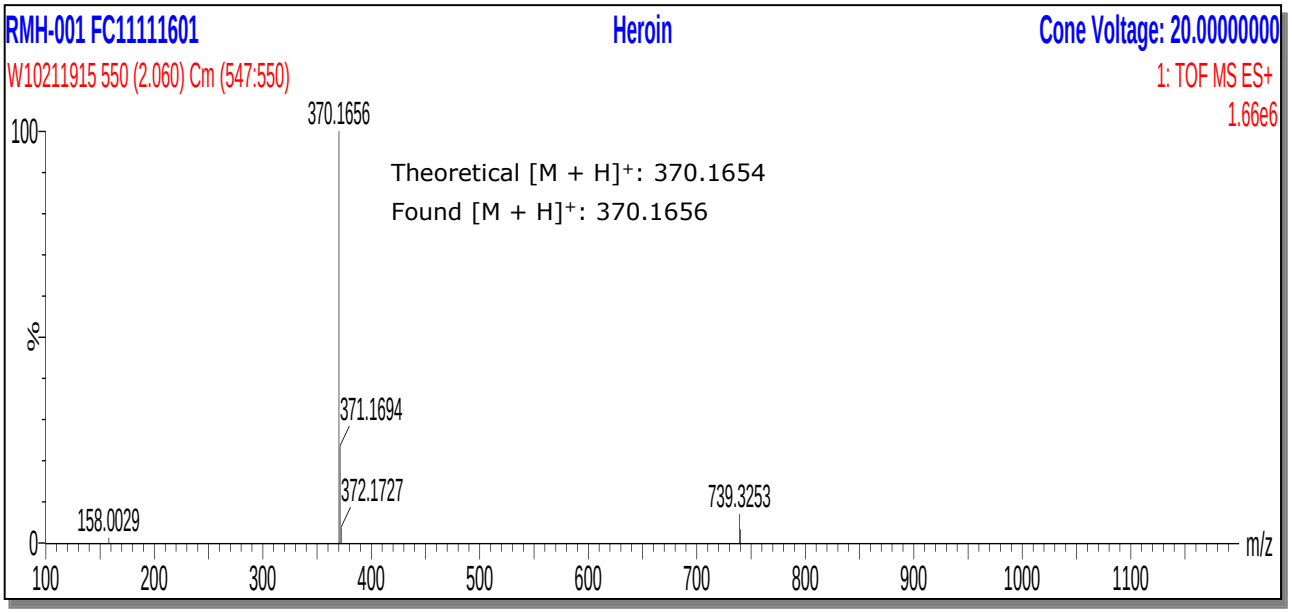
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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	50	50
5.8	50	50
6.0	90	10
8.0	90	10

Flow Rate: 0.4 mL/min
Scan Range: 100-1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: October 21, 2019



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 24, 2020	Initial version.

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Certified Reference Material - Certificate of Analysis

Heroin-D_9, Primary Measurement Standard

7,8-Didehydro-4,5-epoxy-17-trideuteromethyl-morphinan-3,6-diol di[trideuteroacetate]

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: H-037-1ML

Lot No.: FE03022011

Description of CRM: Heroin-D_9 in Acetonitrile (Solution)

Expiration Date: April 2025 See Section "Stability Assessment".

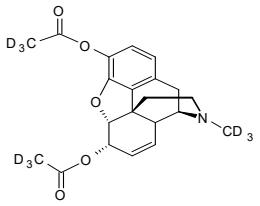
Storage: Store unopened in freezer (-10 °C to -25 °C).

Shipping: Ambient. See Section "Stability Assessment".

Chemical formula: $C_{21}H_{14}D_9NO_5$

CAS No.: 1338713-49-7

Regulatory: USDEA Exempt | Canadian TK # 61-1224



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Heroin-D_9	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability“ on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See “Details about certification process” on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

April 24, 2020

Issue Date

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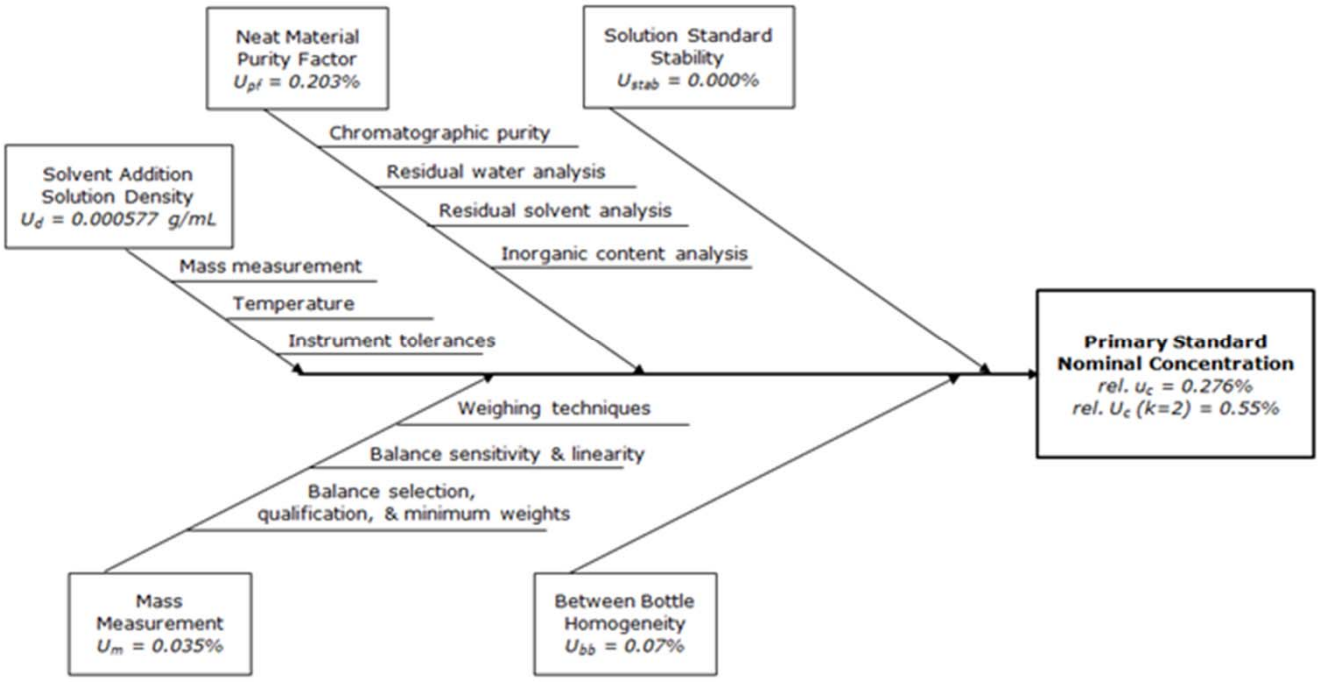
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (20:80)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	235 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03022011	0.997	0.3
Previous Lot	FE05251701	1.010	0.2

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Heroin-D_9	**Chemical Formula:**	$C_{21}H_{14}D_9NO_5$
Material Lot:	FC10151901	**CAS Number:**	1338713-49-7
		Molecular Weight:	378.47

Material Characterization Summary

Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.6% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%	
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure	
Isotopic Purity and Distribution by GC/MS SIM Analysis	SP10-0105	0.02% D_0 vs D_9	
		0.01% D_0 to D_1	0.42% D_6
		0.02% D_2	5.22% D_7
		0.03% D_3 to D_4	17.09% D_8
		0.06% D_5	77.11% D_9
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	0.37%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.28%	

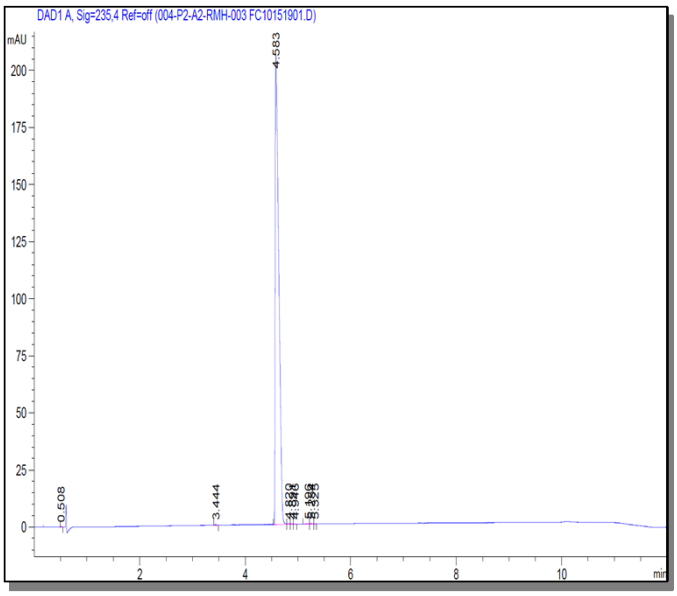
[1] 0.07% 6-Acetylmorphine detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
8.0	50	50
10.0	50	50
10.1	2	98

Flow Rate: 0.8 mL/min

Wavelength: 235 nm

Sample Name: FC10151901

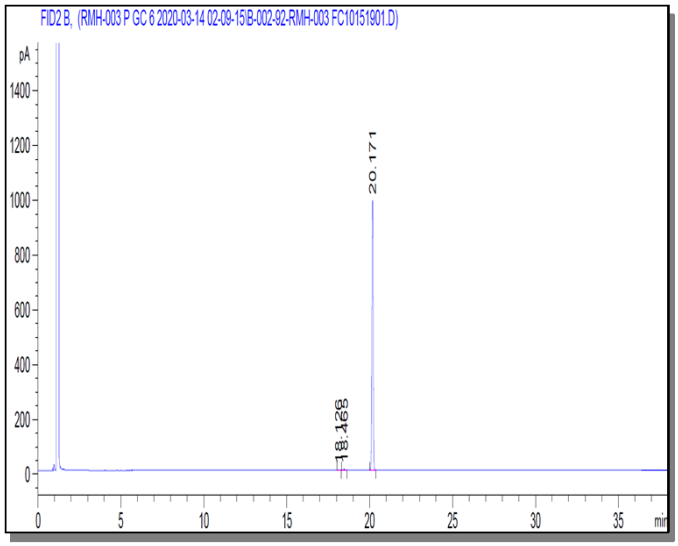
Acquired: March 05, 2020

Peak #	Ret Time	Area %
1	0.51	0.01
2	3.44	0.07
3	4.58	99.67
4	4.82	0.08
5	4.89	0.03
6	4.95	0.01
7	5.20	0.04
8	5.25	0.07
9	5.33	0.03

Peak 2 is identified as 6-Acetylmorphine

Spectral and Physical Data (cont.)

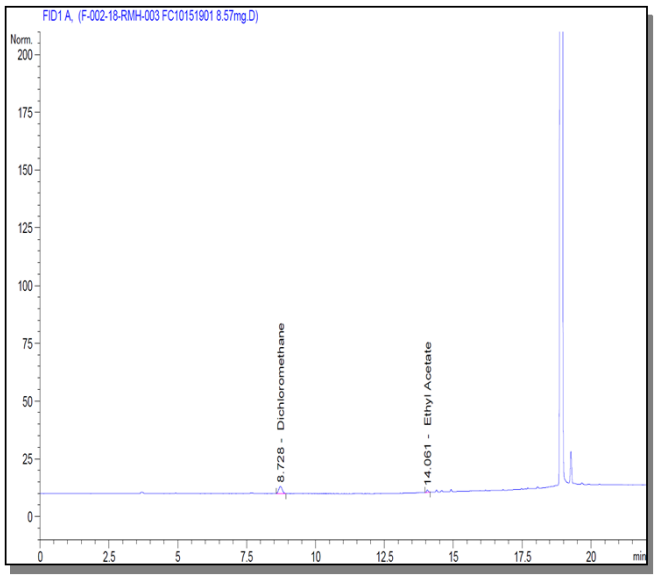
GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 280°C at 5°C /min hold 18 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC10151901
Acquired:	March 14, 2020

Peak #	Ret Time	Area %
1	18.13	0.04
2	18.47	0.16
3	20.17	99.80

Residual Solvent Analysis by GC/FID Headspace



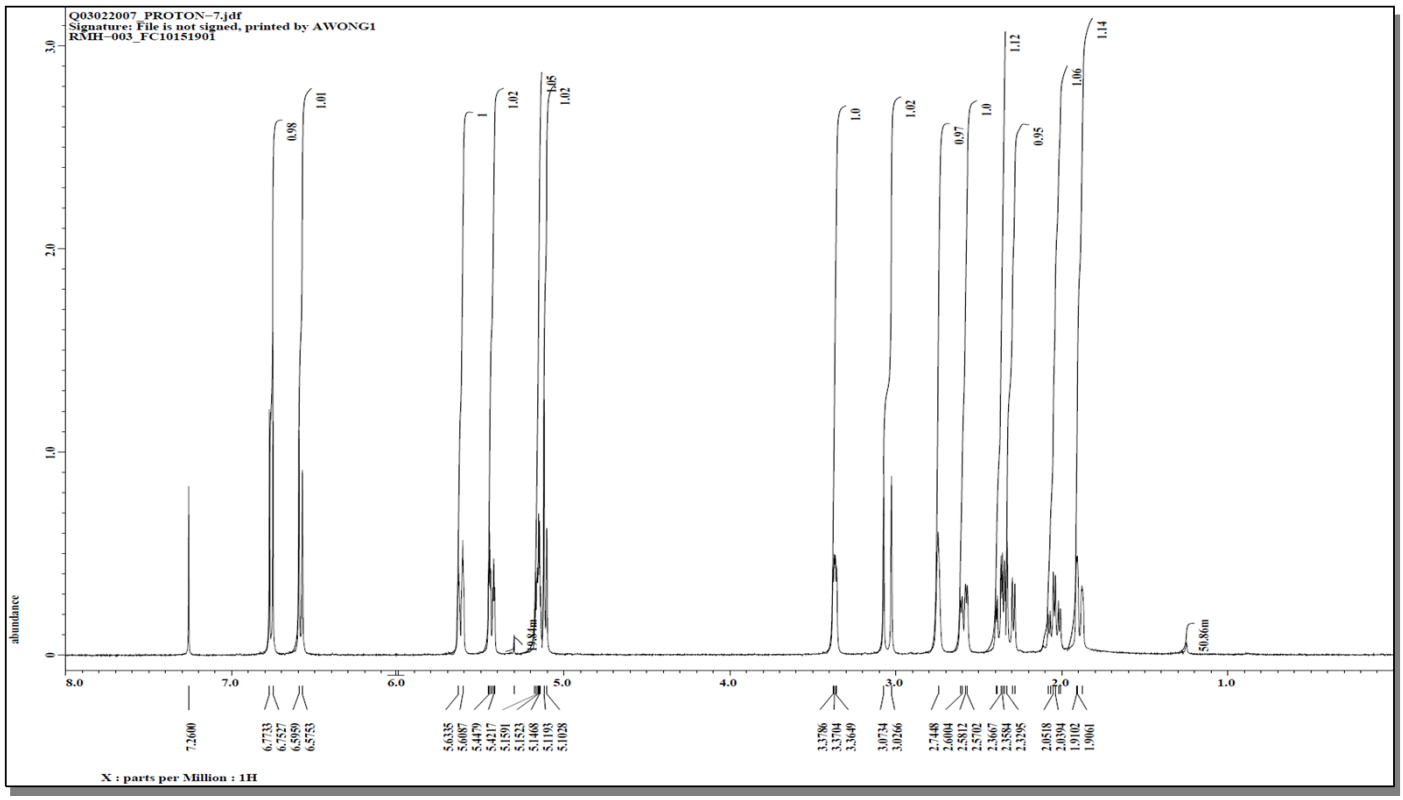
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC10151901
Acquired:	March 04, 2020

Peak	Compound	Area	Weight %
1	Dichloromethane	27.52	0.35
2	Ethyl acetate	4.80	0.02
3	NMP	NA	NA
Total			**0.37**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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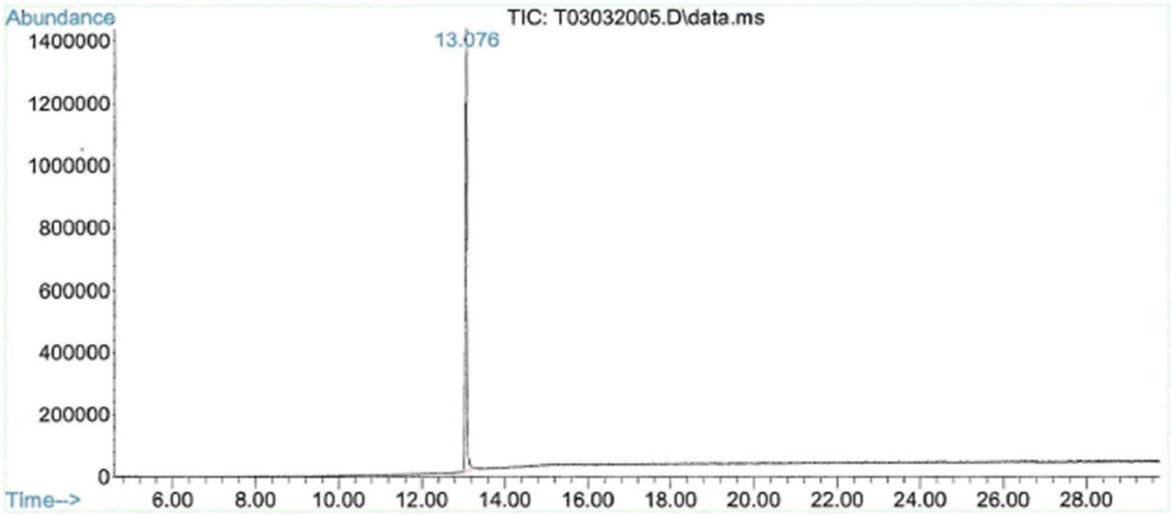
Spectral and Physical Data (cont.)

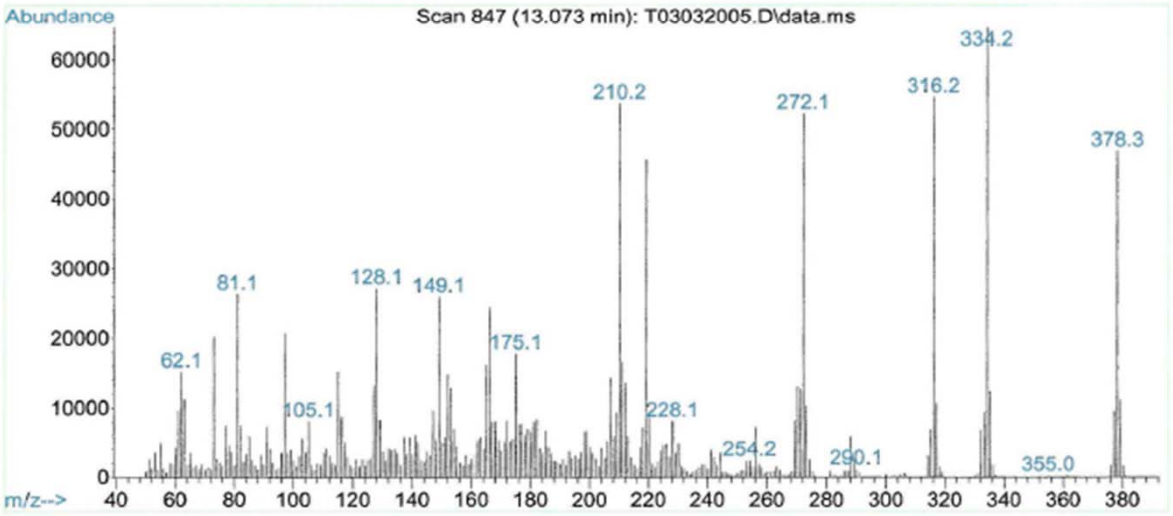
GC / MS

Compound Name	: Heroin-D9
Lot Number	: FC10151901
Instrument	: Agilent GCMS
Operator	: ECM(SGIUFFRE)
Date Reported	: Wed Mar 04 09:35:11 2020
Column Type	: DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	: 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.	: Cool on-column
Carrier Gas	: Helium
Flow Rate (mL\min)	: 0.80 mL/min
Transfer Line Temp.	: 280°C
Scan Range	: 50-500

Total Ion Chromatogram



Mass Spectrum



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

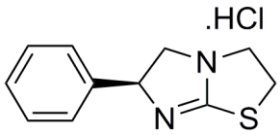
Revision No.	Date	Reason for Revision
00	April 24, 2020	Initial version.

Certified Reference Material - Certificate of Analysis

(-)-Levamisole, Primary Measurement Standard

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: L-025-1ML
Lot No.: FN01142005
Description of CRM: (-)-Levamisole HCl in Methanol (Solution)
Nominal concentration is adjusted for HCl content.
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{11}H_{12}N_2S \bullet HCl$
CAS No.: 16595-80-5



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(-)-Levamisole	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
Nominal concentration is adjusted for HCl content. No adjustment required before use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darren Ellsworth, Quality Assurance Manager

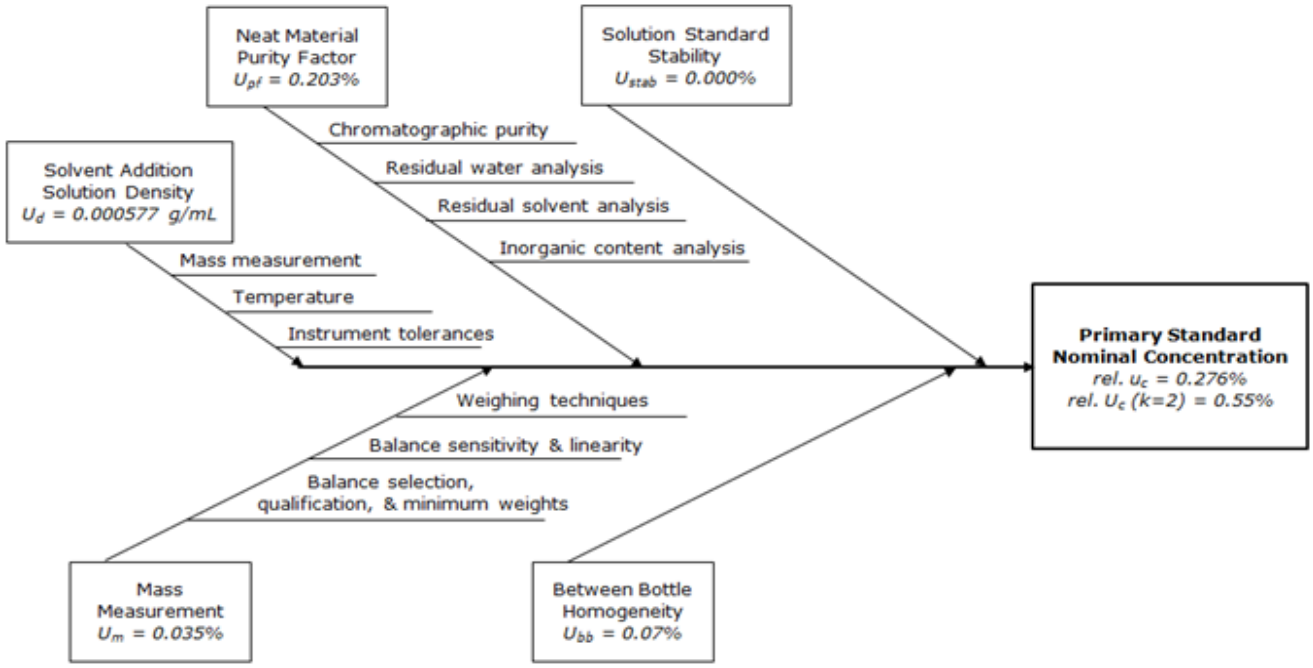
March 03, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (15:85)	**Linearity (r) :**	1.000
Flow Rate:	1.3 mL/min		
Wavelength:	220 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN01142005	0.997	0.7
Previous Lot	FN08261801	0.999	0.6

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(-)-Levamisole HCl	**Molecular Weight (base):**	204.29
Material Lot:	PN030311-02	**Molecular Weight (salt):**	240.75
Chemical Formula:	$C_{11}H_{12}N_2S \bullet HCl$	**Salt Adjustment:**	1.178
CAS Number:	16595-80-5		

Material Characterization Summary

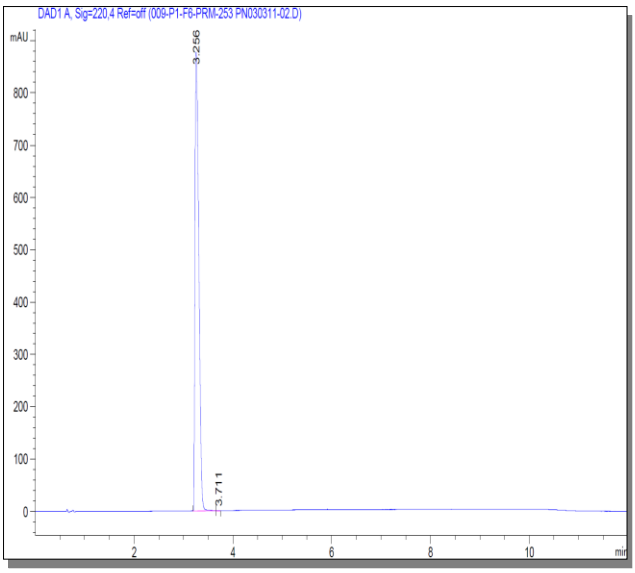
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	> 99.9%
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	> 99.9%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.98%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl
2.7 µm, 3.0 x 100 mm

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

Gradient:

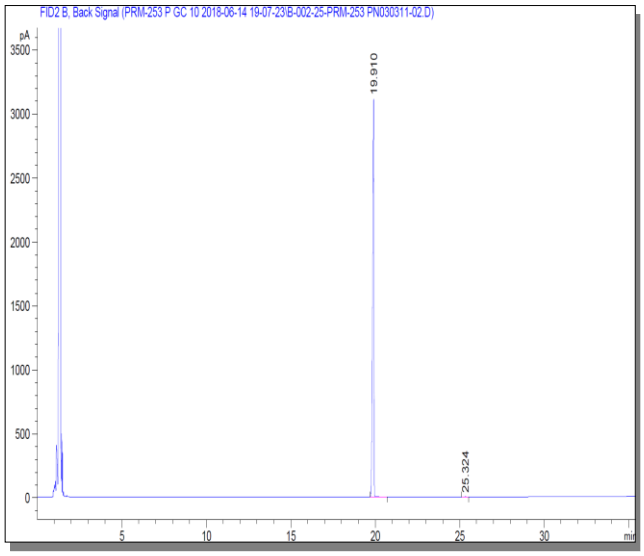
Time (min)	% A	% B
0.0	5	95
0.5	5	95
7.0	70	30
9.0	70	30
9.1	5	95

Flow Rate: 0.7 mL/min
Wavelength: 220 nm

Sample Name: PN030311-02
Acquired: June 21, 2018

Peak #	Ret Time	Area %
1	3.26	99.98
2	3.71	0.02

GC/FID



Column: DB-35ms, 30 m x 0.53 mm ID
1.0 µm film thickness

Temp Program: 40°C to 140°C at 40°C/min
140°C to 280°C at 5°C/min
hold 5 min

Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: PN030311-02
Acquired: June 14, 2018

Peak #	Ret Time	Area %
1	19.91	99.95
2	25.32	0.05

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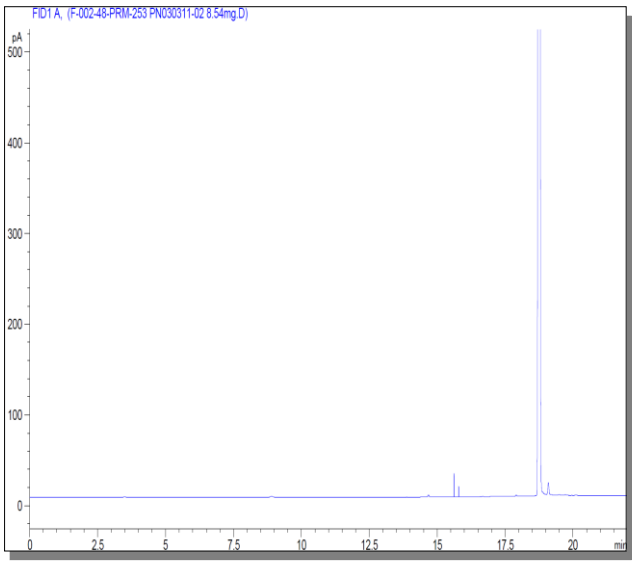
TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



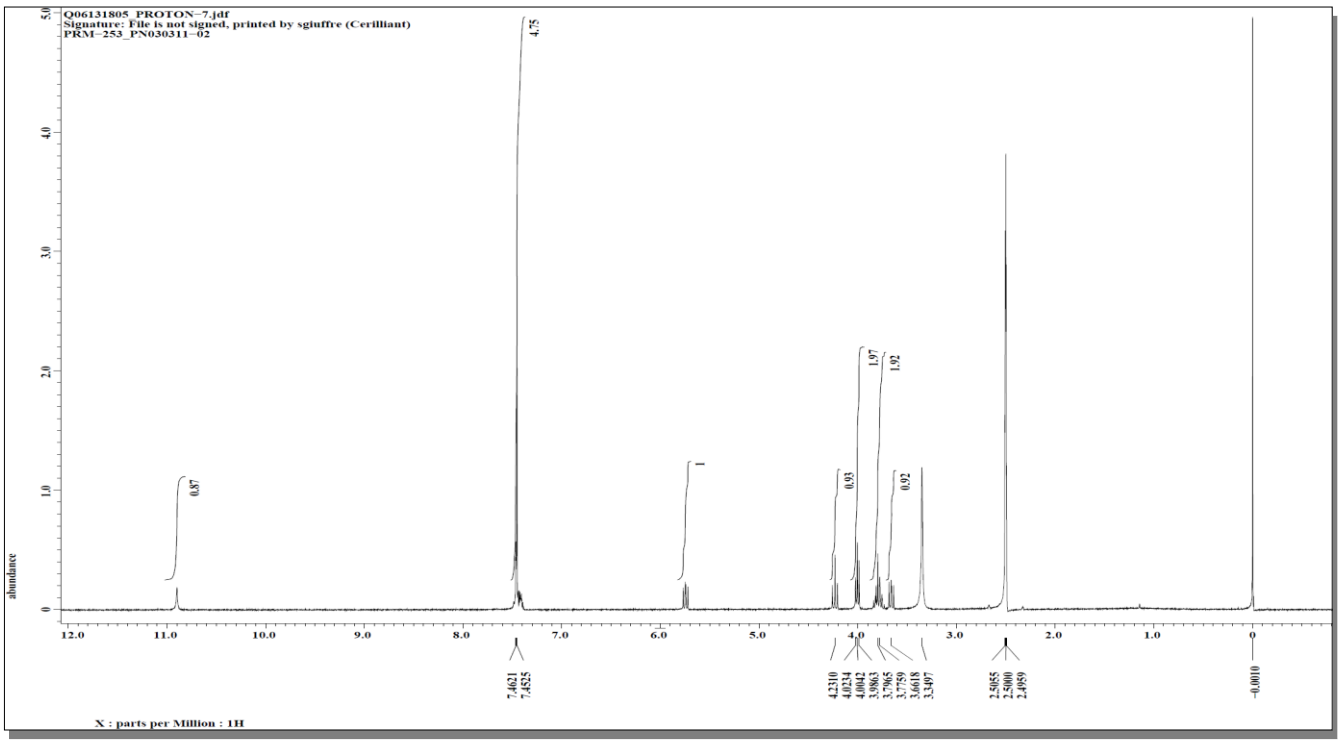
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	PN030311-02
Acquired:	June 19, 2018

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

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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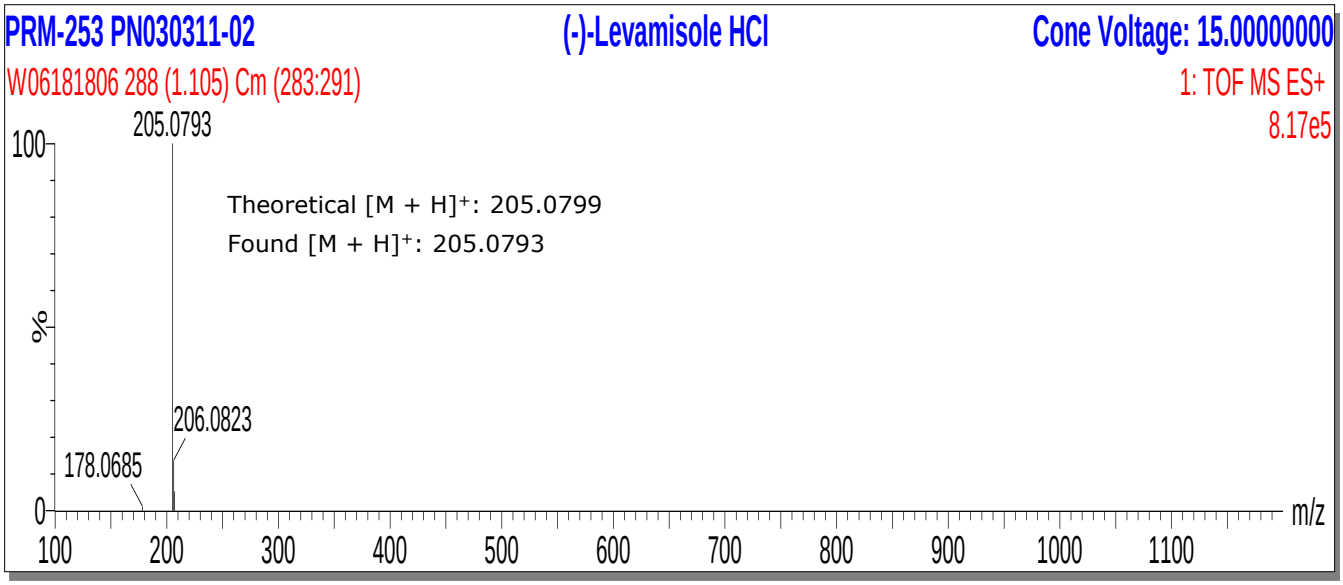
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	June 18, 2018

Time (min)	% A	% B
0.0	90	10
0.5	90	10
4.0	50	50
5.8	50	50
6.0	90	10
8.0	90	10



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 57 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	March 03, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

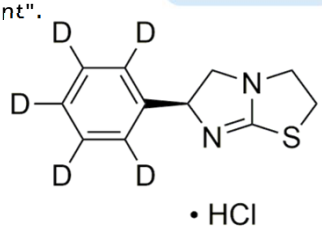
Certified Reference Material - Certificate of Analysis

(-)-Levamisole-D_5, Primary Measurement Standard

(6S)-6-(2,3,4,5,6-Pentadeuteriophenyl)-2,3,5,6-tetrahydroimidazo[2,1-b][1,3]thiazole hydrochloride

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: L-058-1ML
Lot No.: FN03242016
Description of CRM: (-)-Levamisole-D_5 HCl in Methanol (Solution)
Nominal concentration is adjusted for HCl content.
Retest Date: June 2021 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{11}H_7D_5N_2S \cdot HCl$
CAS No.: 1246819-64-6



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(-)-Levamisole-D_5	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Nominal concentration is adjusted for HCl content. No adjustment required before use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 02, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

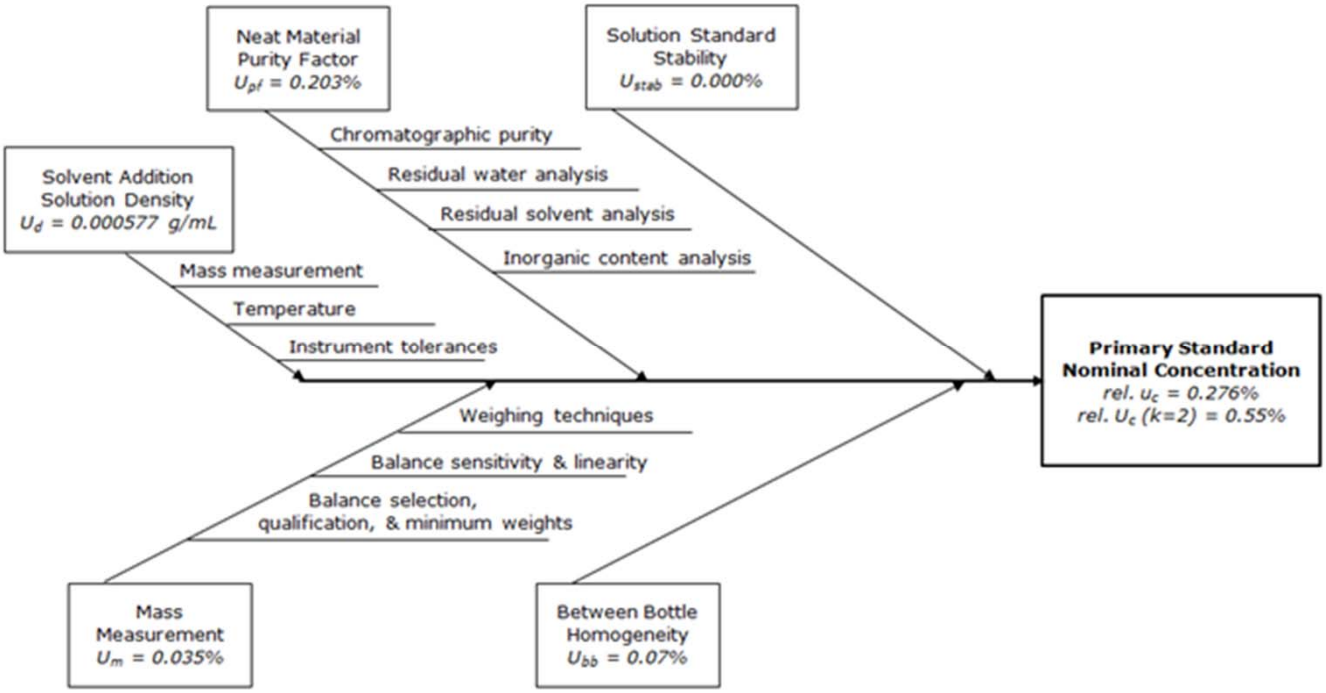
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (12:88)	**Linearity (r) :**	1.000
Flow Rate:	1.7 mL/min		
Wavelength:	220 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN03242016	1.002	0.5

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor and salt adjustment are utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(-)-Levamisole-D_5 HCl	**Molecular Weight (base):**	209.32
Material Lot:	FN10151909	**Molecular Weight (salt):**	245.78
Chemical Formula:	$C_{11}H_7D_5N_2S$ • HCl	**Salt Adjustment:**	1.174
CAS Number:	1246819-64-6		

Material Characterization Summary

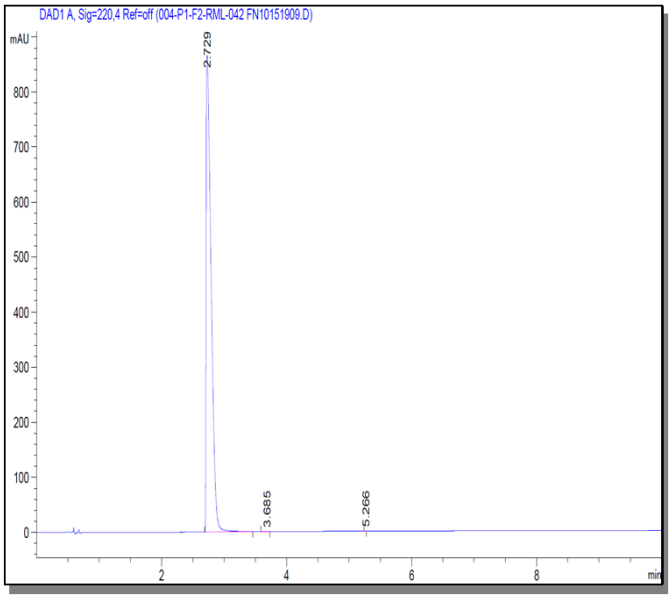
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	> 99.9%	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	> 99.9%	
Chiral Purity by HPLC/UV Analysis	20384348	69.2% ee	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.00% D_0 vs D_5	
		0.00% D_0 to D_2	2.23% D_4
		0.03% D_3	97.73% D_5
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		99.98%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	5	95
0.5	5	95
7.0	70	30
9.0	70	30
9.1	5	95

Flow Rate: 0.7 mL/min

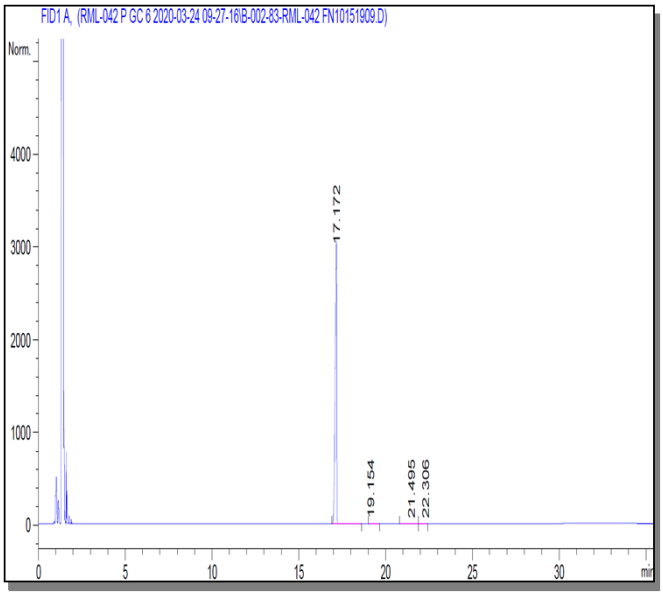
Wavelength: 220 nm

Sample Name: FN10151909

Acquired: March 24, 2020

Peak #	Ret Time	Area %
1	2.73	99.98
2	3.69	0.02
3	5.27	0.00

GC / FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 140°C at 40°C/min
140°C to 280°C at 5°C/min hold 5 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

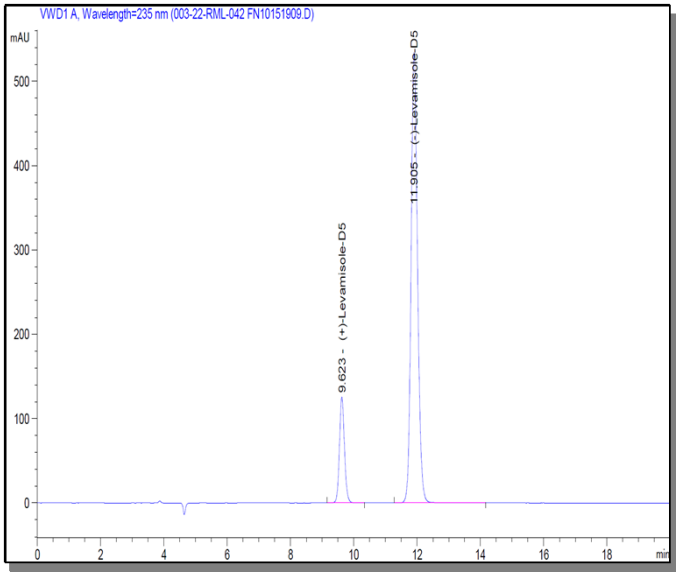
Sample Name: FN10151909

Acquired: March 24, 2020

Peak #	Ret Time	Area %
1	17.17	99.95
2	19.15	0.01
3	21.50	0.02
4	22.31	0.01

Spectral and Physical Data (cont.)

Chiral Purity Analysis by HPLC/UV



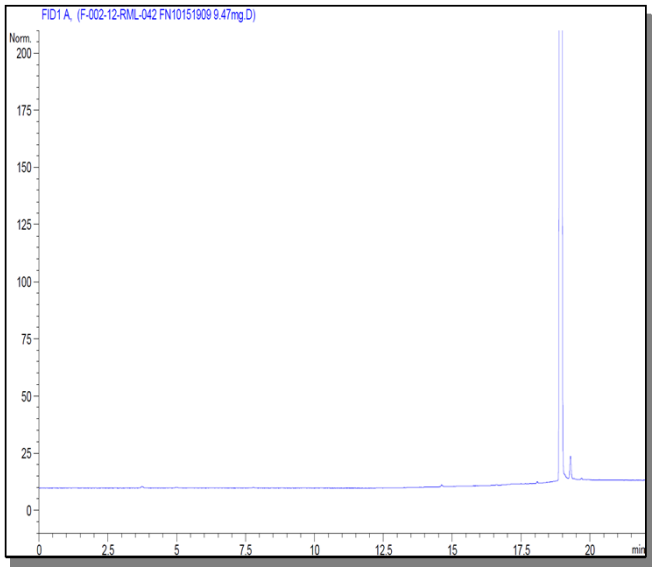
Column: Chiral-Pak AD-H, 5 µm, 4.6 x 250 mm
Mobile Phase: Hexane:Ethanol:Diethylamine (80:20:0.5)
Flow Rate: 0.8 mL/min
Wavelength: 235 nm

Sample Name: FN10151909
Acquired: March 24, 2020

Peak #	Ret Time	Area %	
1	9.62	15.42	(+)-Levamisole-D_5
2	11.91	84.58	(-)-Levamisole-D_5

% ee = 69.16%

Residual Solvent Analysis by GC/FID Headspace



Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C hold 12 min to 220°C at 40°C/min hold 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

Sample Name: FN10151909
Acquired: March 30, 2020

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

ND - None Detected

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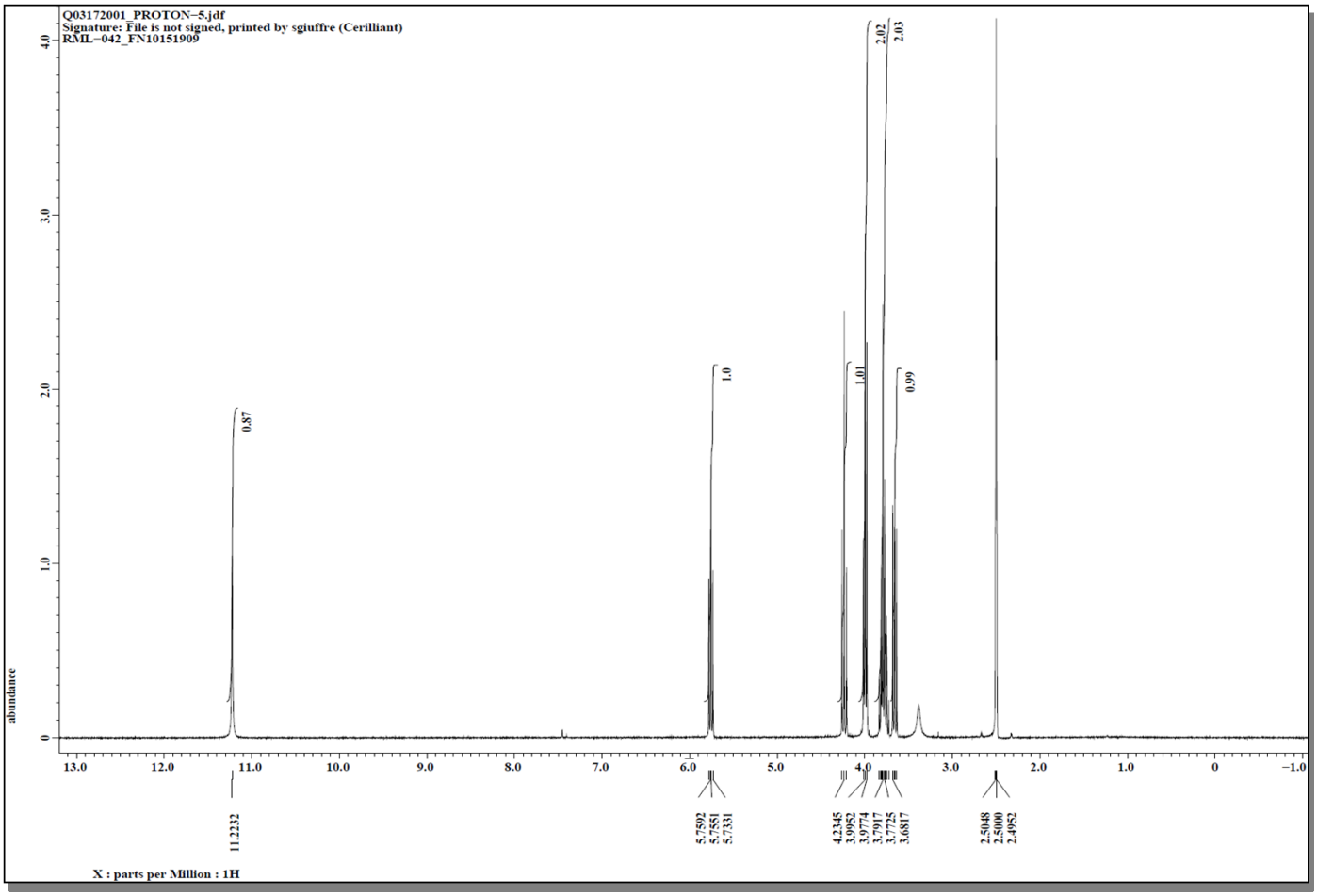
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



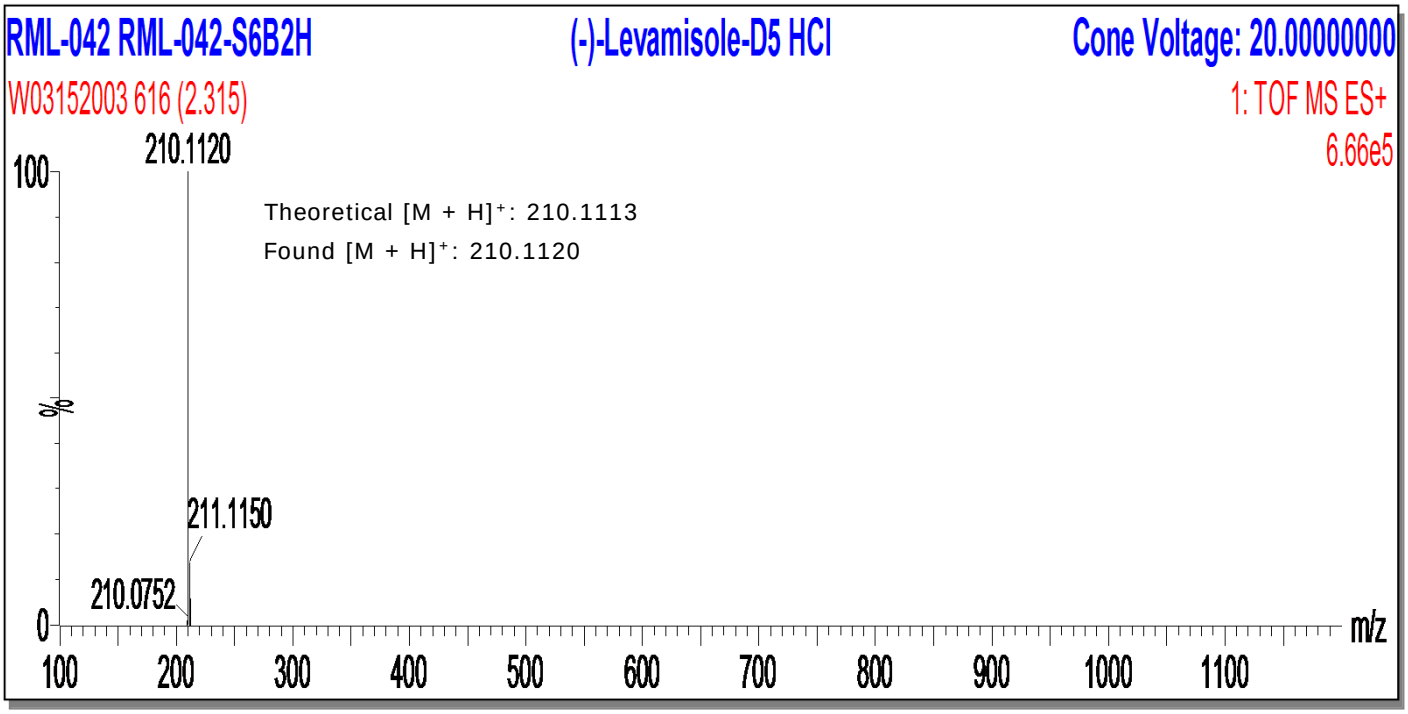
Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 15, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

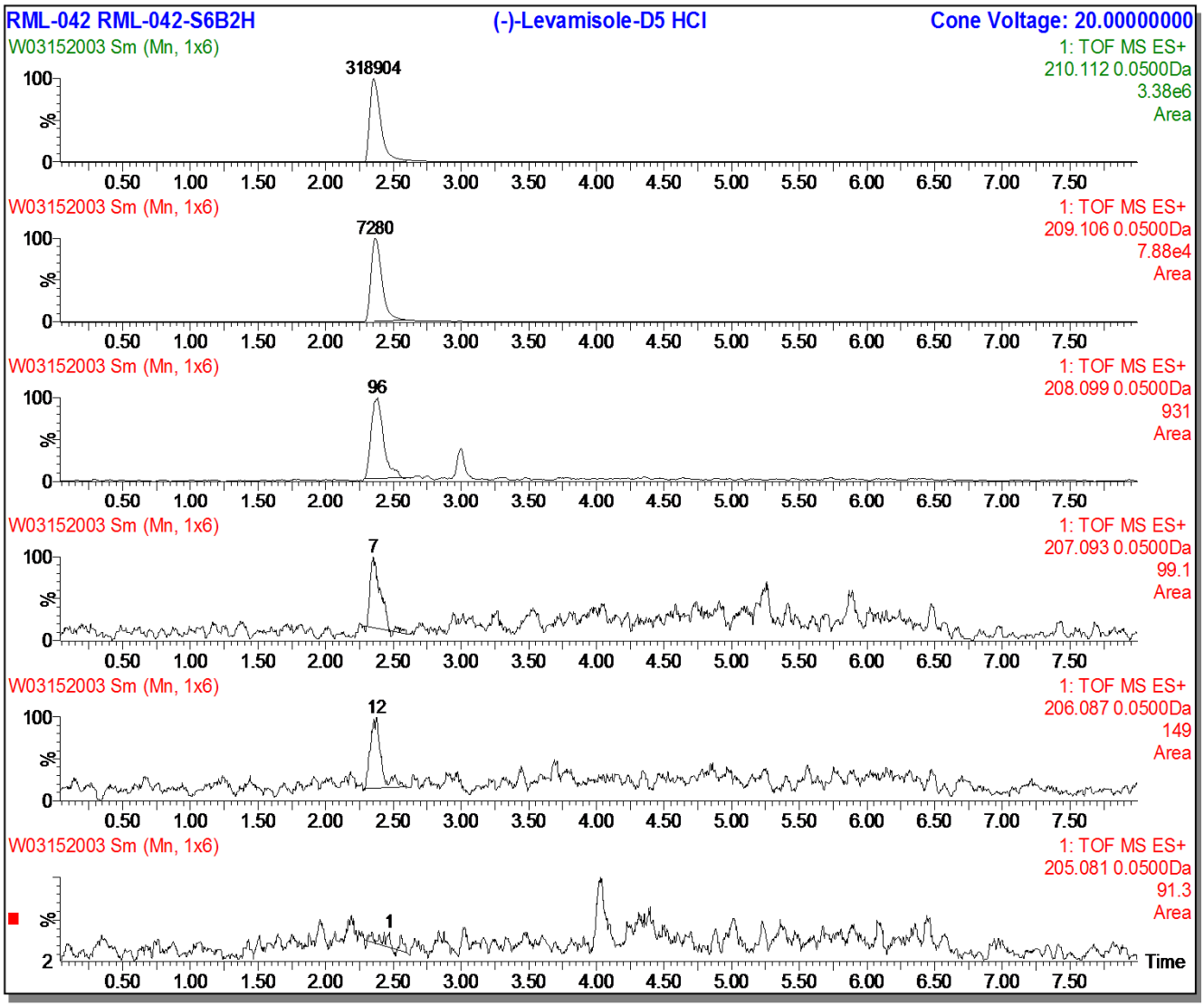
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 205-210 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: March 15, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (L-025, (-)-Levamisole 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 02, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

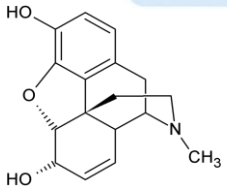
Certified Reference Material - Certificate of Analysis

Morphine, Primary Measurement Standard

(5 α,6 α)-7,8-Didehydro-4,5-epoxy-17-methylmorphinan-3,6-diol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: M-005-1ML
Lot No.: FE01082017
Description of CRM: Morphine in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{19}NO_3$
CAS No.: 57-27-2
Regulatory: USDEA Exempt | Canadian TK # 61-1273



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Morphine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darren Ellsworth, Quality Assurance Manager

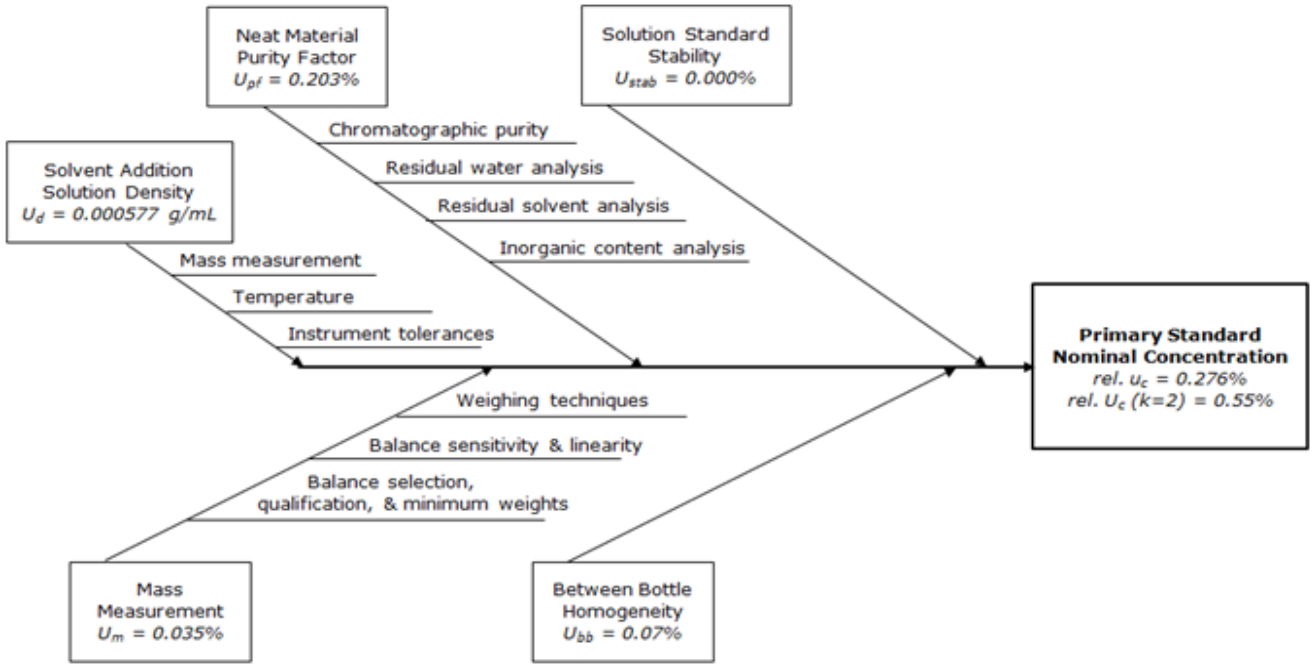
February 17, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (8:92)	**Linearity (r) :**	0.997
Flow Rate:	1.5 mL/min		
Wavelength:	220 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082017	1.012	2.5
Previous Lot	FE08221801	1.010	2.8

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Morphine	**Chemical Formula:**	$C_{17}H_{19}NO_3$
Material Lot:	FC04091901	**CAS Number:**	57-27-2
		Molecular Weight:	285.34

Material Characterization Summary

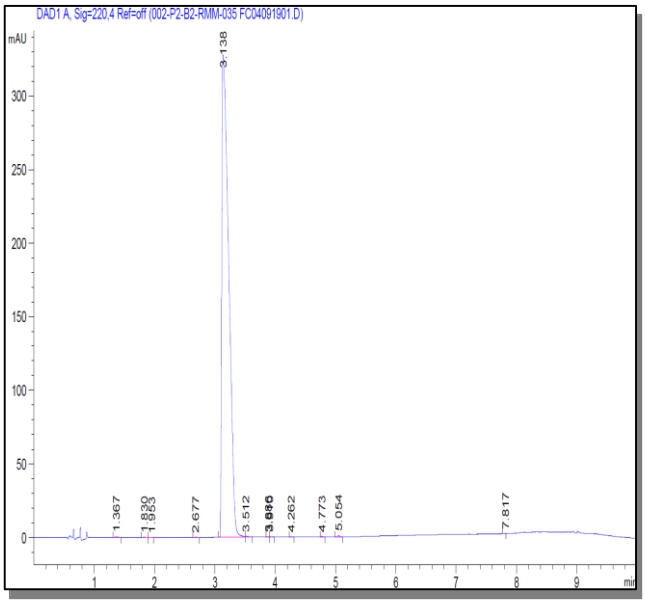
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.7%
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.31%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	1.00%
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		98.41%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
1.0	2	98
4.0	15	85
7.0	70	30
8.0	70	30
8.1	2	98

Flow Rate: 0.7 mL/min

Wavelength: 220 nm

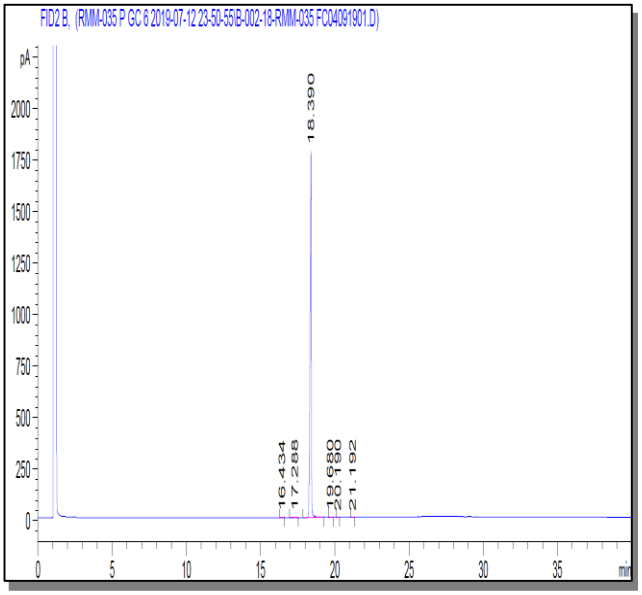
Sample Name: FC04091901

Acquired: July 09, 2019

Peak #	Ret Time	Area %
1	1.37	0.06
2	1.83	0.02
3	1.95	0.01
4	2.68	0.02
5	3.14	99.70
6	3.51	0.07
7	3.89	0.01
8	3.91	0.01
9	4.26	0.01
10	4.77	0.02
11	5.05	0.06
12	7.82	0.01

Spectral and Physical Data (cont.)

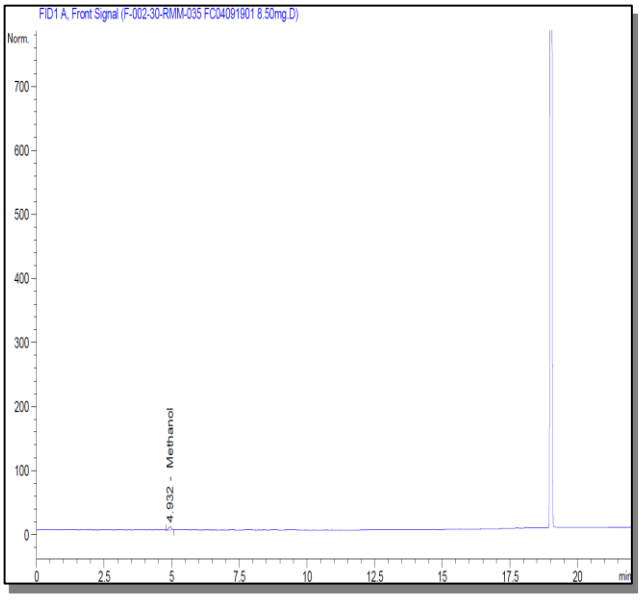
GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 300°C at 5°C/min hold 16 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC04091901
Acquired:	July 13, 2019

Peak #	Ret Time	Area %
1	16.43	0.02
2	17.29	0.09
3	18.39	99.84
4	19.68	0.03
5	20.19	0.01
6	21.19	0.01

Residual Solvent Analysis by GC/FID Headspace



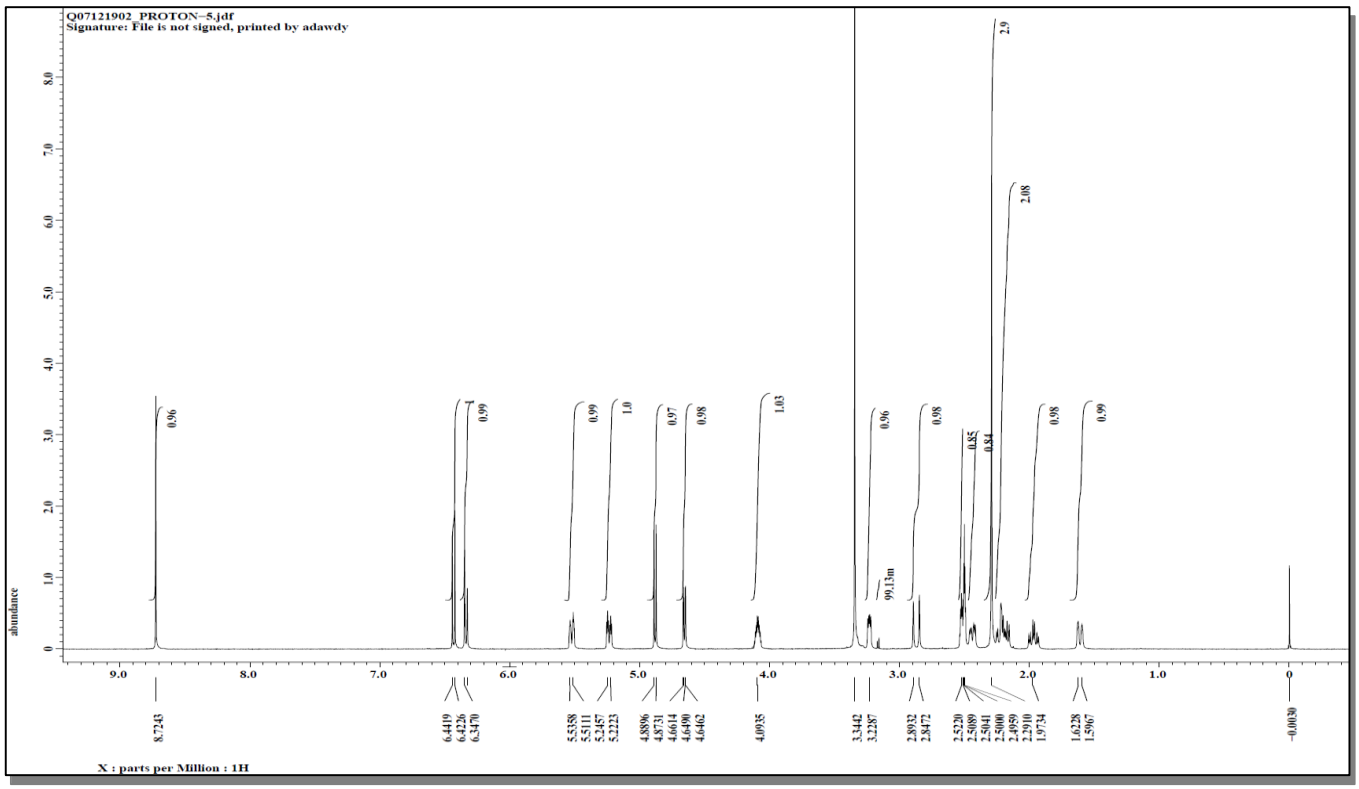
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC04091901
Acquired:	July 09, 2019

Peak	Compound	Area	Weight %
1	Methanol	33.99	0.31
2	NMP	NA	NA
Total			**0.31**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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Spectral and Physical Data (cont.)

LC/MS

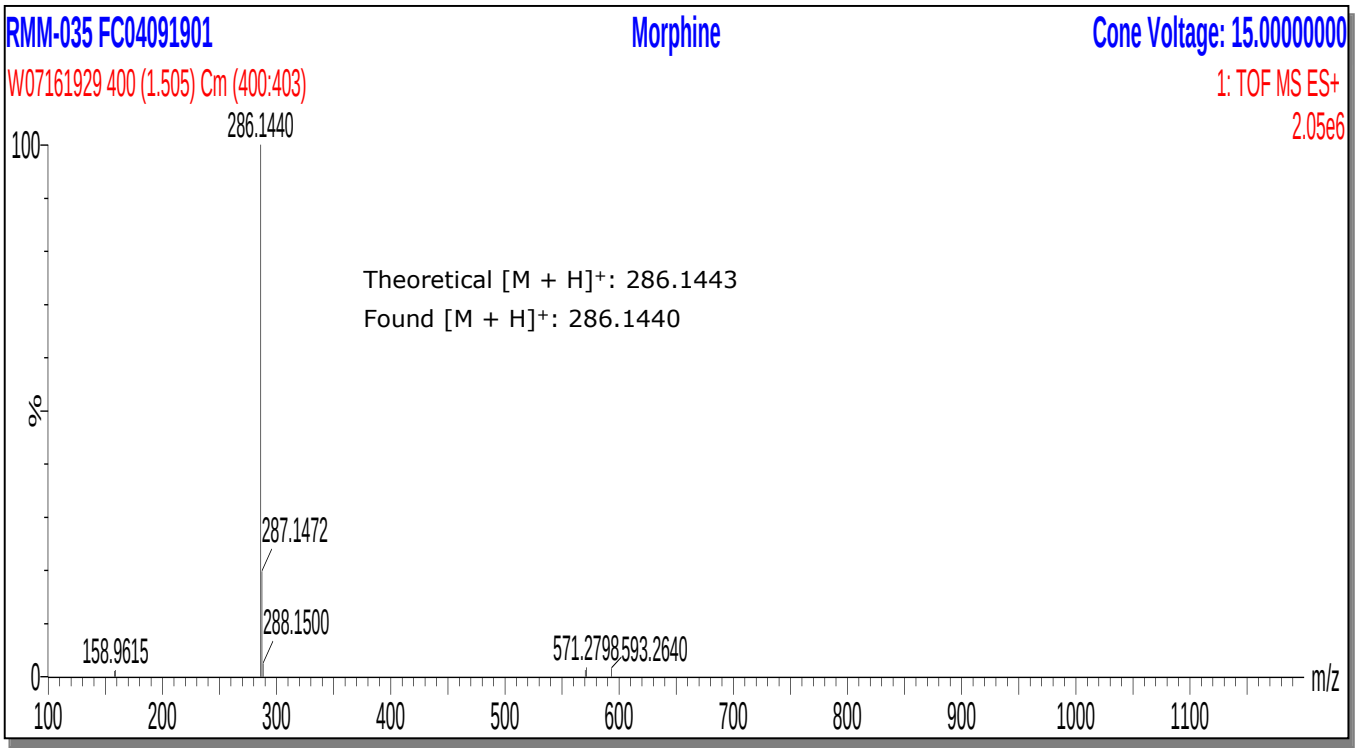
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	40	60
5.8	40	60
6.0	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 100-1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: July 16, 2019



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 17, 2020	Initial version.

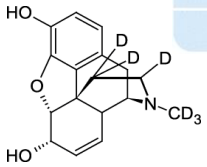
Certified Reference Material - Certificate of Analysis

Morphine-D_6, Primary Measurement Standard

5a,6a-7,8-Didehydro-4,5-epoxy-17-trideuteromethyl-15,15,16-trideutoeromorphinan-3,6-diol

Product No.: M-086-1ML
Lot No.: FE02212001
Description of CRM: Morphine-D_6 in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{13}D_6NO_3$
CAS No.: 1334606-17-5
Regulatory: USDEA Exempt | Canadian TK # 61-1319

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Morphine-D_6	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration.
Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

July 31, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

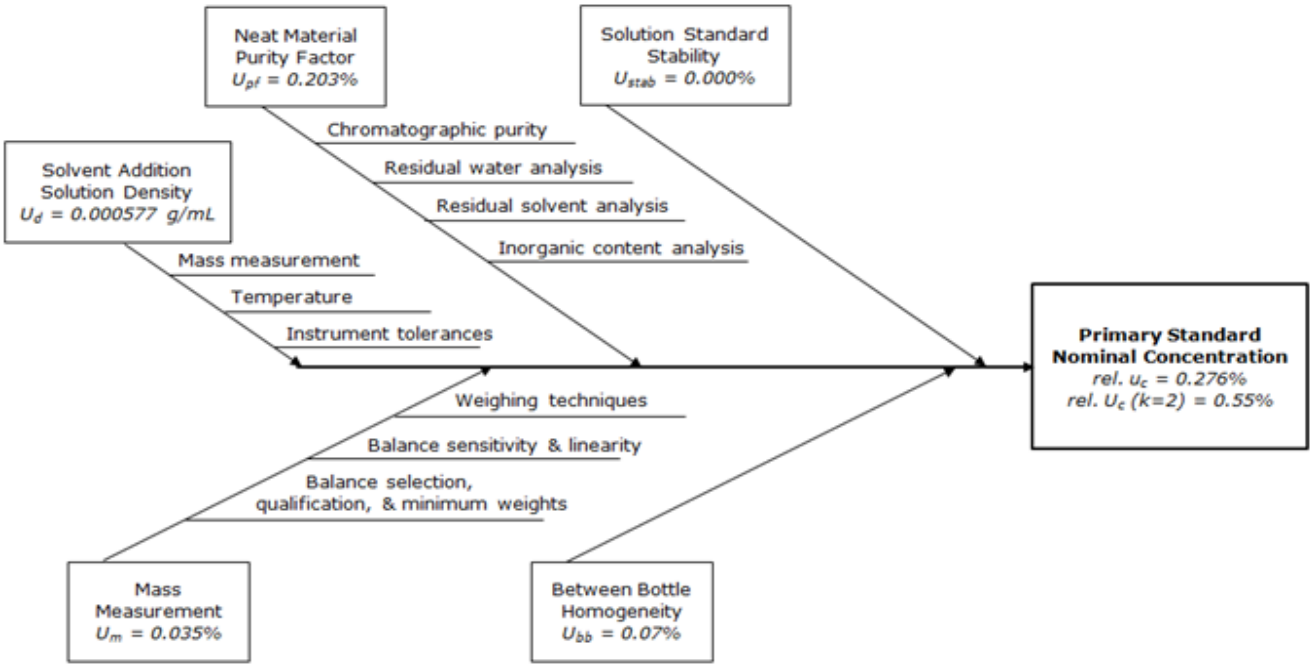
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (5:95)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	210 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02212001	1.000	0.8
Previous Lot	FE05121902	0.999	0.7

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Isotopic Distribution Comparison

The Previous Lot and the New Lot have different isotopic distributions (see table below). The analyzed concentration of the Previous Lot was adjusted for the % of D_6 relative to the New Lot. In MS applications, the New Lot can be expected to have a lower response than the Previous Lot when monitoring the D_6 mass/charge ratio.

Isotopic Distribution of the New Lot (Lot FE02212001)		**Isotopic Distribution of the Previous Lot (Lot FE05121902)**	
$\%D_0$	0.00	$\%D_0$	0.00
$\%D_1$	0.01	$\%D_1$	0.01
$\%D_2$	0.26	$\%D_2$	0.04
$\%D_3$	4.61	$\%D_3$	1.17
$\%D_4$	13.89	$\%D_4$	1.54
$\%D_5$	8.81	$\%D_5$	8.88
$\%D_6$	**70.77**	**$\%D_6$**	**86.57**
$\%D_7$	1.58	$\%D_7$	1.68
$\%D_8$	0.07	$\%D_8$	0.12
$\%D_0$ vs D_6	0.00	$\%D_0$ vs D_6	0.00

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Morphine-D_6	**Chemical Formula:**	$C_{17}H_{13}D_6NO_3$
Material Lot:	FC07311901	**CAS Number:**	1334606-17-5
		Molecular Weight:	291.37

Material Characterization Summary

Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.3% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	> 99.9%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis [2]	20384217	0.00% D_0 vs D_6	
		0.00% D_0	8.81% D_5
		0.01% D_1	70.77% D_6
		0.26% D_2	1.58% D_7
		4.61% D_3	0.07% D_8
		13.89% D_4	
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [3]	1.33%	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [3]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		97.96%	

[1] 0.01% 6-Acetylmorphine detected by HPLC/UV analysis

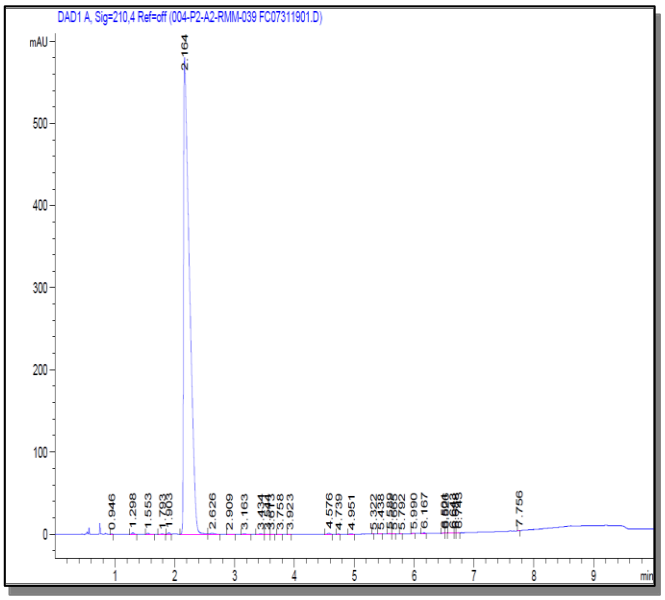
[2] Isotopic distribution values are adjusted for the natural abundance of isotopes (M + 1 adjusted 19.03%; M + 2 adjusted 2.33%).

[3] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
1.0	2	98
4.0	10	90
7.0	50	50
9.0	50	50
9.1	2	98

Flow Rate: 0.8 mL/min

Wavelength: 210 nm

Sample Name: FC07311901

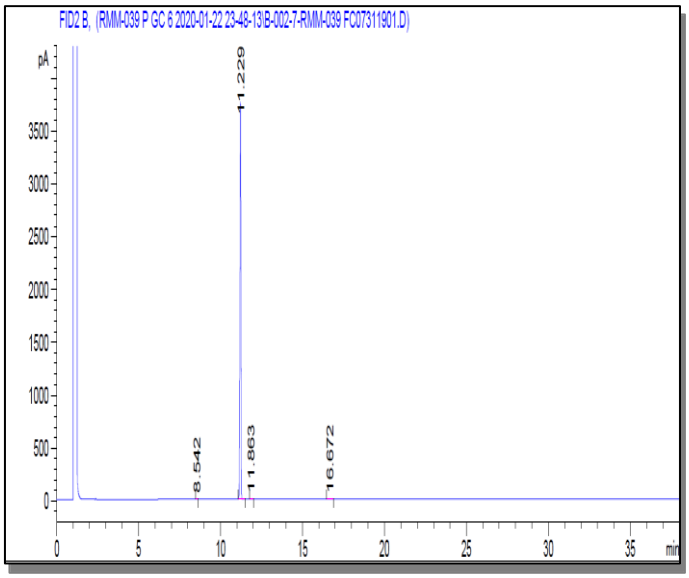
Acquired: January 30, 2020

Peak #	Ret Time	Area %
1	0.95	0.01
2	1.30	0.10
3	1.55	0.07
4	1.79	0.03
5	1.90	0.09
6	2.16	99.24
7	2.63	0.12
8	2.91	0.02
9	3.16	0.04
10	3.43	0.03
11	3.54	0.02
12	3.61	0.01
13	3.76	0.00
14	3.92	0.00
15	4.58	0.07
16	4.74	0.01
17	4.95	0.01
18	5.32	0.00
19	5.44	0.02
20	5.59	0.01
21	5.67	0.01
22	5.79	0.00
23	5.99	0.00
24	6.17	0.04
25	6.50	0.01
26	6.53	0.01
27	6.64	0.01
28	6.69	0.00
29	6.74	0.01
30	7.76	0.01

Peak #21 has been identified as 6-Acetylmorphine.

Spectral and Physical Data (cont.)

GC/FID

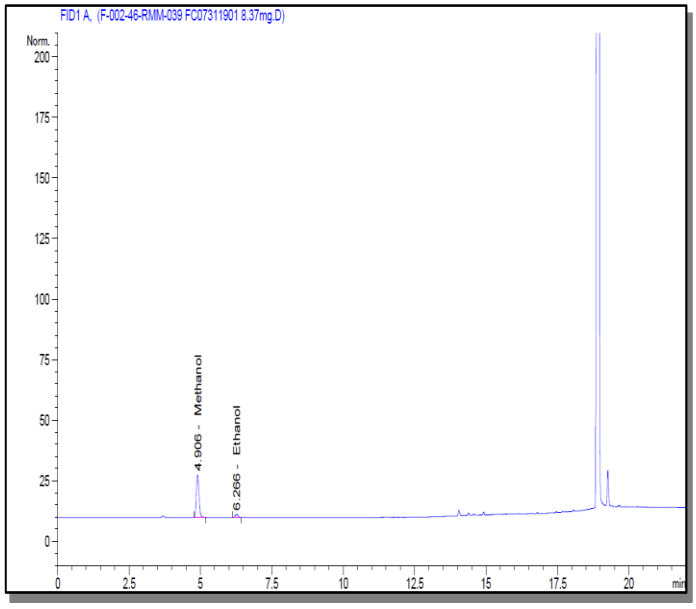


Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC07311901
Acquired: January 23, 2020

Peak	Ret Time	Area %
1	8.54	0.01
2	11.23	99.98
3	11.86	0.01
4	16.67	0.01

Residual Solvent Analysis by GC/FID Headspace



Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C hold 12 min to 220°C at 40°C/min hold 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

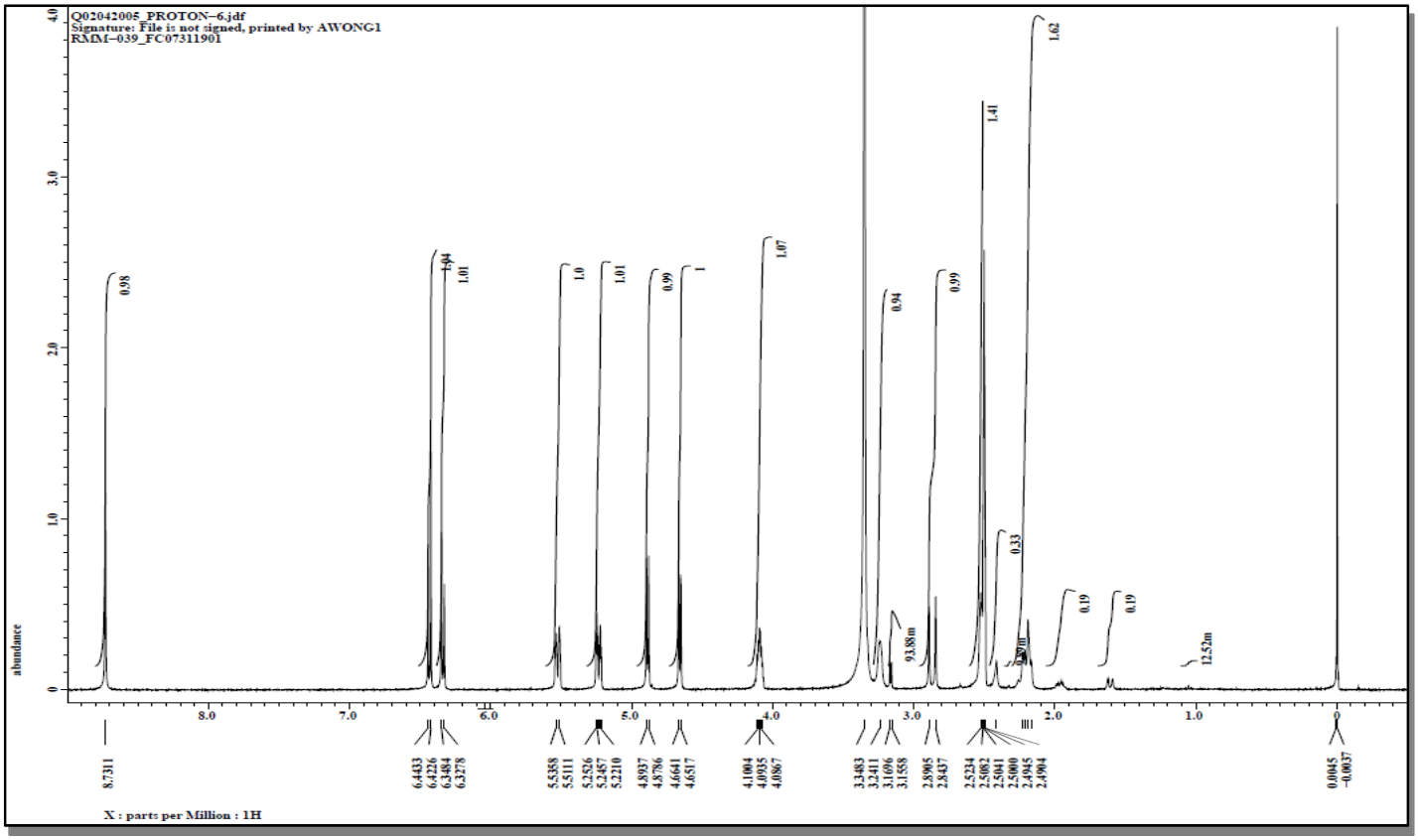
Sample Name: FC07311901
Acquired: January 07, 2020

Peak	Compound	Area	Weight %
1	Methanol	116.52	1.22
2	Ethanol	9.73	0.11
3	NMP	NA	NA
Total			**1.33**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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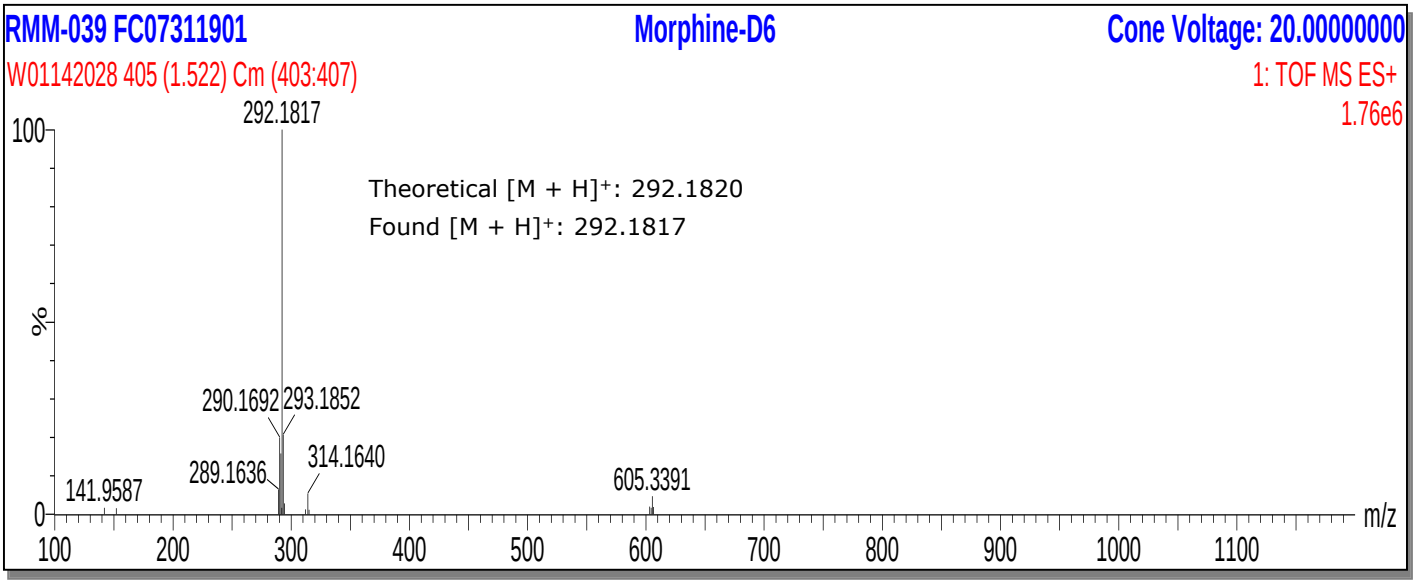
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 14, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

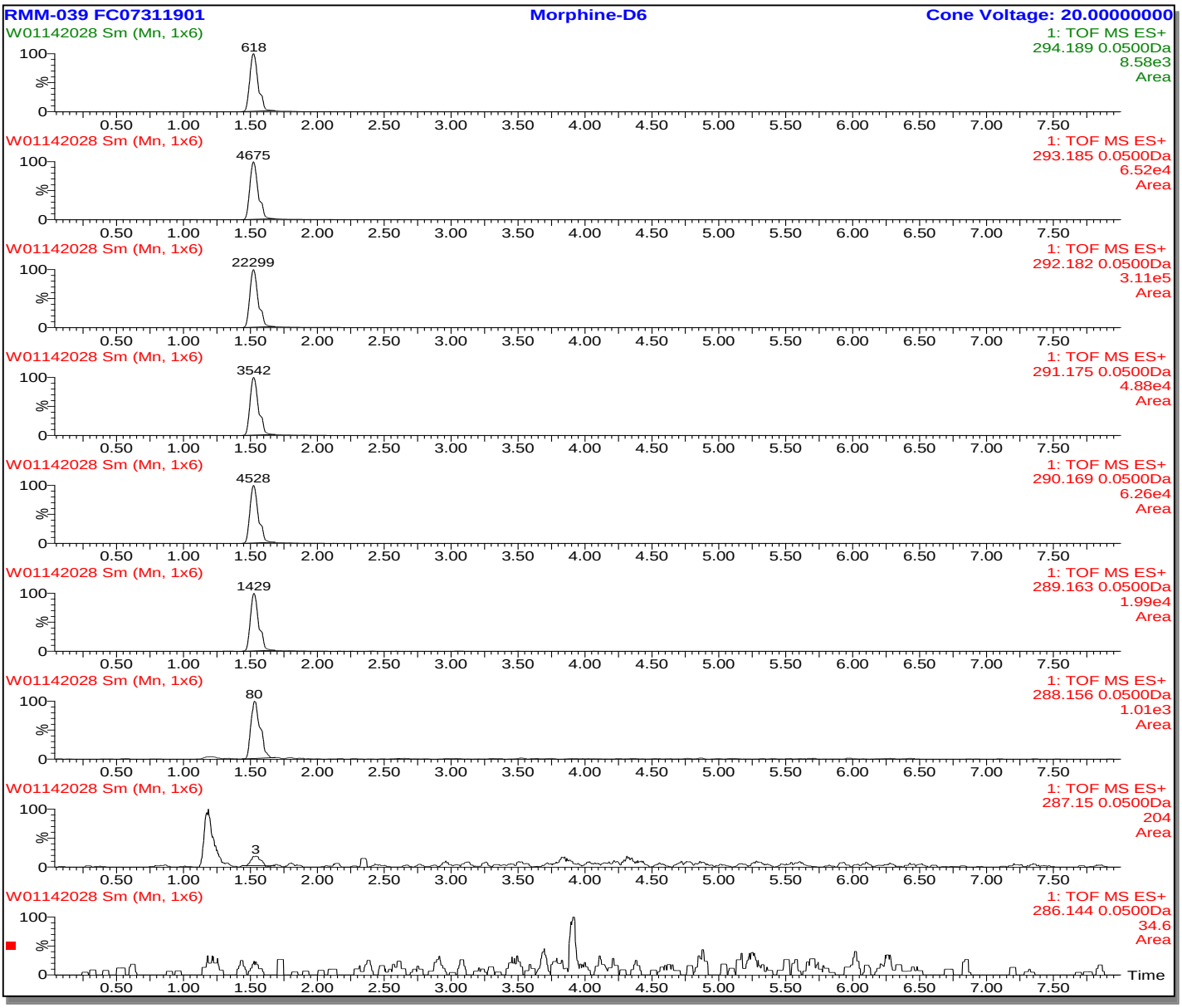
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 286-294 amu
Ionization: Electrospray, Negative Ion
Instrument: Waters XEVO G2 QTOF
Acquired: January 14, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (M-109, Morphine) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 08, 2020	Initial version.
01	June 23, 2020	Added Isotopic Distribution Comparison table.
02	July 31, 2020	Corrected Isotopic Distribution Comparison to state "lower response".

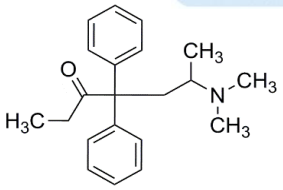
Certified Reference Material - Certificate of Analysis

(±)-Methadone, Primary Measurement Standard

(±)-6-Dimethylamino-4,4-diphenyl-3-heptanone

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: M-007-1ML
Lot No.: FE02272002
Description of CRM: (±)-Methadone in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{21}H_{27}NO$
CAS No.: 76-99-3
Regulatory: USDEA Exempt | Canadian TK # 61-1275



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Methadone	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

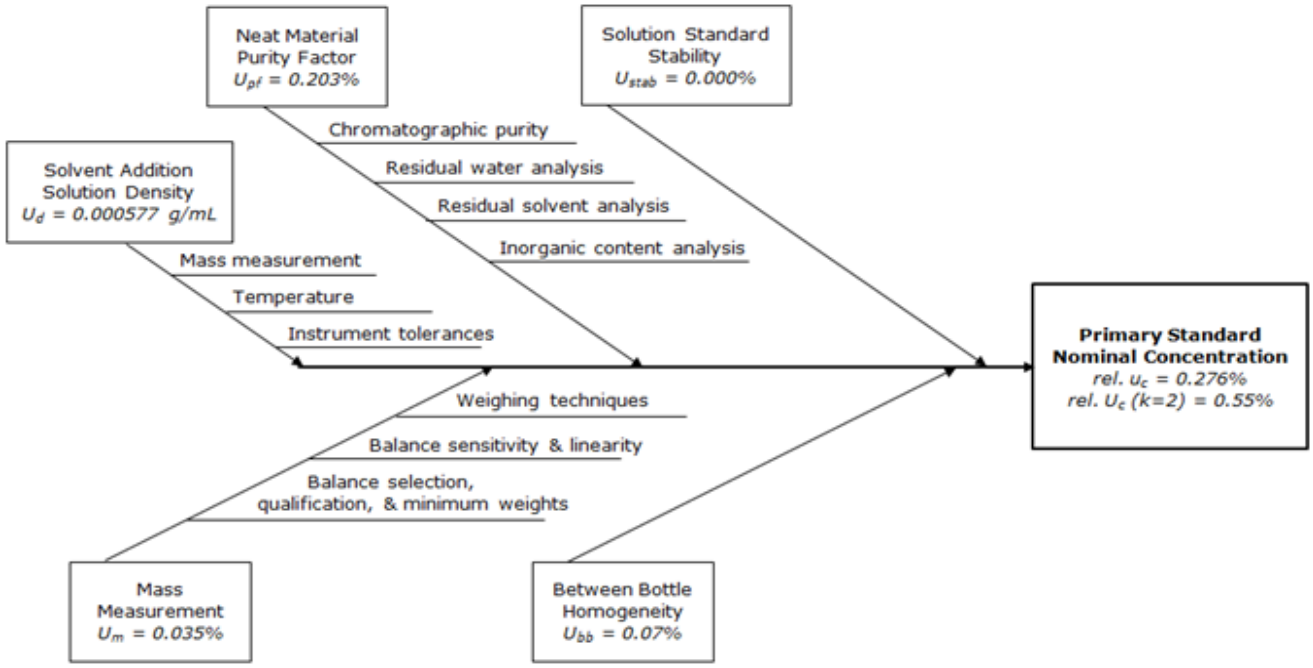
April 06, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms 30 m x 0.53 mm ID, 1.5 µm film thickness	**Number of Points:**	4
Temp Program:	60°C to 280°C at 40°C/min hold 7 min	**Linearity (r) :**	1.000
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02272002	0.995	0.3
Previous Lot	FE08091801	0.993	0.5

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Methadone	**Chemical Formula:**	$C_{21}H_{27}NO$
Material Lot:	FC08301902	**CAS Number:**	76-99-3
		Molecular Weight:	309.45

Material Characterization Summary

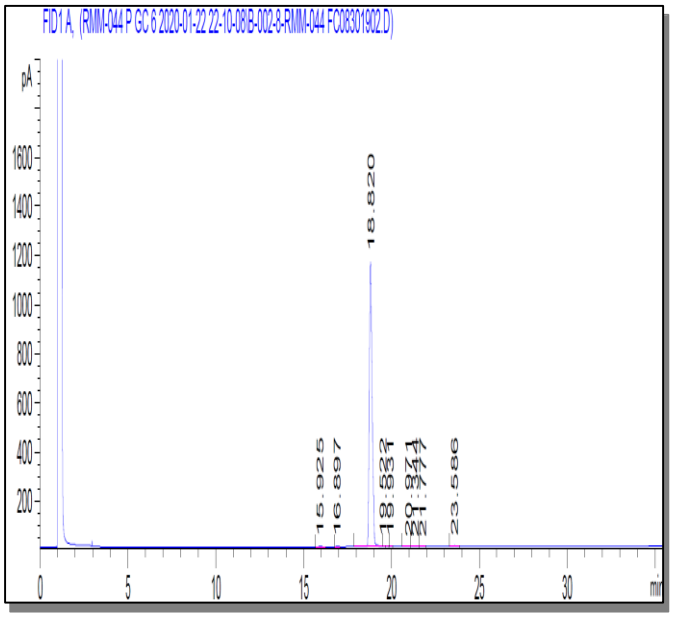
Analytical Test	Method	Results
Primary Chromatographic Purity by GC/FID Analysis	20384346	99.7%
Secondary Chromatographic Purity by HPLC/UV Analysis	20384348	> 99.9%
Identity by GC/MS Analysis	20384214	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	0.05%
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.69%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

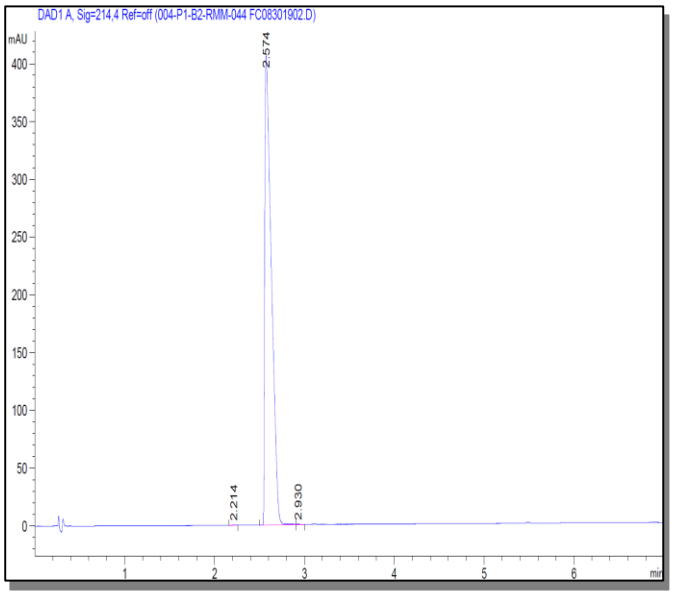
GC/FID



Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 180°C at 40°C/min 180°C to 280°C at 5°C/min hold 12 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC08301902
Acquired:	January 22, 2020

Peak #	Ret Time	Area %
1	15.93	0.05
2	16.90	0.03
3	18.82	99.67
4	19.52	0.01
5	19.93	0.00
6	20.97	0.03
7	21.34	0.04
8	21.78	0.05
9	23.59	0.12

HPLC/UV



Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm
Mobile Phase:	A: Acetonitrile B: 0.1% Phosphoric acid in Water

Gradient:

Time (min)	% A	% B
0.0	20	80
5.0	80	20
6.0	80	20
6.1	20	80

Flow Rate:	0.8 mL/min
Wavelength:	214 nm
Sample Name:	FC08301902
Acquired:	January 03, 2020

Peak #	Ret Time	Area %
1	2.21	0.01
2	2.57	99.96
3	2.93	0.03

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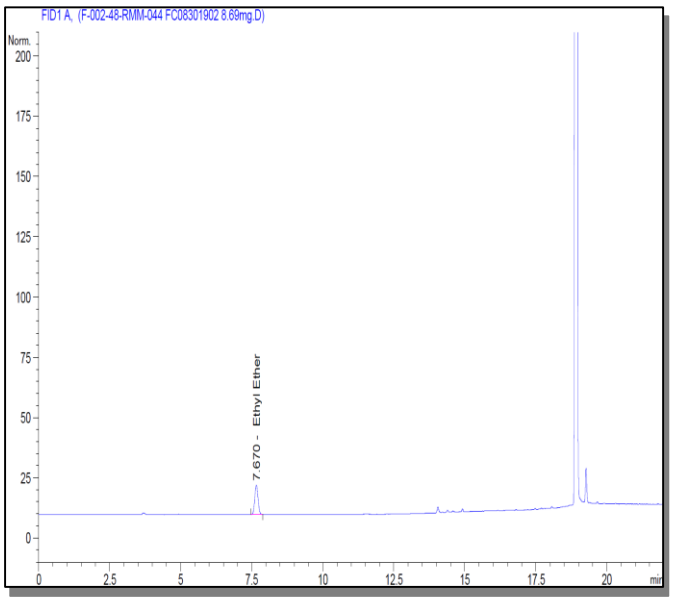
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

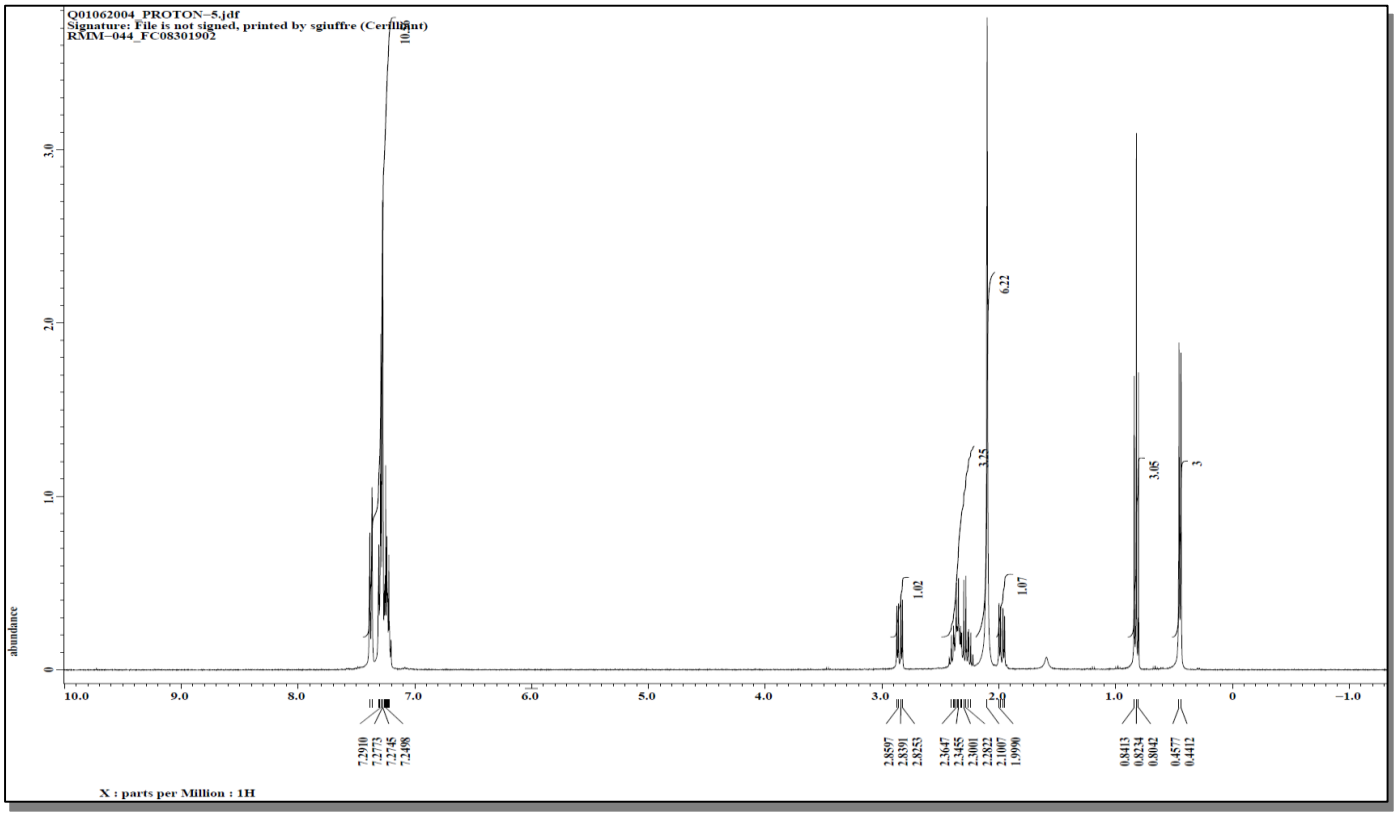


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC08301902
Acquired:	January 07, 2020

Peak	Compound	Area	Weight %
1	Ethyl ether	98.75	0.05
2	NMP	NA	NA
Total			**0.05**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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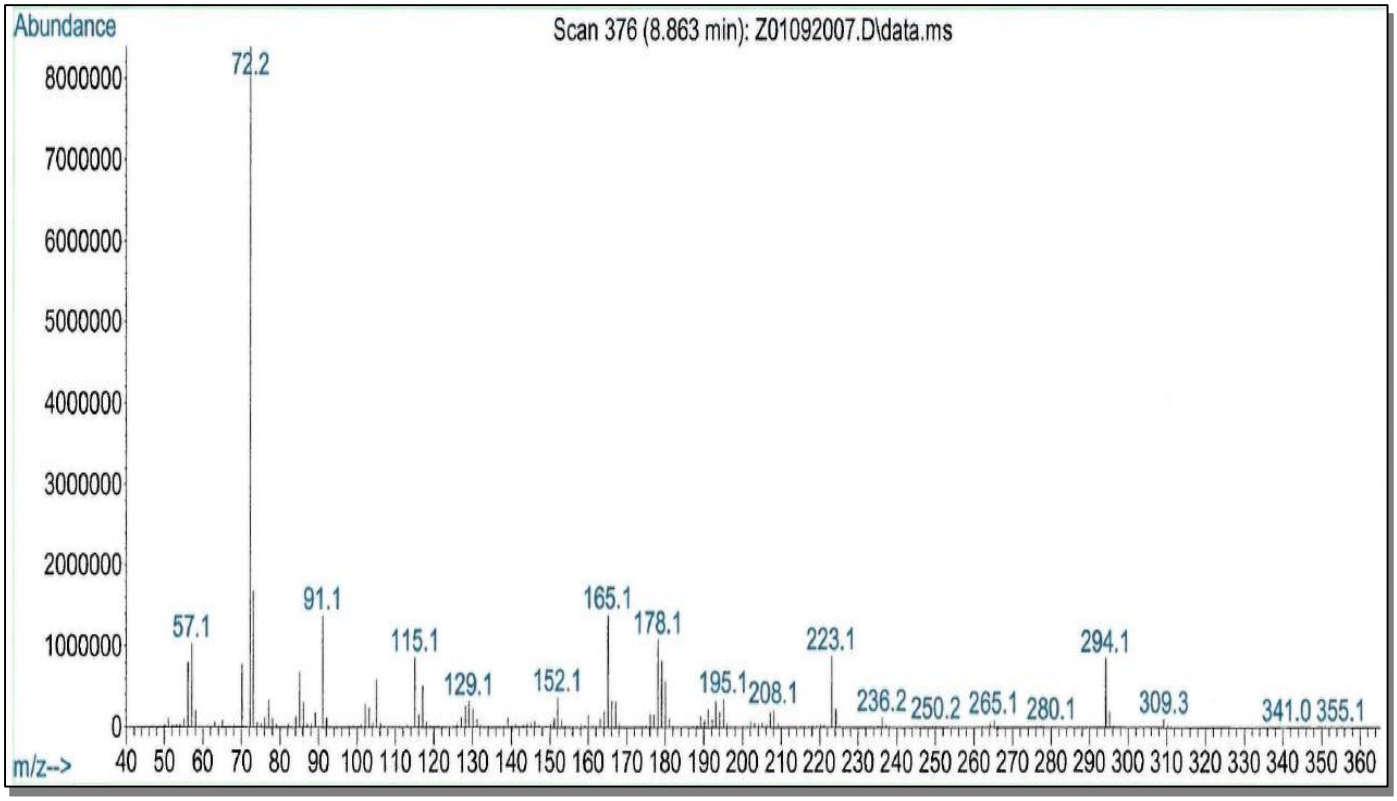
Spectral and Physical Data (cont.)

GC/MS

Column:	DB-5ms 30 m x 0.25 mm ID, 0.25 µm film thickness	**Scan Range:**	50-500 amu
		Instrument:	Agilent GC/MS
Temp Program:	50°C to 200°C at 40°C/min 200°C to 300°C at 10°C/min hold 16 min	**Acquired:**	January 09, 2020



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (M-008, (±)-Methadone-D_3) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 06, 2020	Initial version.

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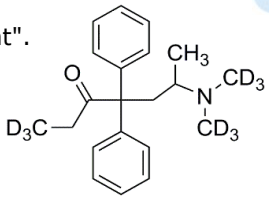
Certified Reference Material - Certificate of Analysis

(±)-Methadone-D_9, Primary Measurement Standard

(±)-6-Di(trideuteromethyl)amino-4,4-diphenyl-1-1-1,1-trideuteromethyl-3-heptanone

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: M-089-1ML
Lot No.: FE01082012
Description of CRM: (±)-Methadone-D_9 in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{21}H_{18}D_9NO$
CAS No.: 1435933-74-6
Regulatory: USDEA Exempt | Canadian TK # 61-1321



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Methadone-D_9	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

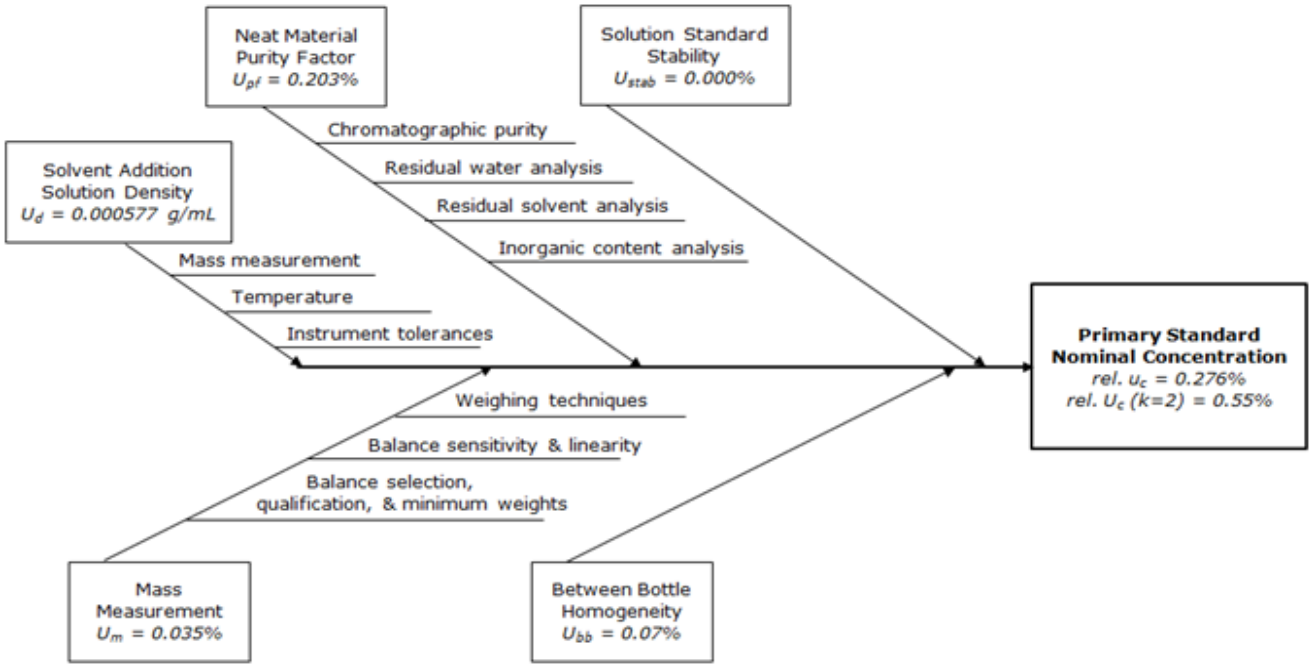
February 18, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms 30 m x 0.53 mm ID, 1.5 µm film thickness	**Number of Points:**	4
Temp Program:	60°C to 280°C at 40°C/min hold 7 min	**Linearity (r) :**	1.000
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082012	0.992	0.4
Previous Lot	FE05101801	0.985	0.6

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Methadone-D_9	**Chemical Formula:**	$C_{21}H_{18}D_9NO$
Material Lot:	FC07311801	**CAS Number:**	1435933-74-6
		Molecular Weight:	318.50

Material Characterization Summary

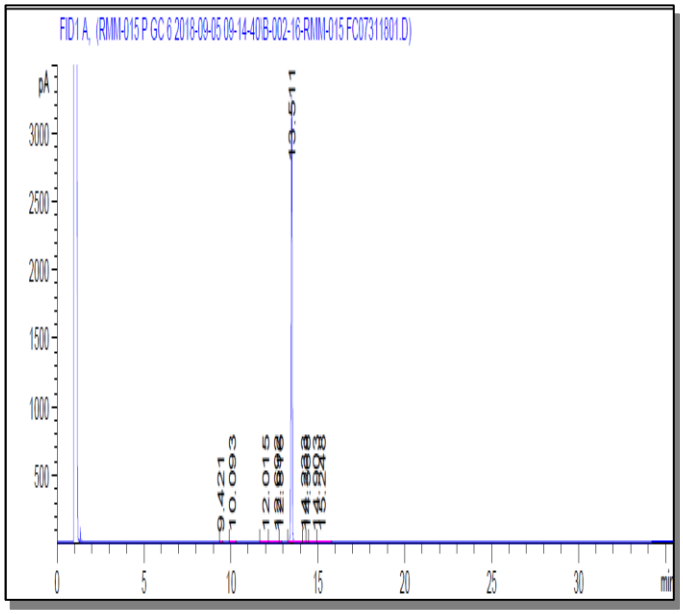
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.8%	
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	> 99.9%	
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure	
Isotopic Purity and Distribution by GC/MS SIM Analysis	SP10-0105	0.06% D_0 vs D_9	
		0.05% D_0	0.41% D_5
		0.07% D_1	1.23% D_6
		0.13% D_2	2.66% D_7
		0.18% D_3	12.40% D_8
		0.50% D_4	82.38% D_9
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.00% D_0 vs D_9	
		0.00% D_0 to D_7	98.31% D_9
		1.69% D_8	
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.02%	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	None Detected	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.75%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

GC/FID

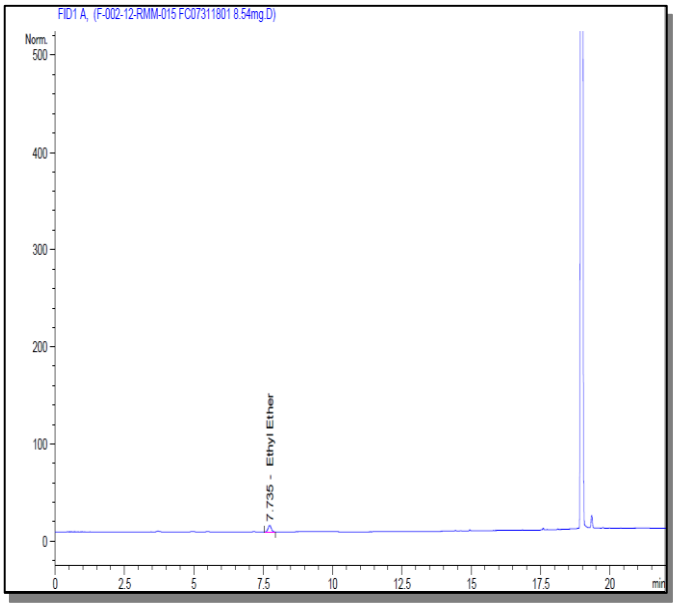


Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 180°C at 40°C/min
180°C to 280°C at 5°C/min
hold 12 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC07311801
Acquired: September 05, 2018

Peak #	Ret Time	Area %
1	9.42	0.00
2	10.09	0.01
3	12.02	0.02
4	12.69	0.02
5	12.82	0.00
6	13.51	99.81
7	14.23	0.02
8	14.37	0.02
9	14.90	0.04
10	15.25	0.06

HPLC/UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm
Mobile Phase: A: Acetonitrile
B: 0.1% Phosphoric acid in Water
Gradient:

Time (min)	% A	% B
0.0	20	80
5.0	80	20
6.0	80	20
6.1	20	80

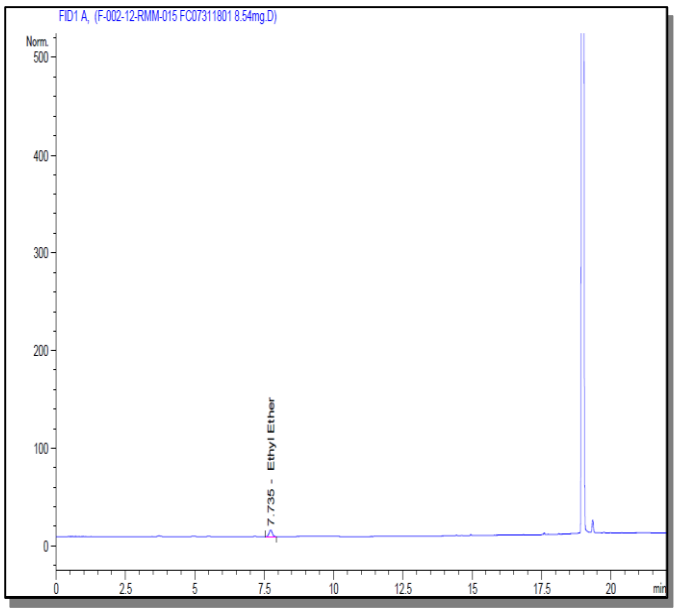
Flow Rate: 0.8 mL/min
Wavelength: 214 nm

Sample Name: FC07311801
Acquired: August 30, 2018

Peak #	Ret Time	Area %
1	2.54	99.98
2	3.31	0.02

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

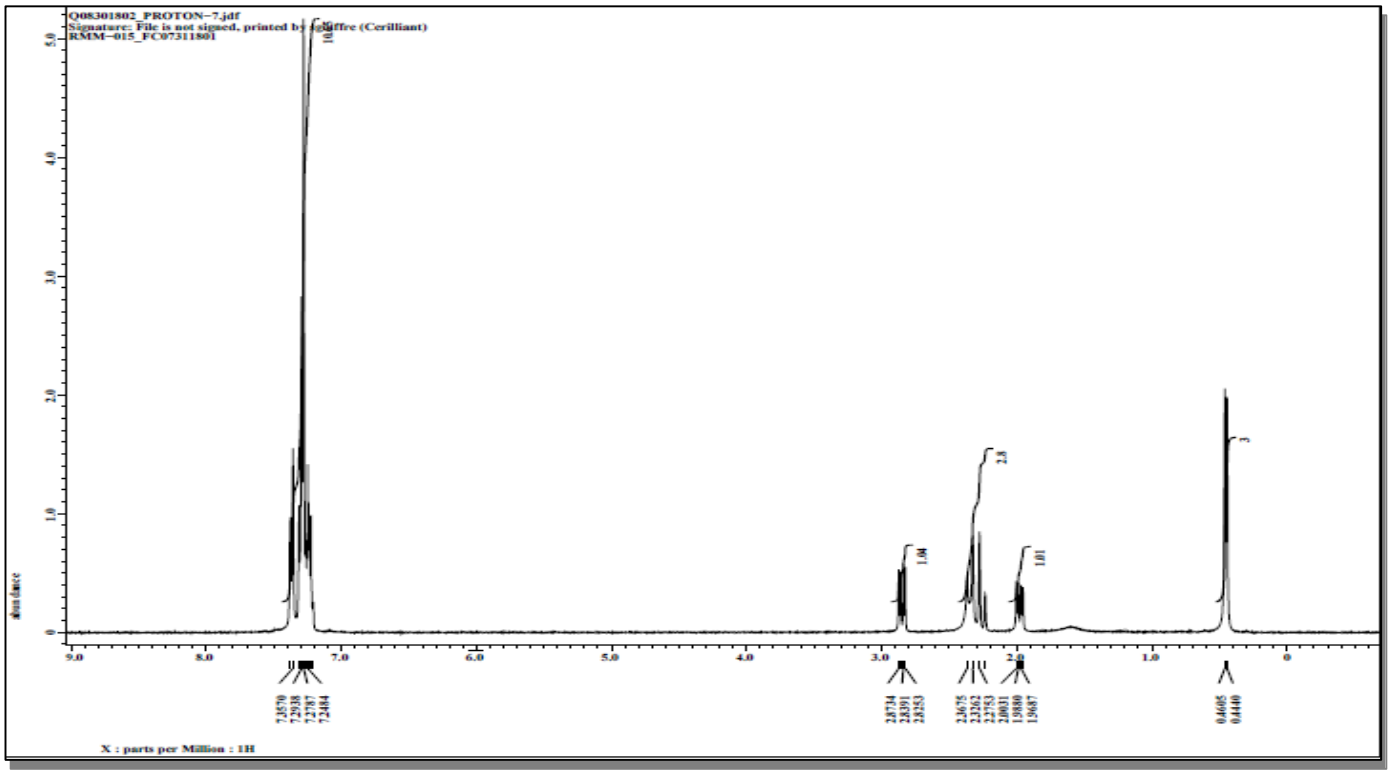


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC07311801
Acquired:	September 14, 2018

Peak	Compound	Area	Weight %
1	Ethyl ether	53.59	0.02
2	NMP	NA	NA
Total			**0.02**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

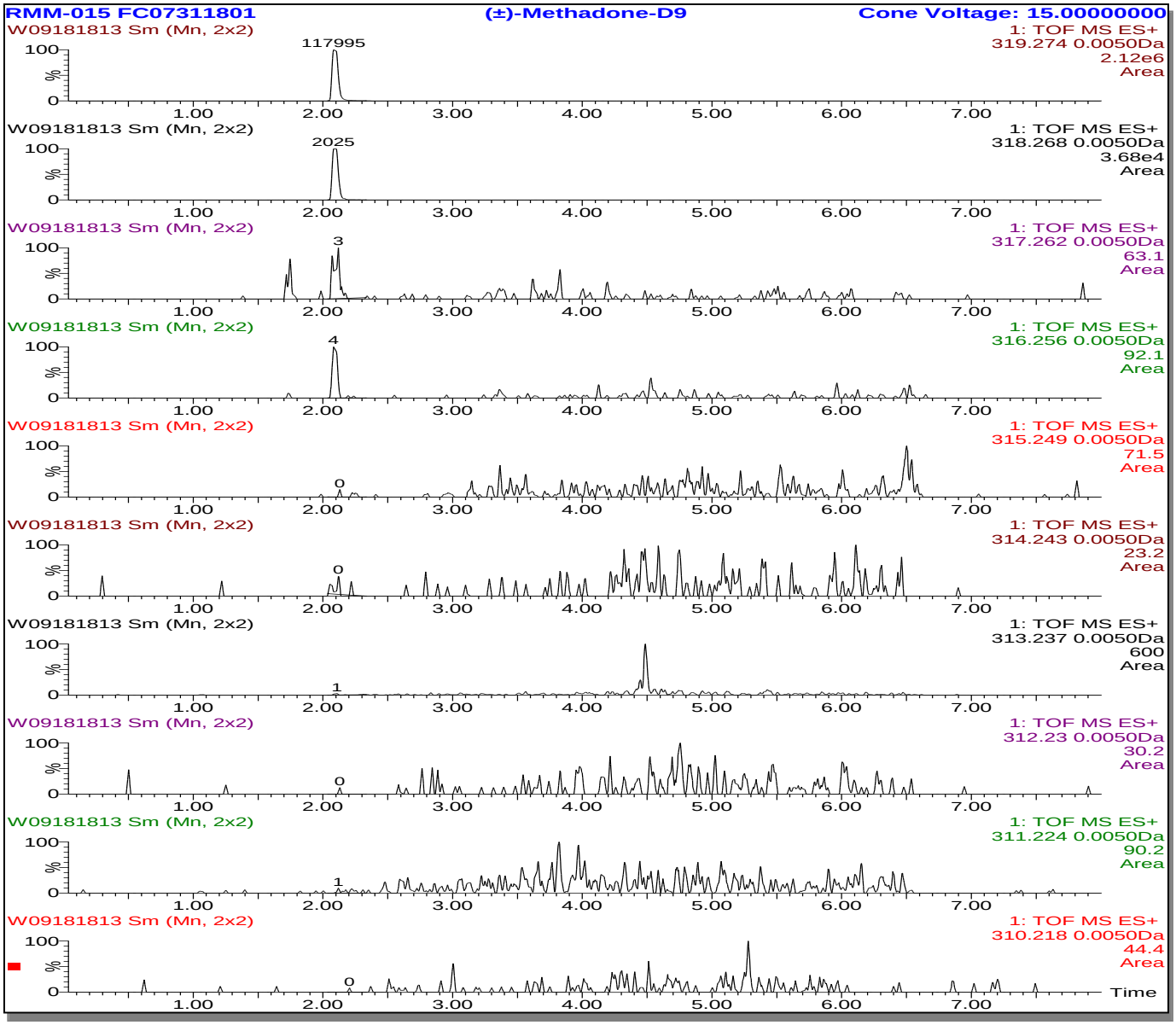
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	80	20
0.5	80	20
4.0	20	80
5.8	20	80
6.0	80	20
8.0	80	20

Flow Rate: 0.4 mL/min
Scan Range: 310-319 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: September 18, 2018



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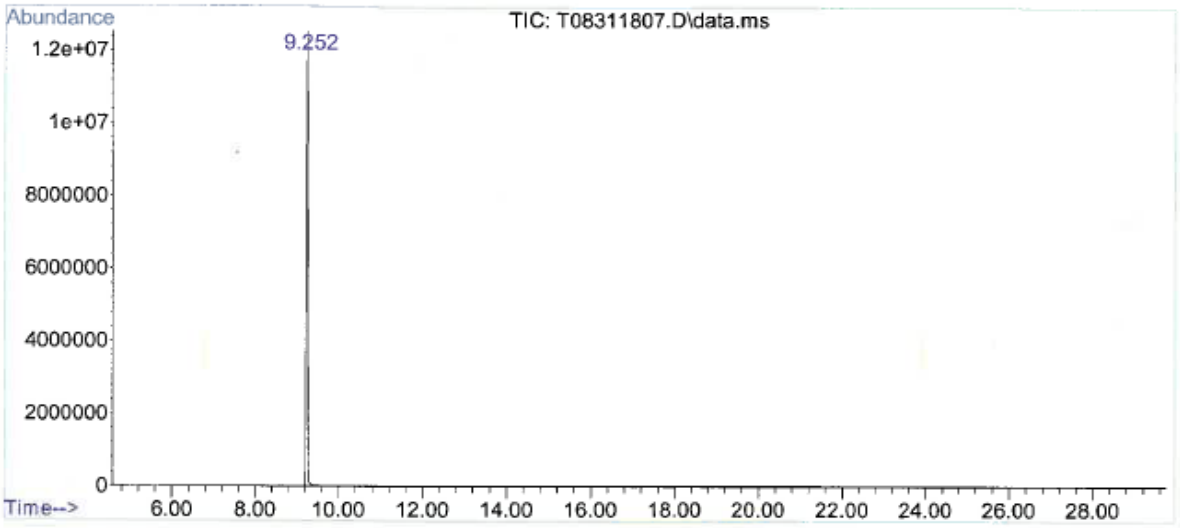
Spectral and Physical Data (cont.)

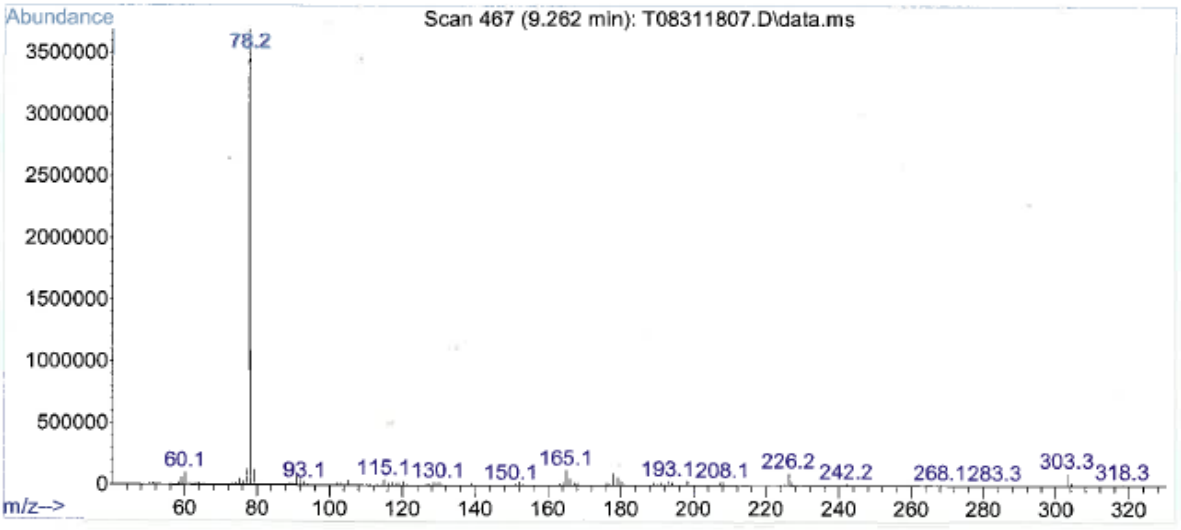
GC/MS

```
Compound Name        : (±)-Methadone-D9
Lot Number           : FC07311801
Instrument           : Agilent GCMS
Operator             : ECM(SGIUFFRE)
Date Reported        : Tue Sep 04 07:43:31 2018
Column Type          : DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program        : 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.       : Cool on-column
Carrier Gas          : Helium
Flow Rate (mL\min)   : 0.80 mL/min
Transfer Line Temp.  : 280°C
Scan Range           : 50-500
```

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (M-019, (±)-Methadone) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 18, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

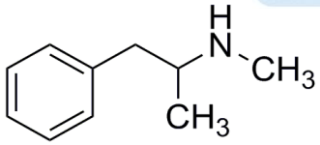
Certified Reference Material - Certificate of Analysis

(±)-Methamphetamine, Primary Measurement Standard

1-Phenyl-2-methylaminopropane

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: M-009-1ML
Lot No.: FE03022006
Description of CRM: (±)-Methamphetamine in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{10}H_{15}N$
CAS No.: 7632-10-2
Regulatory: USDEA Exempt | Canadian TK # 61-1277



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Methamphetamine	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

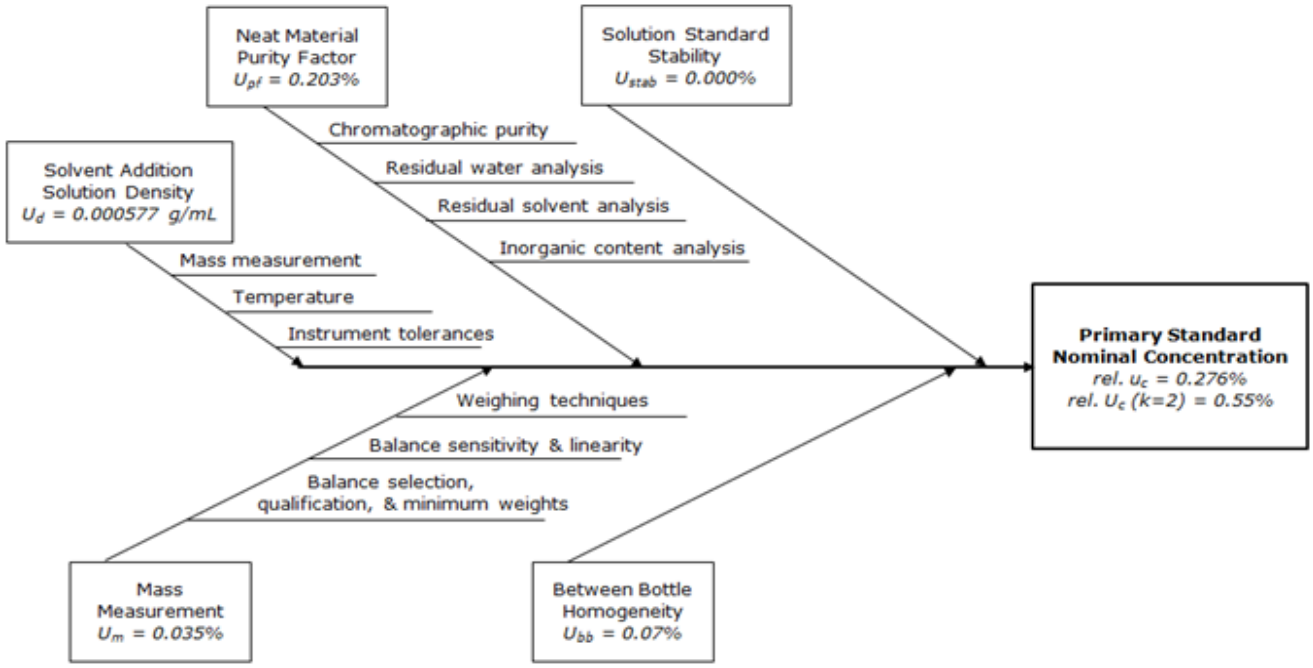
July 16, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms 30 m x 0.53 mm ID, 1.5 µm film thickness	**Number of Points:**	4
Temp Program:	60°C to 260°C at 20°C/min hold 1 min	**Linearity (r) :**	1.000
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE03022006	1.015	0.6
Previous Lot	FE01152002	1.018	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Methamphetamine	**Chemical Formula:**	$C_{10}H_{15}N$
Material Lot:	FC12131901	**CAS Number:**	7632-10-2
		Molecular Weight:	149.23

Material Characterization Summary

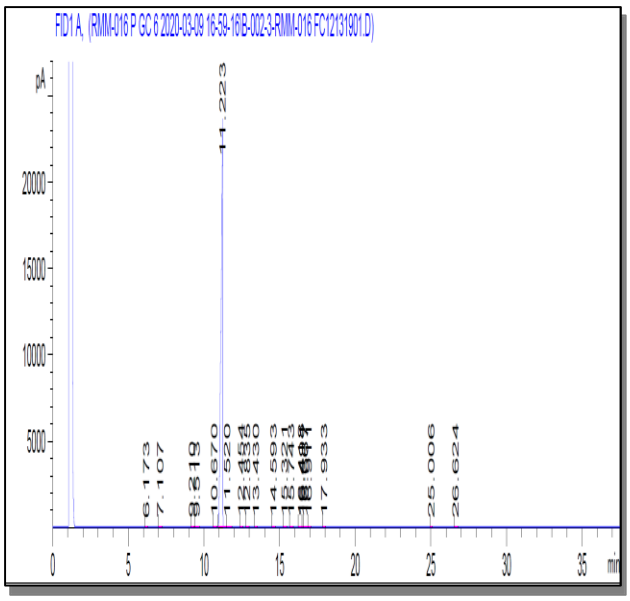
Analytical Test	Method	Results
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.9%
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.9%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	None Detected
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit
Mass Balance Purity Factor		99.89%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

GC/FID



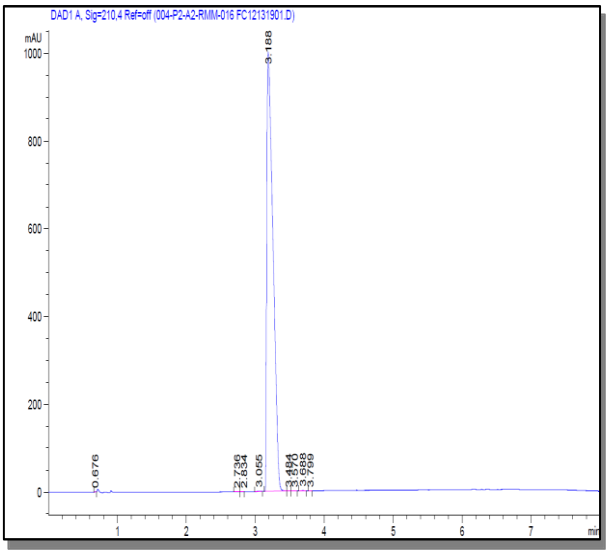
Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 80°C at 40°C/min
80°C to 175°C at 5°C/min
175°C to 300°C at 10°C/min
hold 5 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC12131901
Acquired: March 09, 2020

Peak #	Ret Time	Area %
1	6.17	0.01
2	7.11	0.00
3	9.21	0.00
4	9.51	0.02
5	10.67	0.03
6	11.22	99.88
7	11.52	0.01
8	12.45	0.00
9	12.84	0.01
10	13.43	0.00
11	14.59	0.03
12	15.32	0.00
13	15.74	0.00
14	16.42	0.00
15	16.49	0.00
16	16.67	0.00
17	16.91	0.00
18	17.93	0.00
19	25.01	0.00
20	26.62	0.00

Spectral and Physical Data (cont.)

HPLC/UV



Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm
Mobile Phase:	A: Acetonitrile B: 0.1% Phosphoric acid in Water

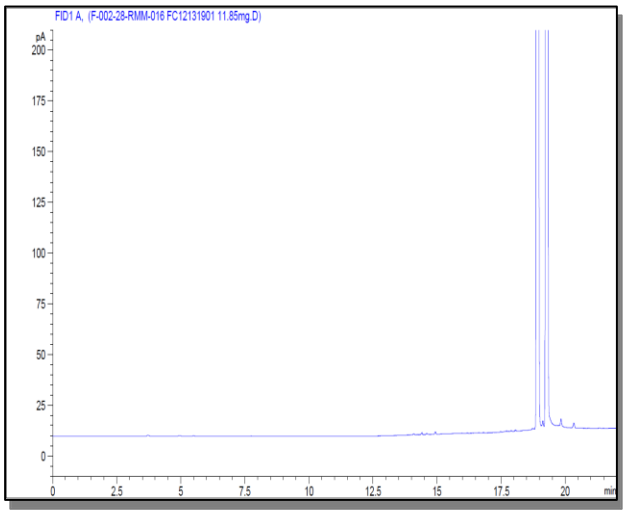
Gradient:

Time (min)	% A	% B
0.0	5	95
0.5	5	95
4.5	70	30
6.0	70	30
6.1	5	95

Flow Rate:	0.6 mL/min
Wavelength:	210 nm
Sample Name:	FC12131901
Acquired:	February 18, 2020

Peak #	Ret Time	Area %
1	0.68	0.01
2	2.74	0.01
3	2.83	0.00
4	3.06	0.02
5	3.19	99.89
6	3.48	0.02
7	3.57	0.01
8	3.69	0.03
9	3.80	0.00

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FC12131901
Acquired:	February 18, 2020

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

ND- None Detected

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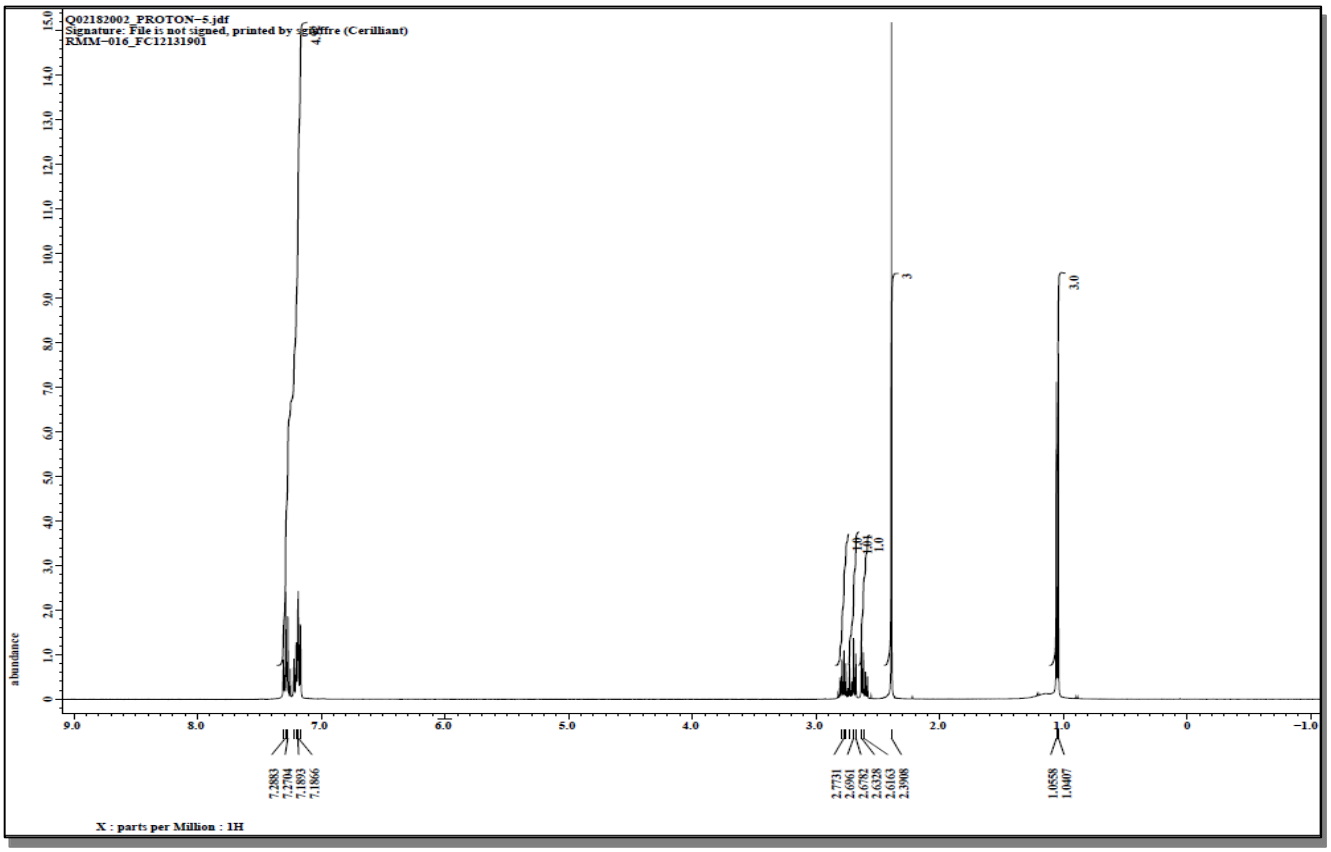
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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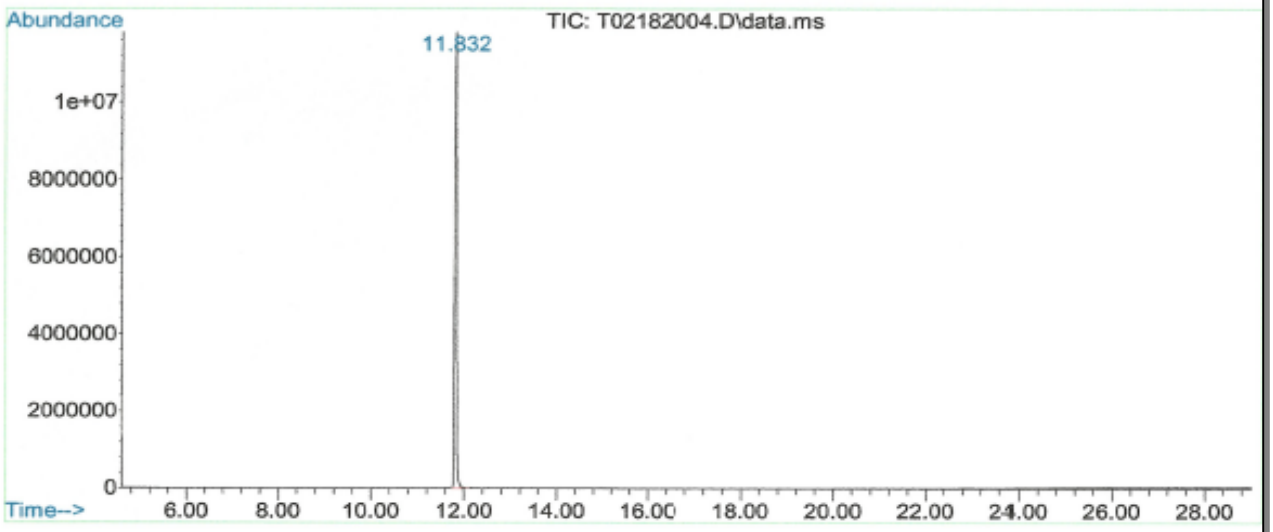
Spectral and Physical Data (cont.)

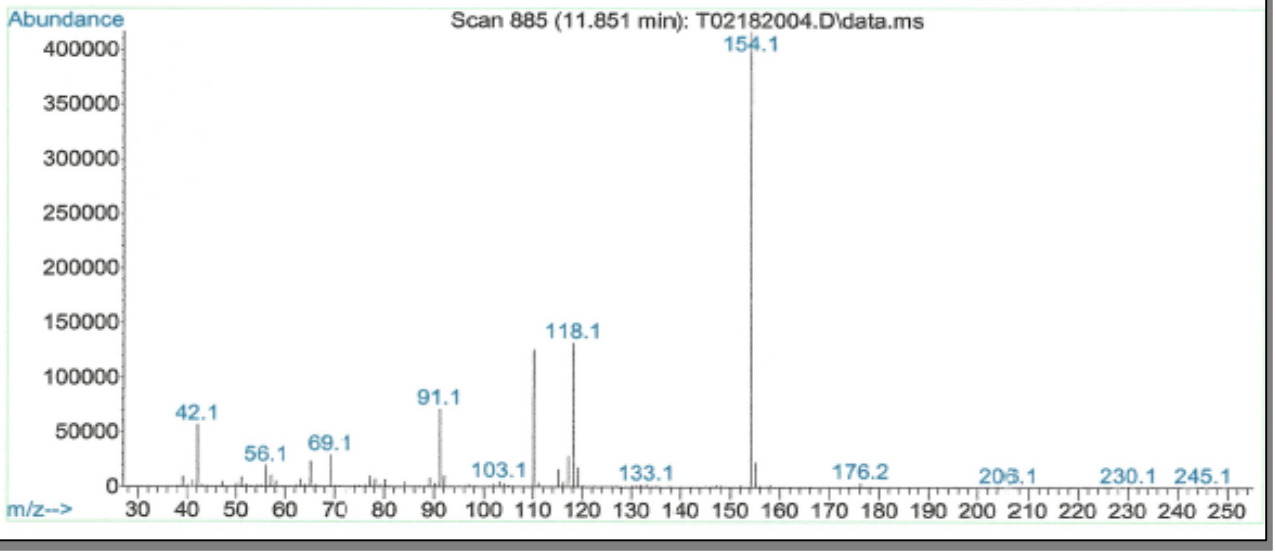
GC/MS

Compound Name	:	(±)-Methamphetamine
Lot Number	:	FC12131901
Instrument	:	Agilent GCMS
Operator	:	ECM(SGIUFFRE)
Date Reported	:	Tue Feb 18 08:21:55 2020
Column Type	:	DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	:	50°C to 300°C @ 10°C/min (hold for 4 min)
Injector Temp.	:	Cool on-column
Carrier Gas	:	Helium
Flow Rate (mL\min)	:	0.80 mL/min
Transfer Line Temp.	:	280°C
Scan Range	:	35-600

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (M-112, S(+)-Amphetamine) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	July 16, 2020	Initial version.

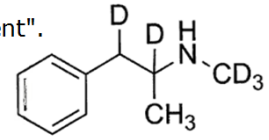
Certified Reference Material - Certificate of Analysis

(±)-Methamphetamine-D_5, Primary Measurement Standard

(±)-1-Phenyl-1,2-dideutero-2-(trideuteromethyl)aminopropane

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: M-023-1ML
Lot No.: FE01212014
Description of CRM: (±)-Methamphetamine-D_5 in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{10}H_{10}D_5N$
CAS No.: 60124-88-1
Regulatory: USDEA Exempt | Canadian TK # 61-1291



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(±)-Methamphetamine-D_5	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 19, 2020
Issue Date

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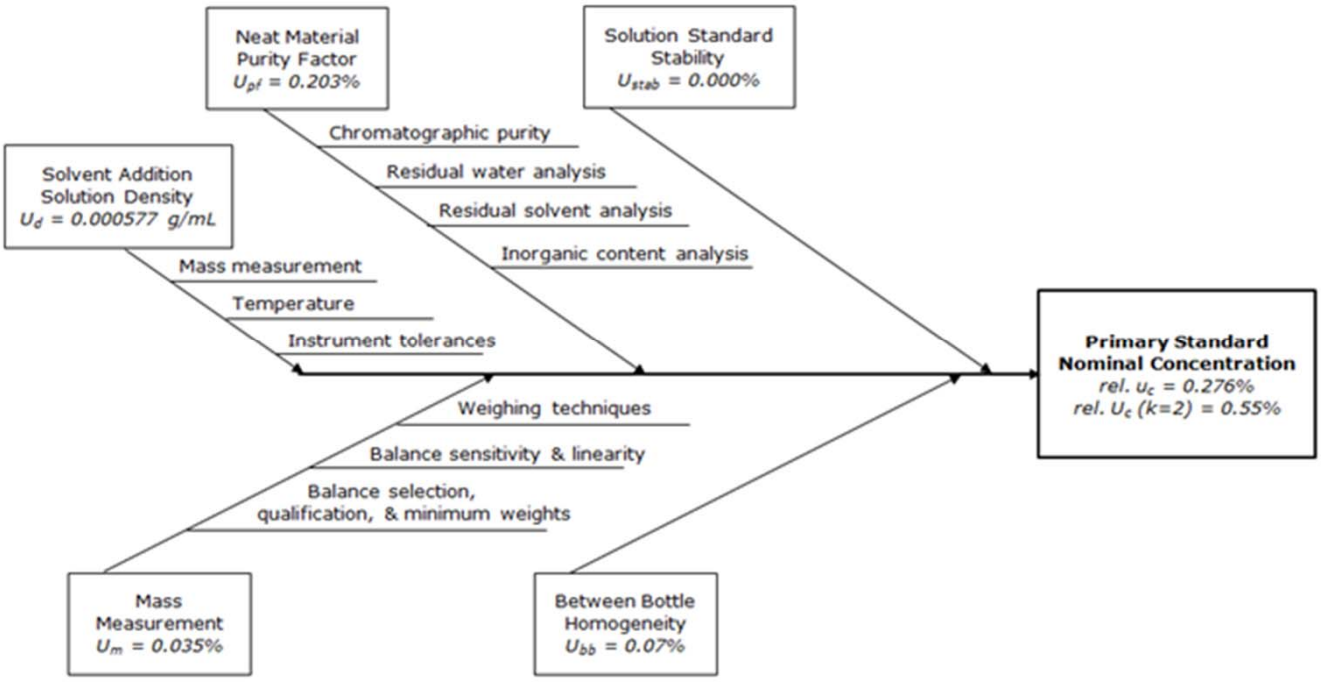
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	GC/FID	**Calibration Curve:**	Linear Regression
Column:	DB-5ms, 30 m x 0.53 mm ID,	**Number of Points:**	4
	1.5 µm film thickness	**Linearity (r) :**	1.000
Temp Program:	60°C to 260°C at 20°C/min hold 1 min		
Injector Temp:	Cool-on-Column		
Detector Temp:	325°C		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01212014	1.010	0.6
Previous Lot	FE03031704	1.008	0.7

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(±)-Methamphetamine-D_5	**Chemical Formula:**	$C_{10}H_{10}D_5N$
Material Lot:	FC11081601	**CAS Number:**	60124-88-1
		Molecular Weight:	154.26

Material Characterization Summary

Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.9% [1]	
Secondary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.7% [1]	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure [1]	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.00% D_0 vs D_5	
		0.00% D_0 to D_2	2.55% D_4
		0.01% D_3	97.44% D_5
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	0.15%	
Mass Balance Purity Factor		99.71%	

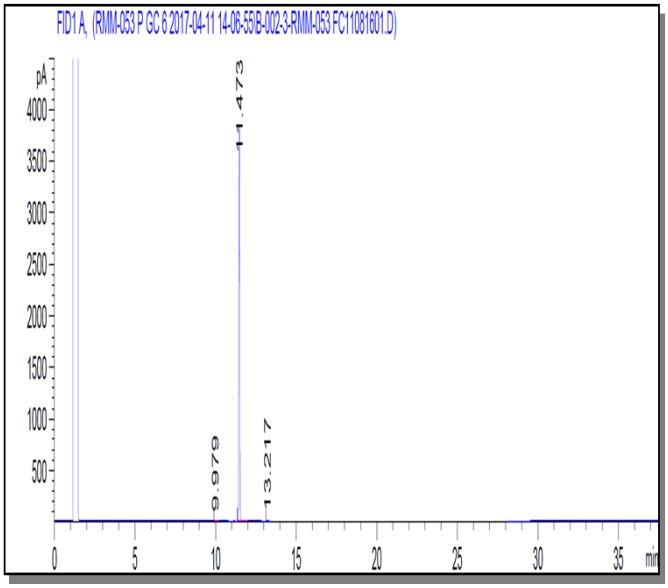
[1] 0.13% Amphetamine-D_2 detected by GC/FID analysis. 0.18% Amphetamine-D_2 detected by HPLC/UV analysis. 0.29% Amphetamine-D_2 detected by LC/MS analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

GC/FID



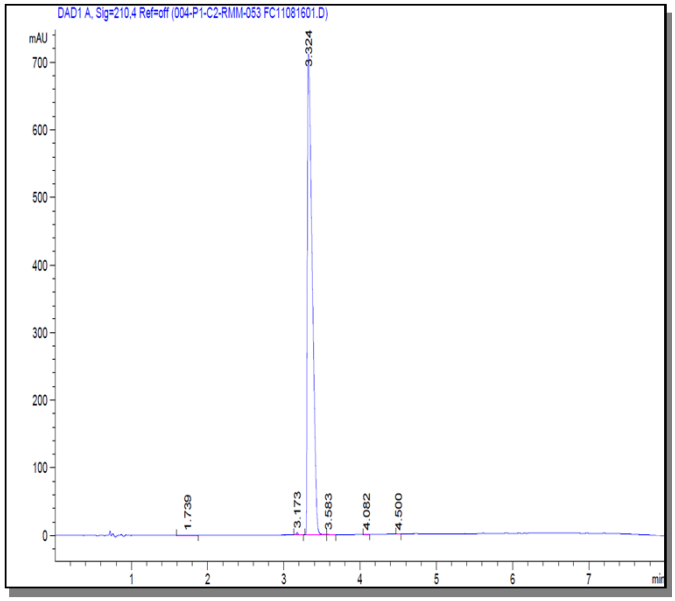
Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 40°C to 80°C at 40°C/min
80°C to 175°C at 5°C/min
175°C to 300°C at 10°C/min
hold 5 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC11081601
Acquired: April 11, 2017

Peak #	Ret Time	Area %
1	9.98	0.13
2	11.47	99.86
3	13.22	0.01

Peak 1 has been identified as Amphetamine-D_2

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm
Mobile Phase: A: Acetonitrile
B: 0.1% Phosphoric acid
Gradient:

Time (min)	%A	%B
0.0	5	95
0.5	5	95
4.5	70	30
6.0	70	30
6.1	5	95

Flow Rate: 0.6 mL/min
Wavelength: 210 nm

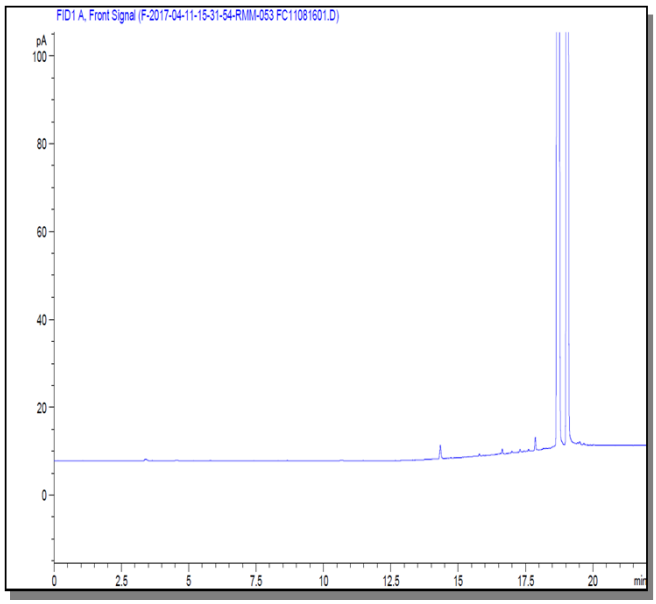
Sample Name: FC11081601
Acquired: April 12, 2017

Peak #	Ret Time	Area %
1	1.74	0.05
2	3.17	0.18
3	3.32	99.70
4	3.58	0.04
5	4.08	0.02
6	4.50	0.01

Peak 2 has been identified as Amphetamine-D_2

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



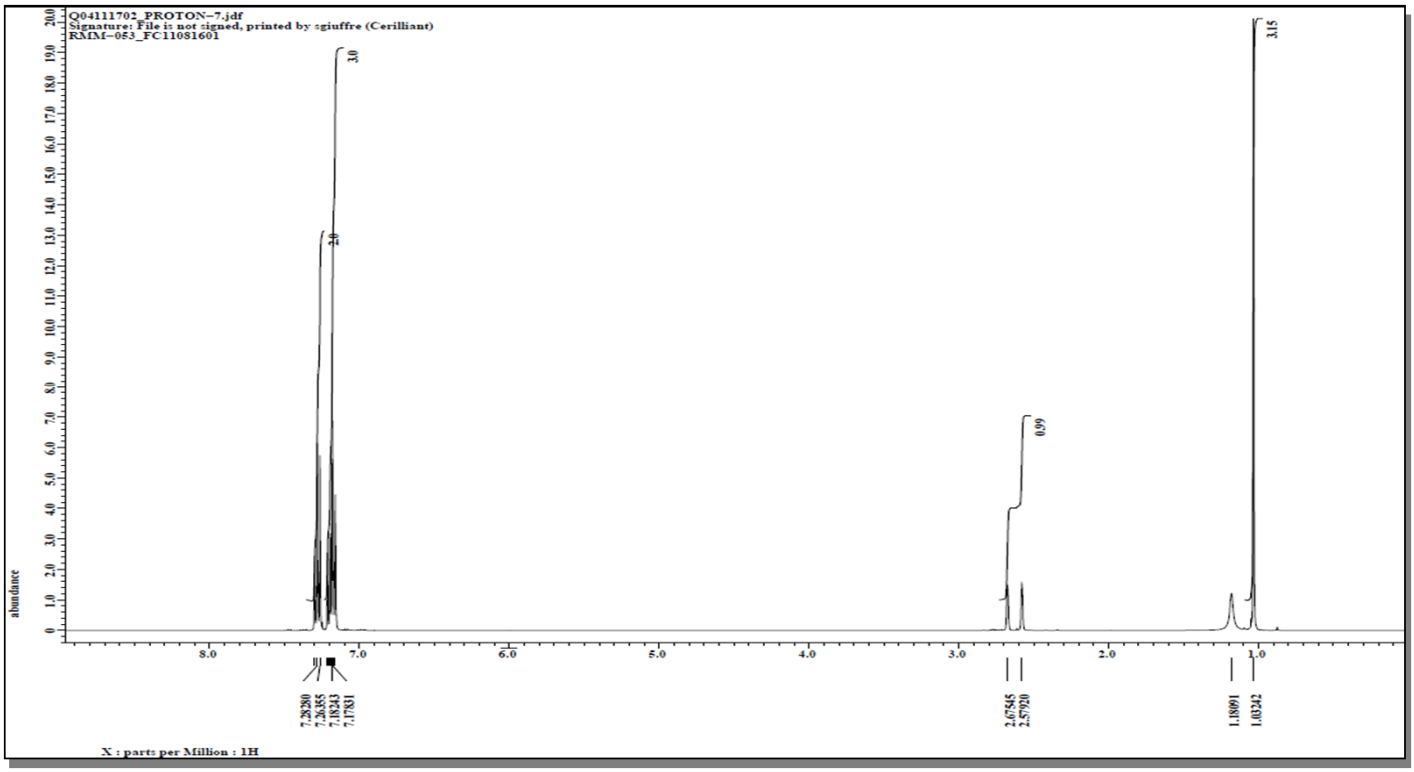
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC11081601
Acquired:	April 11, 2017

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

ND - None Detected

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	Chloroform-D



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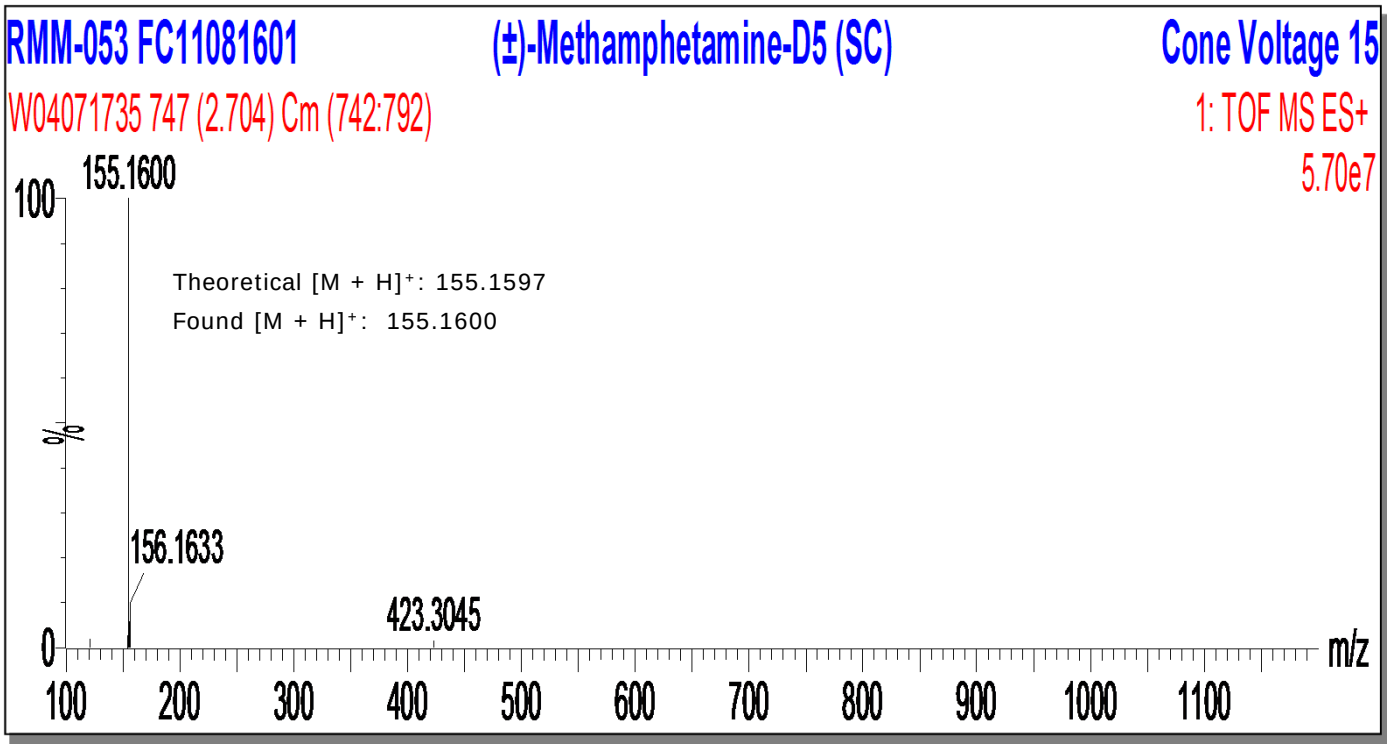
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	April 07, 2017

Time (min)	% A	% B
0.0	98	2
5.0	80	20
6.0	80	20
6.1	98	2
8.0	98	2



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

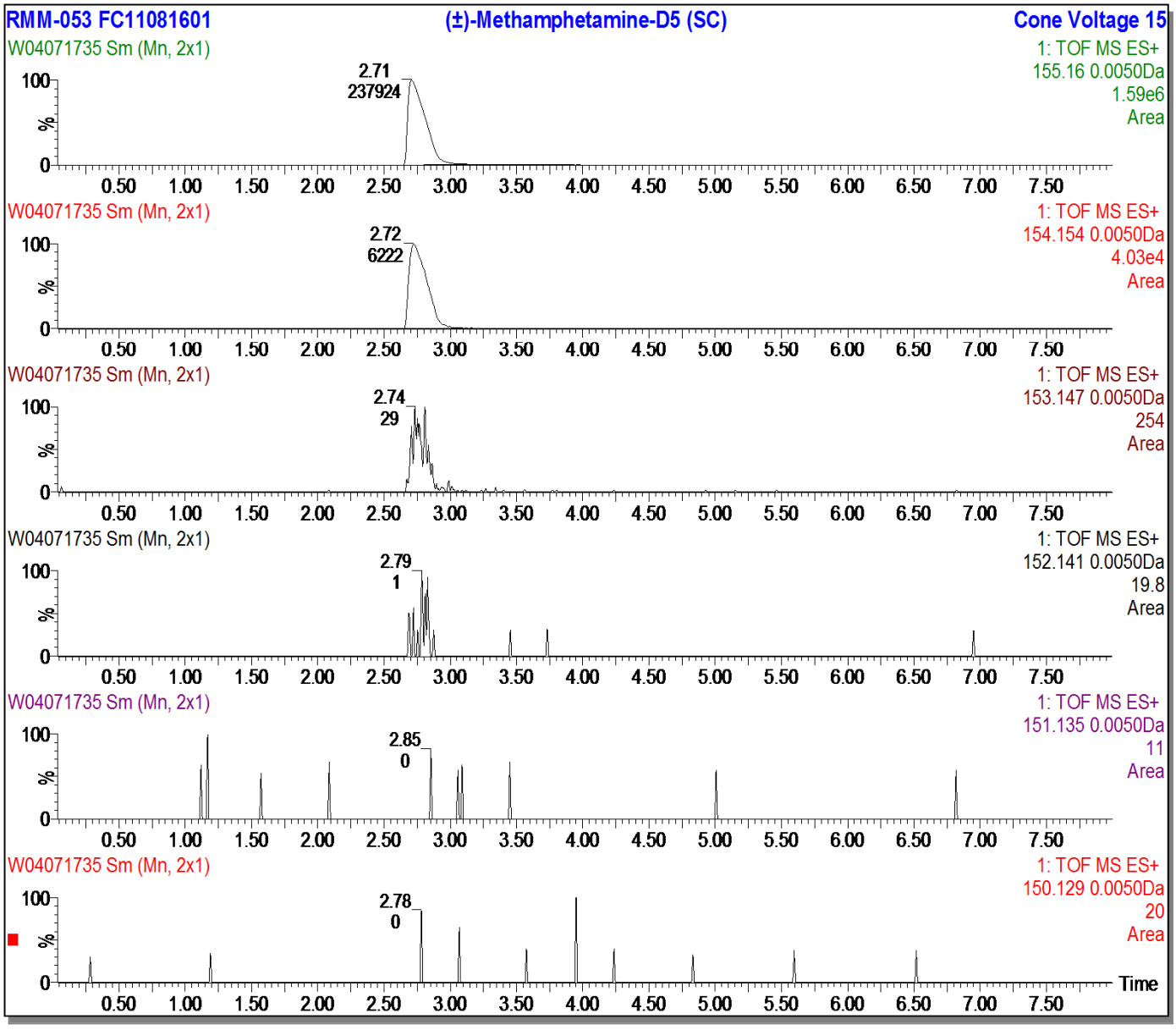
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
5.0	80	20
6.0	80	20
6.1	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 150-155 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: April 07, 2017



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (M-034, (±)-Methamphetamine-D_8) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 19, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

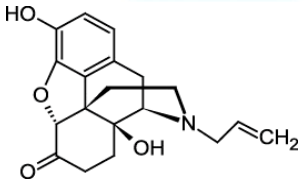
Certified Reference Material - Certificate of Analysis

Naloxone, Primary Measurement Standard

(5α)-4,5-Epoxy-3,14-dihydroxy-17-(2-propenyl)morphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: N-004-1ML
Lot No.: FN02212003
Description of CRM: Naloxone in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{19}H_{21}NO_4$
CAS No.: 465-65-6



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Naloxone	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

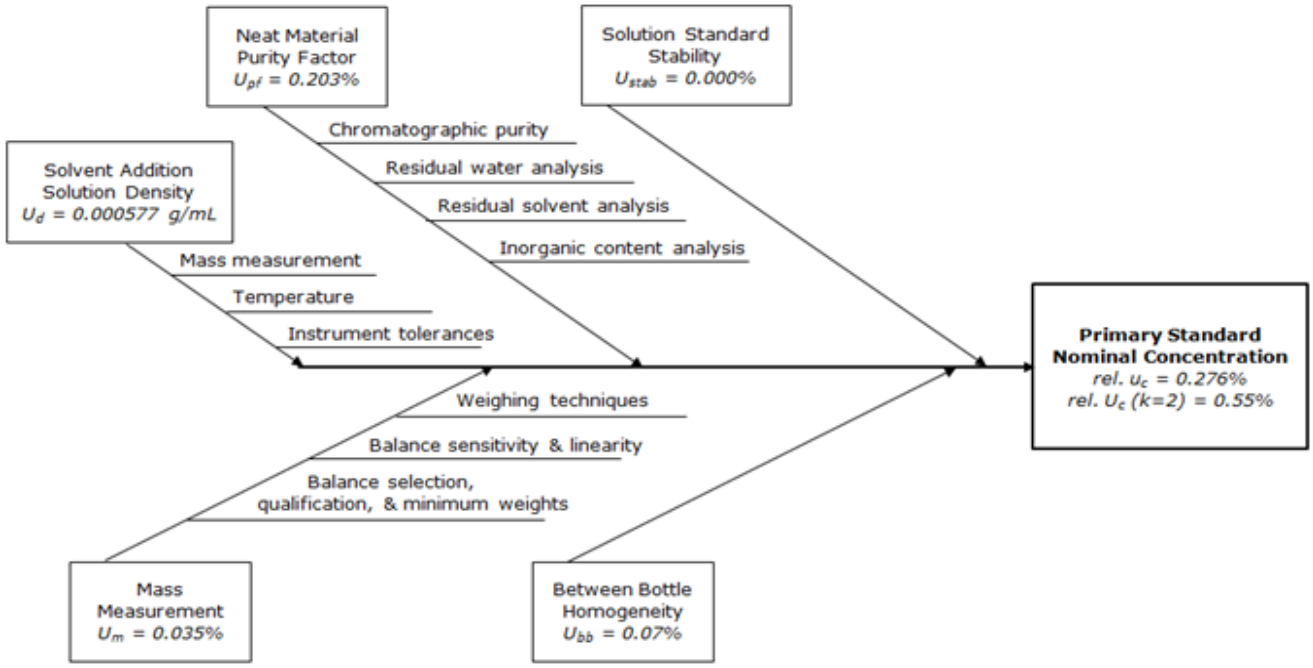
April 02, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (7:93)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN02212003	1.019	0.8
Previous Lot	FN02211902	1.007	0.5

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Naloxone	**Chemical Formula:**	$C_{19}H_{21}NO_4$
Material Lot:	FN10141906	**CAS Number:**	465-65-6
		Molecular Weight:	327.37

Material Characterization Summary

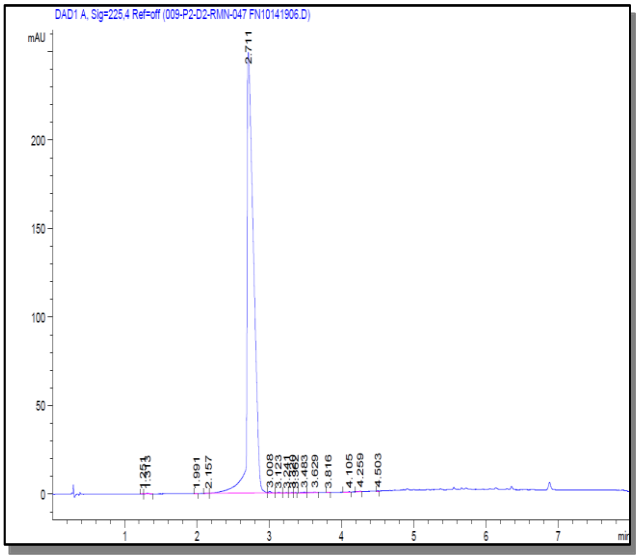
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.4%
Secondary Chromatographic Purity by GC/FID Analysis	20384346	99.9%
Identity by LC/MS Analysis	20384217	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	0.09%
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	20384350	< 0.2%
Mass Balance Purity Factor		99.34%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
3.0	15	85
5.0	50	50
7.0	50	50
7.1	2	98

Flow Rate: 0.8 mL/min

Wavelength: 225 nm

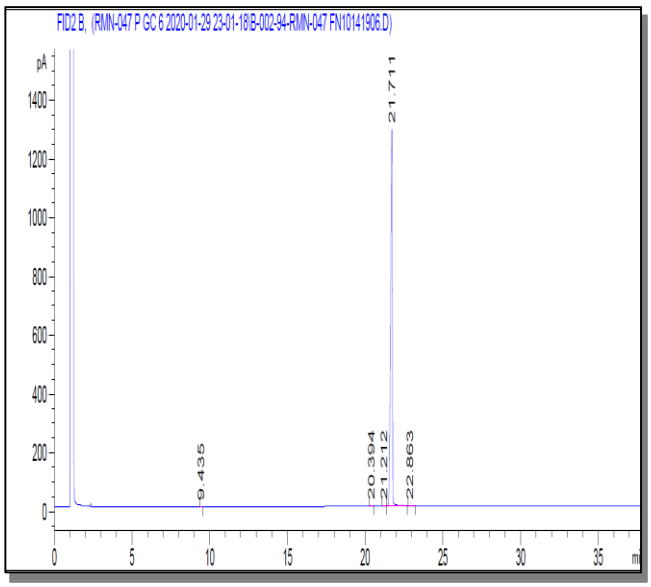
Sample Name: FN10141906

Acquired: February 03, 2020

Peak #	Ret Time	Area %
1	1.25	0.01
2	1.31	0.07
3	1.99	0.01
4	2.16	0.03
5	2.71	99.43
6	3.01	0.15
7	3.12	0.05
8	3.24	0.03
9	3.32	0.02
10	3.36	0.01
11	3.48	0.05
12	3.63	0.07
13	3.82	0.01
14	4.11	0.02
15	4.26	0.03
16	4.50	0.01

Spectral and Physical Data (cont.)

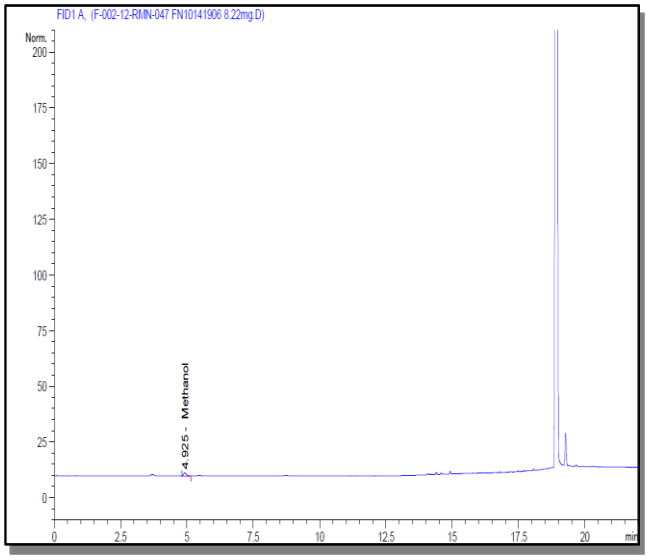
GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 280°C at 5°C/min hold 18 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FN10141906
Acquired:	January 30, 2020

Peak #	Ret Time	Area %
1	9.44	0.01
2	20.39	0.03
3	21.21	0.00
4	21.71	99.95
5	22.86	0.02

Residual Solvent Analysis by GC/FID Headspace



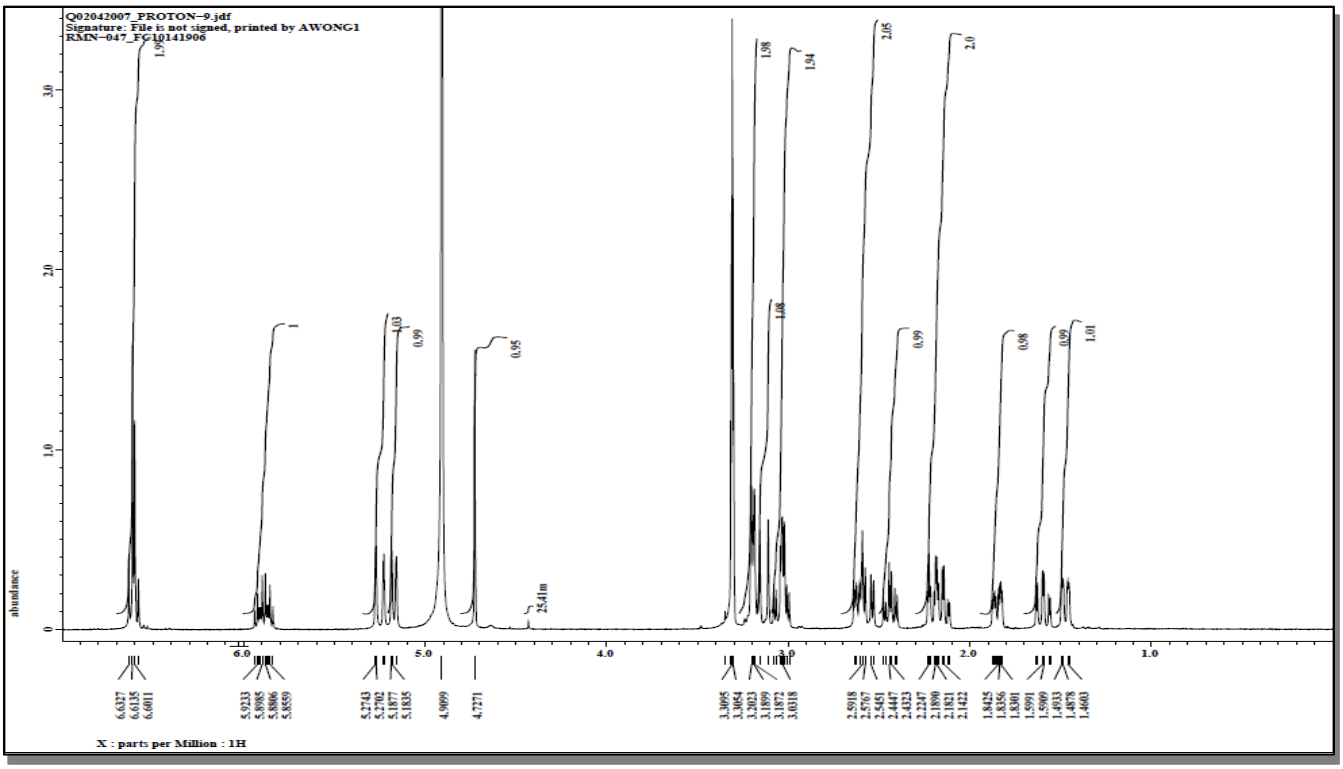
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FN10141906
Acquired:	January 31, 2020

Peak	Compound	Area	Weight %
1	Methanol	9.36	0.09
2	NMP	NA	NA
Total			**0.09**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Methanol-D_4



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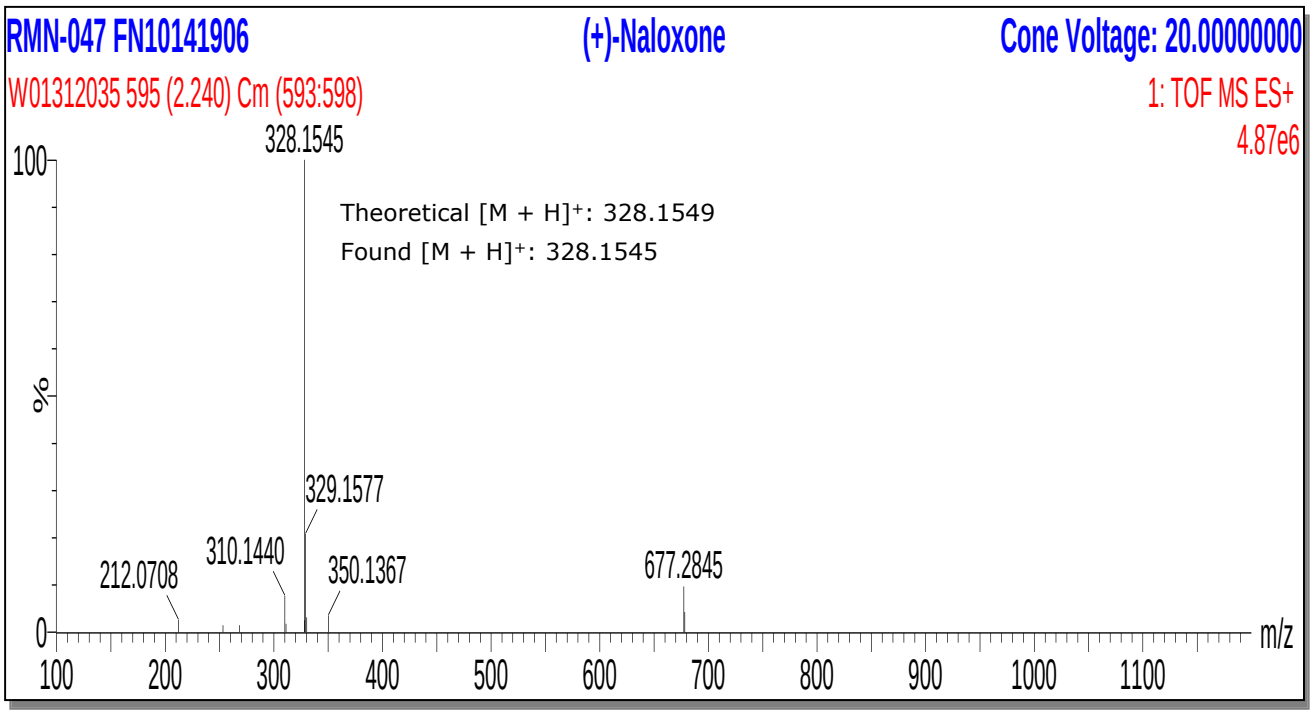
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	January 31, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 02, 2020	Initial version.

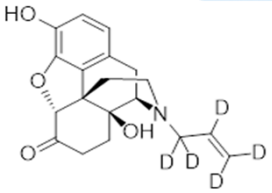
Certified Reference Material - Certificate of Analysis

Naloxone-D_5, Primary Measurement Standard

(5 α)-3,14-dihydroxy-17-prop-2-en-1-yl)-4,5-epoxymorphinan-6-one-D_5

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: N-115-1ML
Lot No.: FN03022013
Description of CRM: Naloxone-D_5 in Methanol (Solution)
Expiration Date: April 2023 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{19}H_{16}D_5NO_4$
CAS No.: 1261079-38-2



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Naloxone-D_5	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 02, 2020
Issue Date

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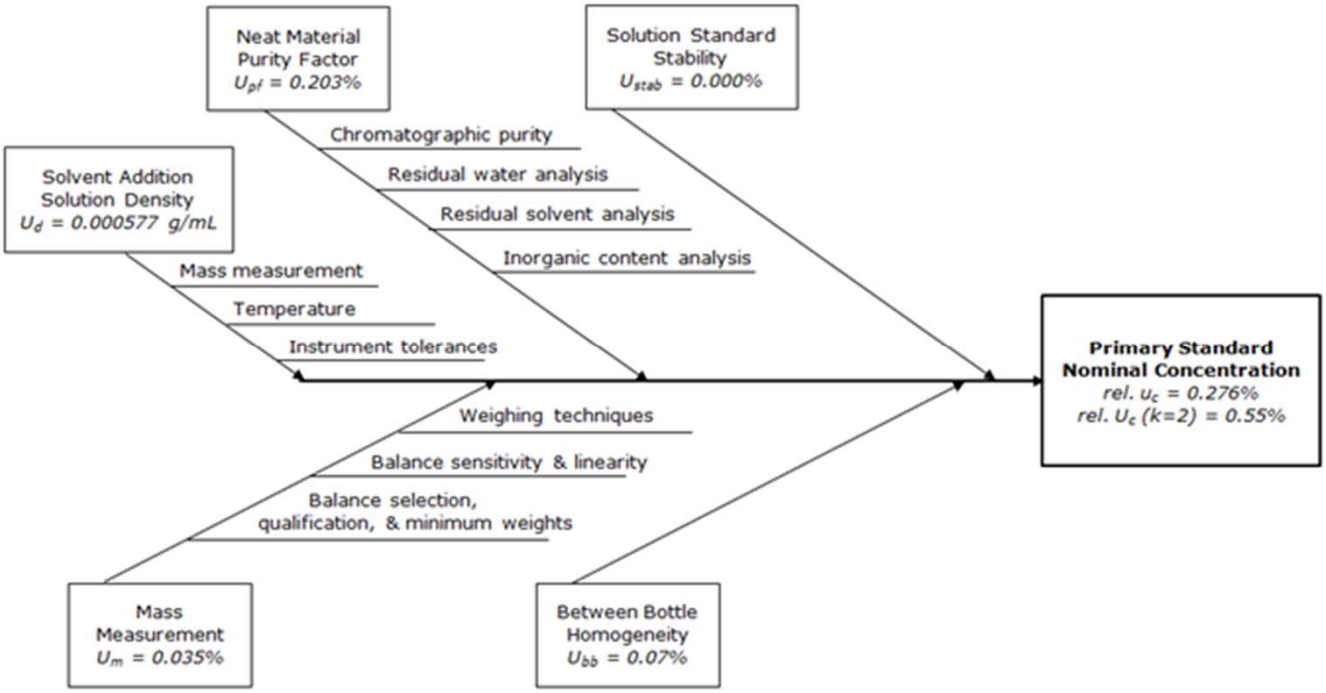
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (8:92)	**Linearity (r) :**	1.000
Flow Rate:	1.2 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FN03022013	1.016	1.0
Previous Lot	FN02131802	1.015	0.6

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Naloxone-D_5	**Chemical Formula:**	$C_{19}H_{16}D_5NO_4$
Material Lot:	FN11261902	**CAS Number:**	1261079-38-2
		Molecular Weight:	332.41

Material Characterization Summary

Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.9% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	> 99.9%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.01% D_0 vs D_5	
		0.01% D_0 to D_2	6.96% D_4
		0.23% D_3	92.78% D_5
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [2]	0.17%	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [2]	Not Detected	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		99.74%	

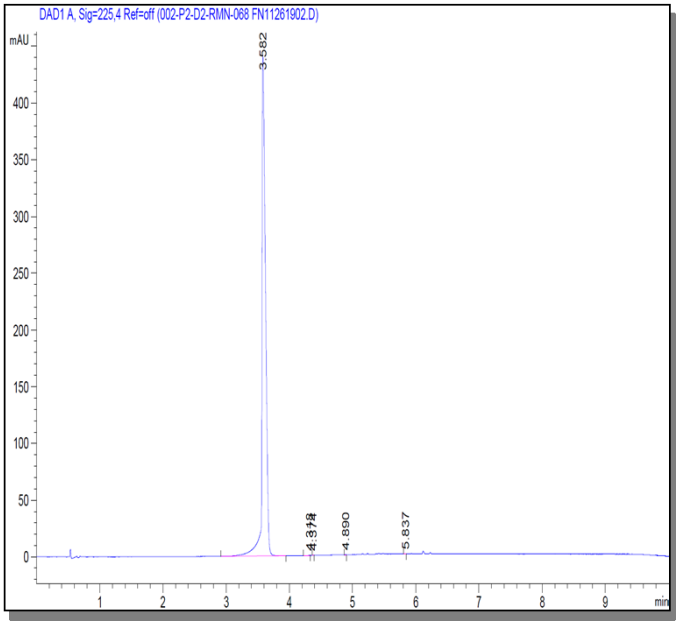
[1] No Noroxymorphone detected by HPLC/UV analysis.

[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.00	2	98
0.50	2	98
3.00	15	85
5.00	50	50
8.50	50	50
8.51	2	98

Flow Rate: 0.8 mL/min

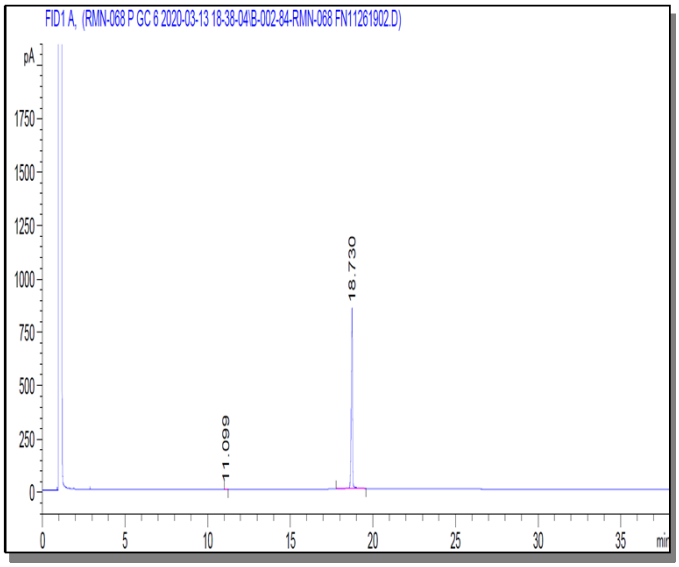
Wavelength: 225 nm

Sample Name: FN11261902

Acquired: February 25, 2020

Peak #	Ret Time	Area %
1	3.58	99.95
2	4.32	0.02
3	4.37	0.00
4	4.89	0.01
5	5.84	0.01

GC / FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C /min hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

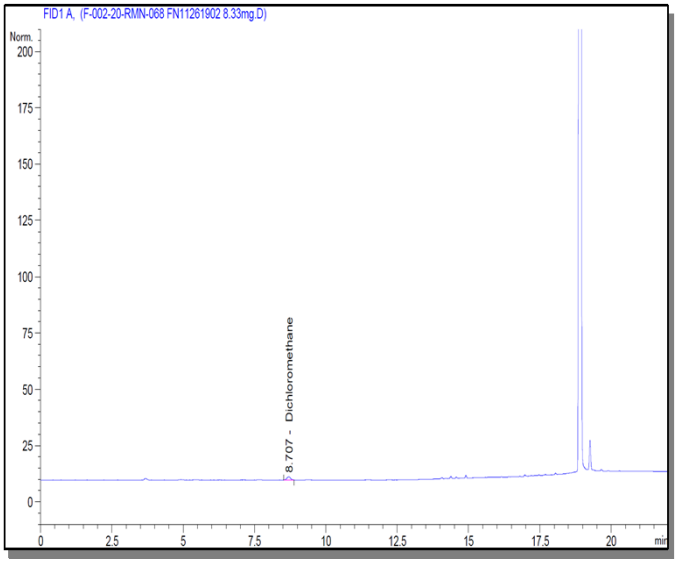
Sample Name: FN11261902

Acquired: March 13, 2020

Peak #	Ret Time	Area %
1	11.10	0.02
2	18.73	99.98

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

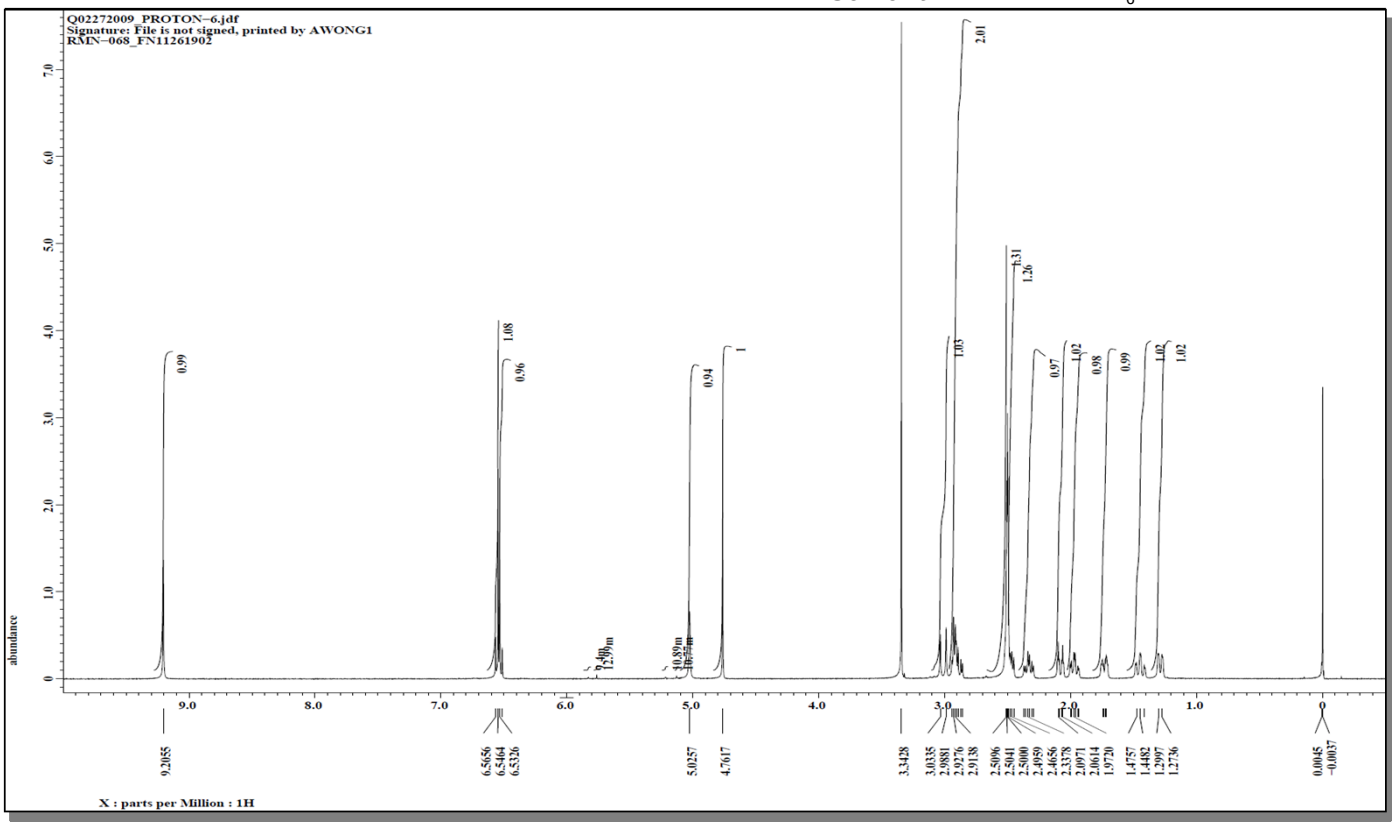


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FN11261902
Acquired:	February 28, 2020

Peak	Compound	Area	Weight %
1	Dichloromethane	12.64	0.17
2	NMP	NA	NA
Total			**0.17**

^{1}H NMR

Instrument:	JEOL ECS 400
Solvent:	DMSO-D_6



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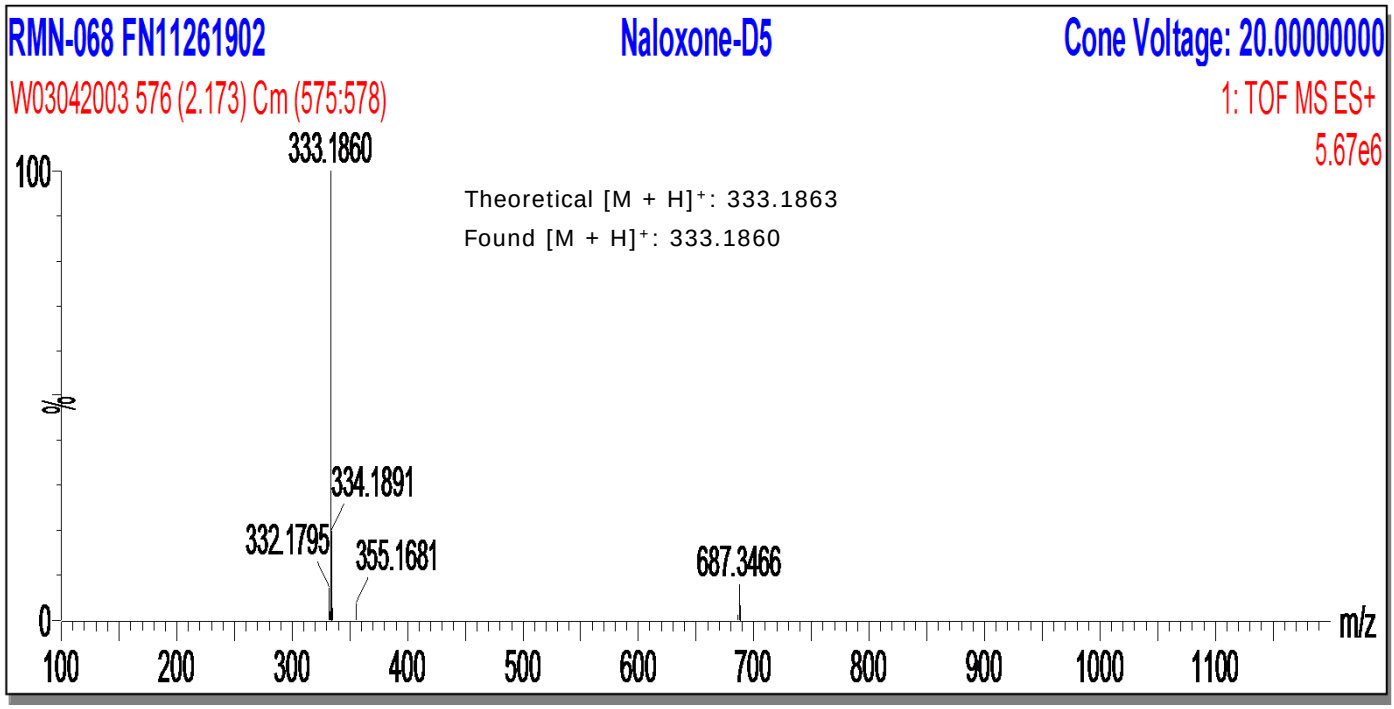
Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	March 04, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

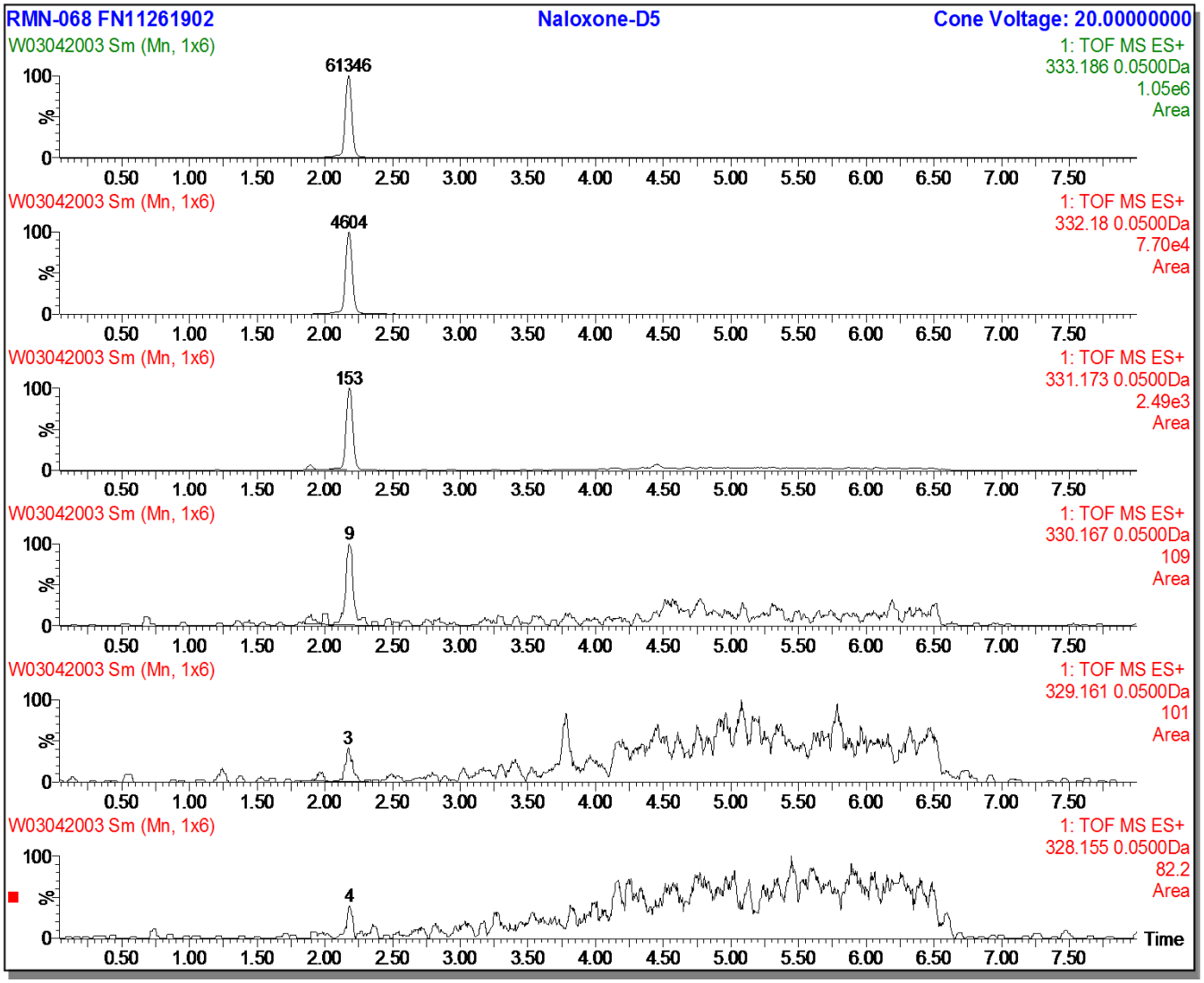
Column: Ascentis Express C18, 2.7 µm, 3.0 x 50 mm

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

Gradient:

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2

Flow Rate: 0.4 mL/min
Scan Range: 328-333 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: March 04, 2020



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (N-004, Naloxone) 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 41 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 02, 2020	Initial version.

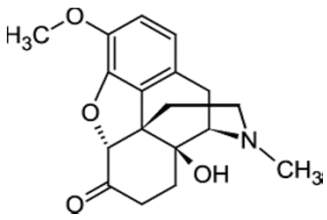
Certified Reference Material - Certificate of Analysis

Oxycodone, Primary Measurement Standard

4,5-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: O-002-1ML
Lot No.: FE01082008
Description of CRM: Oxycodone in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{21}NO_4$
CAS No.: 76-42-6
Regulatory: USDEA Exempt | Canadian TK # 61-1414



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Oxycodone	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability“ on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See “Details about certification process” on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

July 29, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

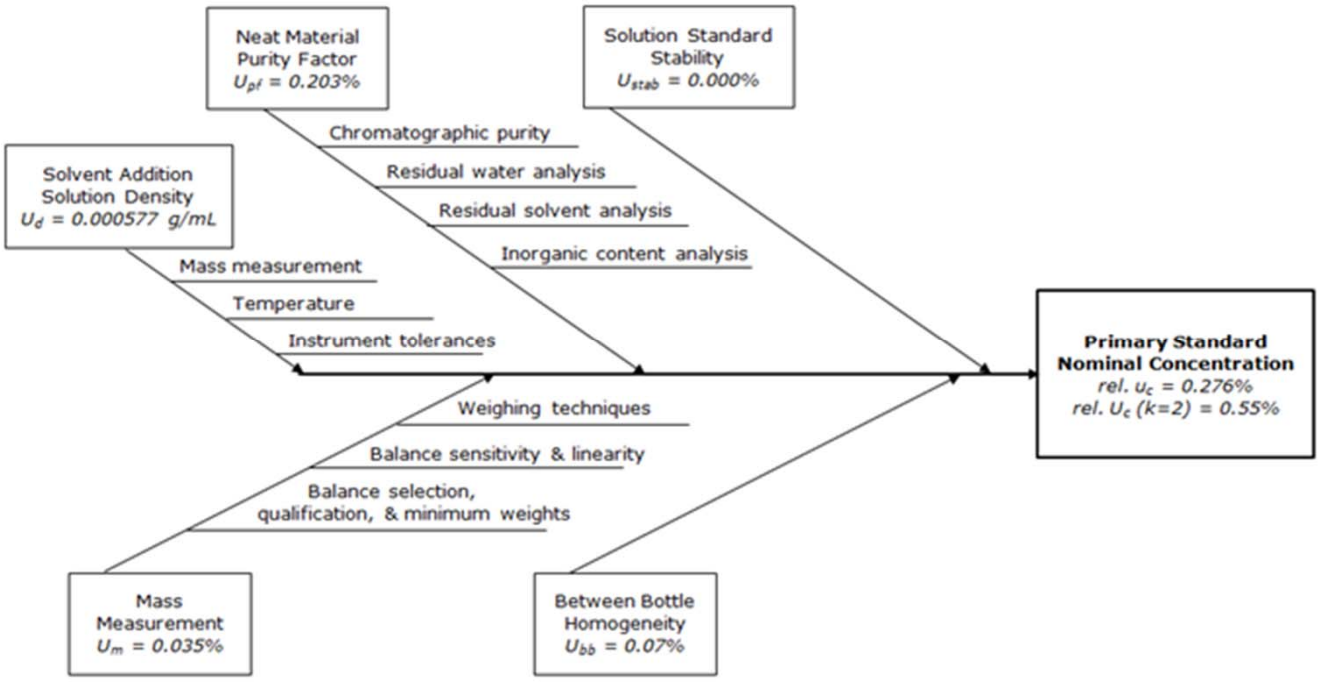
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (10:90)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	230 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082008	0.995	1.5
Previous Lot	FE08241701	0.999	0.6

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Oxycodone	**Chemical Formula:**	$C_{18}H_{21}NO_4$
Material Lot:	PC04111701	**CAS Number:**	76-42-6
		Molecular Weight:	315.36

Material Characterization Summary

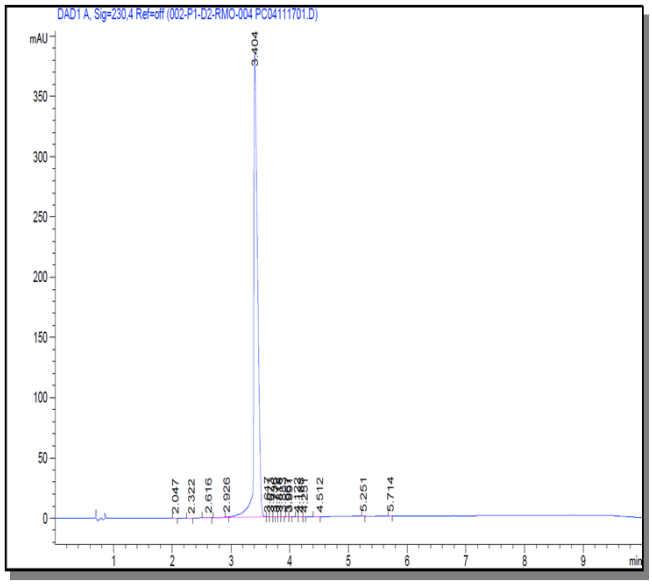
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8%
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.9%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	Below Quantitation Limit
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.82%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

Mobile Phase: A: Acetonitrile
B: 0.05% Phosphoric acid in Water

Gradient:

Time (min)	% A	% B
0.0	5	95
0.5	5	95
7.0	65	35
8.0	65	35
8.1	5	95

Flow Rate: 0.6 mL/min

Wavelength: 230 nm

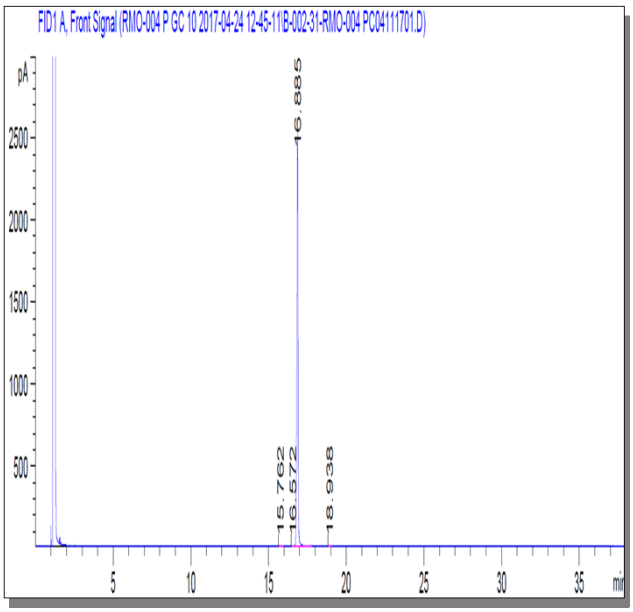
Sample Name: PC04111701

Acquired: March 25, 2019

Peak #	Ret Time	Area %
1	2.05	0.01
2	2.32	0.01
3	2.62	0.03
4	2.93	0.02
5	3.40	99.81
6	3.62	0.03
7	3.67	0.02
8	3.74	0.00
9	3.77	0.02
10	3.82	0.00
11	3.88	0.00
12	3.97	0.01
13	3.99	0.01
14	4.12	0.01
15	4.19	0.01
16	4.25	0.00
17	4.51	0.01
18	5.25	0.01
19	5.71	0.00

Spectral and Physical Data (cont.)

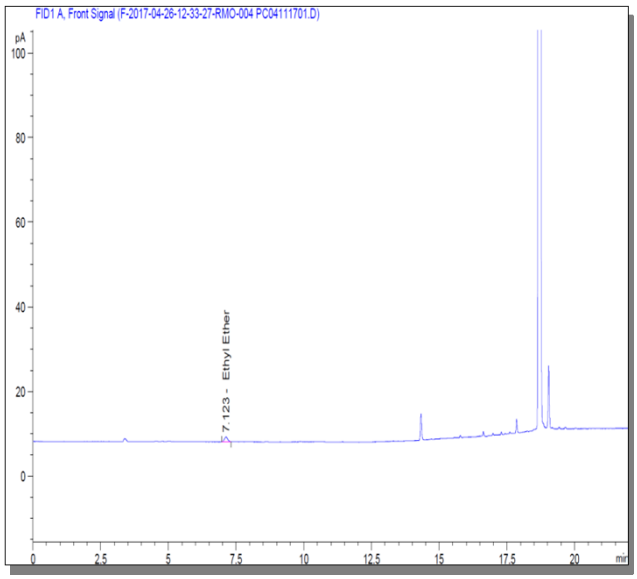
GC/FID



Column:	DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 280°C at 5°C/min hold 18 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	PC04111701
Acquired:	April 24, 2017

Peak #	Ret Time	Area %
1	15.76	0.02
2	16.57	0.04
3	16.89	99.93
4	18.94	0.02

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	PC04111701
Acquired:	April 26, 2017

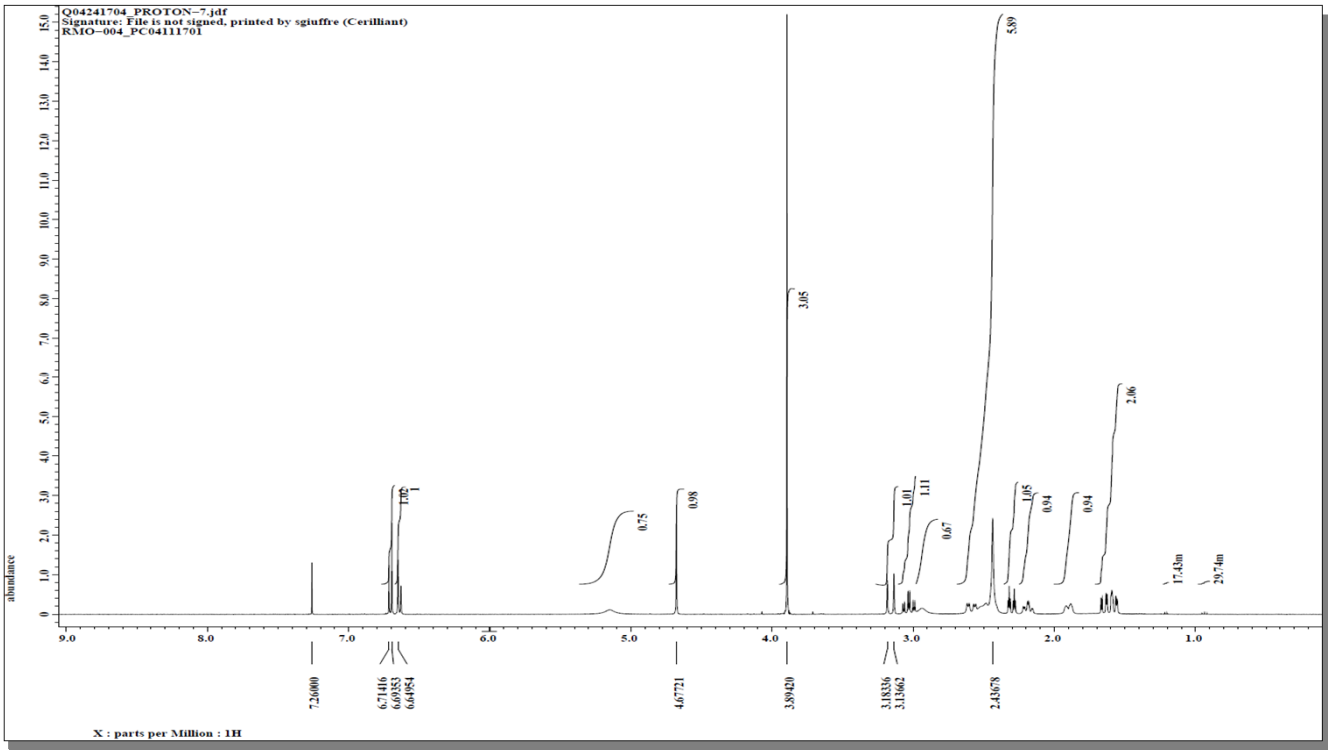
Peak	Compound	Area	Weight %
1	Ethyl ether	9.82	BQL
2	NMP	NA	NA
Total			**BQL**

BQL - Below Quantitation Limit

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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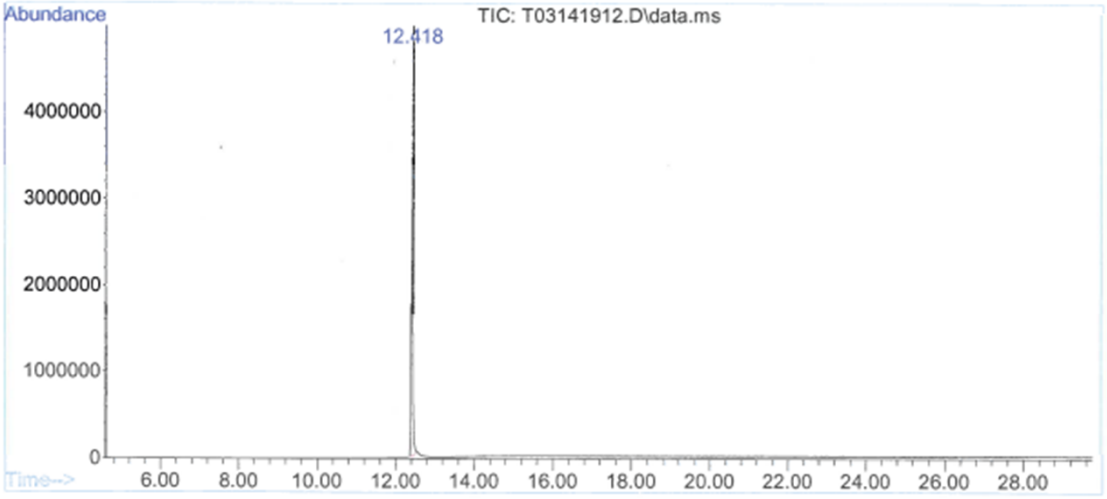
Spectral and Physical Data (cont.)

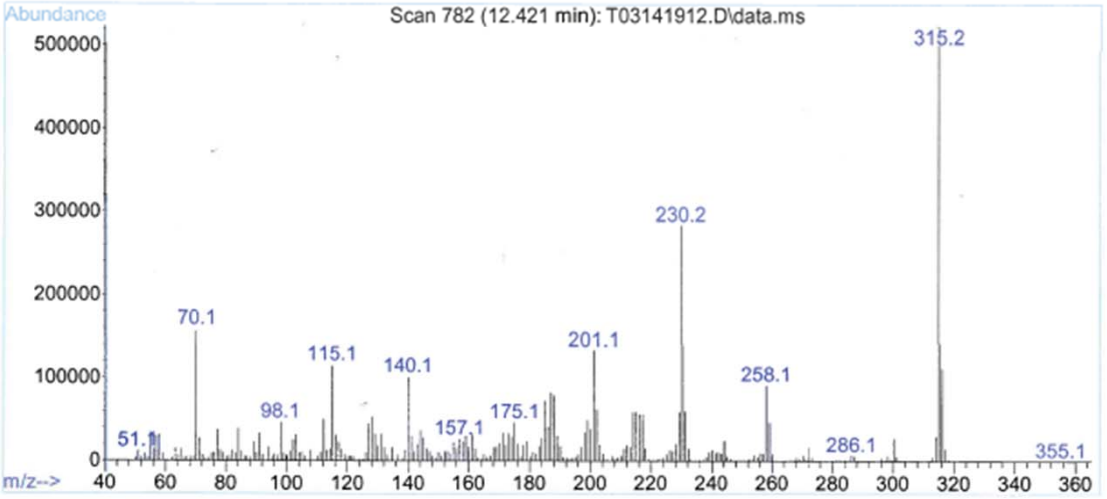
GC / MS

```
Compound Name        : Oxycodone
Lot Number           : PC04111701
Instrument           : Agilent GCMS
Operator             : ECM(SGIUFFRE)
Date Reported        : Fri Mar 15 07:54:29 2019
Column Type          : DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program        : 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.       : Cool on-column
Carrier Gas          : Helium
Flow Rate (mL\min)   : 0.80 mL/min
Transfer Line Temp.  : 280°C
Scan Range           : 50-500
```

Total Ion Chromatogram



Mass Spectrum



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	July 29, 2020	Initial version.

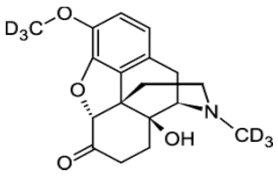
Certified Reference Material - Certificate of Analysis

Oxycodone-D_6, Primary Measurement Standard

4,5-Epoxy-14-hydroxy-3-trideuteromethoxy-17-[trideuteromethyl]morphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: O-008-1ML
Lot No.: FE02042002
Description of CRM: Oxycodone-D_6 in Methanol (Solution)
Expiration Date: March 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{18}H_{15}D_6NO_4$
CAS No.: 152477-91-3
Regulatory: USDEA Exempt | Canadian TK # 61-1420



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Oxycodone-D_6	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.

Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

April 13, 2020
Issue Date

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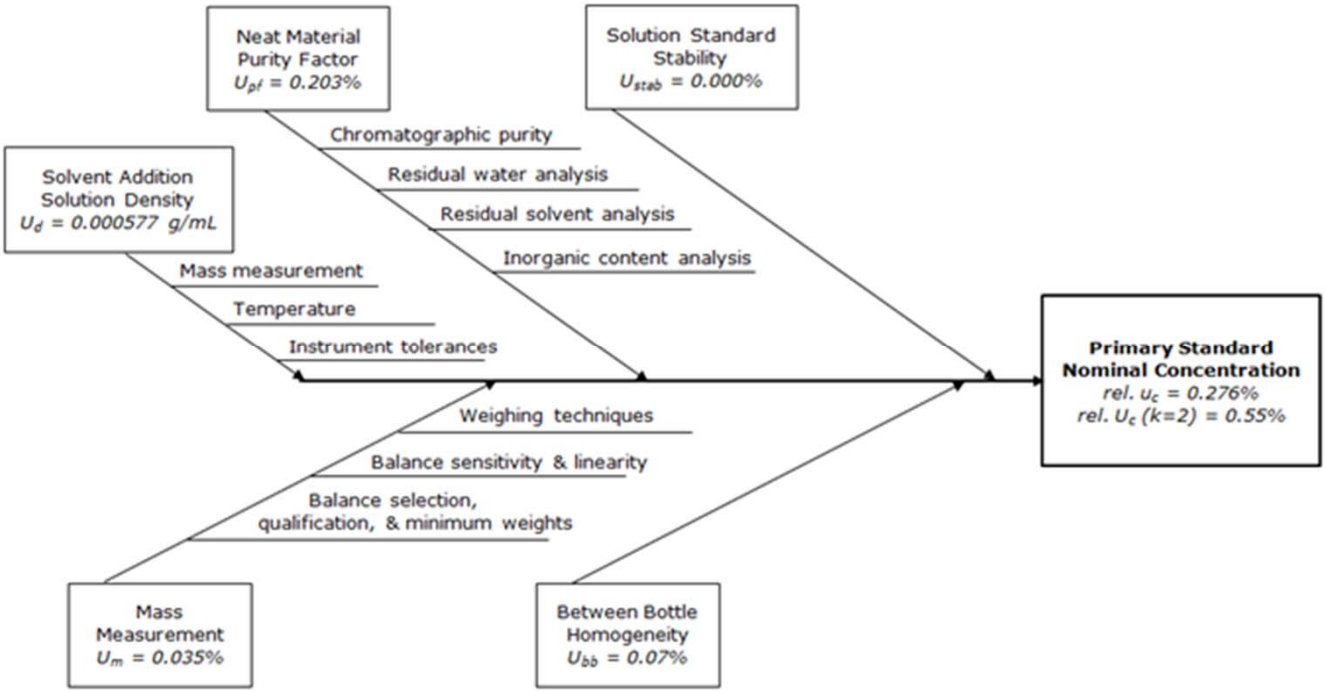
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



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Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.

- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.

- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.

- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.

- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express C18, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (10:90)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02042002	0.999	1.3
Previous Lot	FE05191703	1.008	0.6

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Oxycodone-D_6	**Chemical Formula:**	$C_{18}H_{15}D_6NO_4$
Material Lot:	FC12181501	**CAS Number:**	152477-91-3
		Molecular Weight:	321.40

Material Characterization Summary

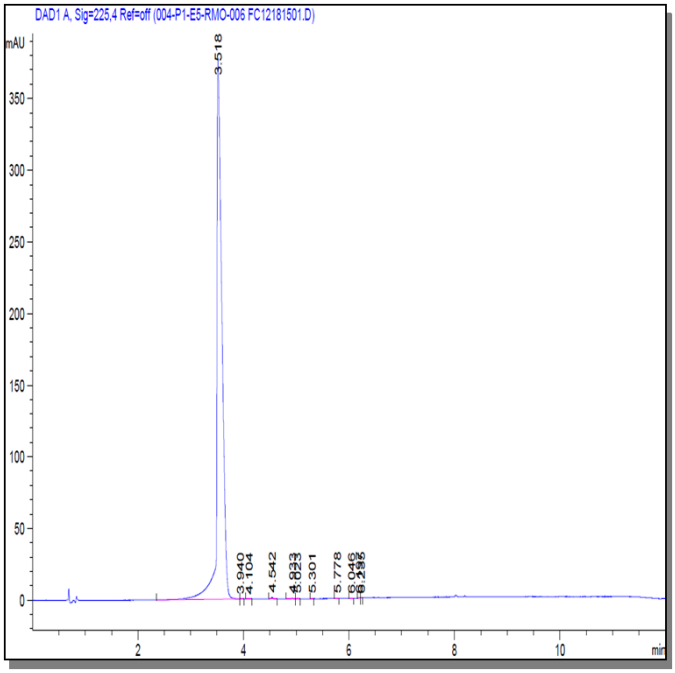
Analytical Test	Method	Results	
Primary Chromatographic Purity by HPLC/UV Analysis	20384348	99.8%	
Secondary Chromatographic Purity by GC/FID Analysis	20384346	99.9%	
Identity by LC/MS Analysis	20384217	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	20384217	0.03% D_0 vs D_6	
		0.03% D_0	0.18% D_4
		0.01% D_1 to D_2	0.77% D_5
		0.20% D_3	98.80% D_6
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	20397799 [1]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	20398075 [1]	Not Detected	
Inorganic Content by Microash Analysis	20384350	< 0.2%	
Mass Balance Purity Factor		99.76%	

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



Column: Ascentis Express C18, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	5	95
4.0	20	80
8.0	60	40
10.0	60	40
10.1	5	95

Flow Rate: 0.6 mL/min

Wavelength: 225 nm

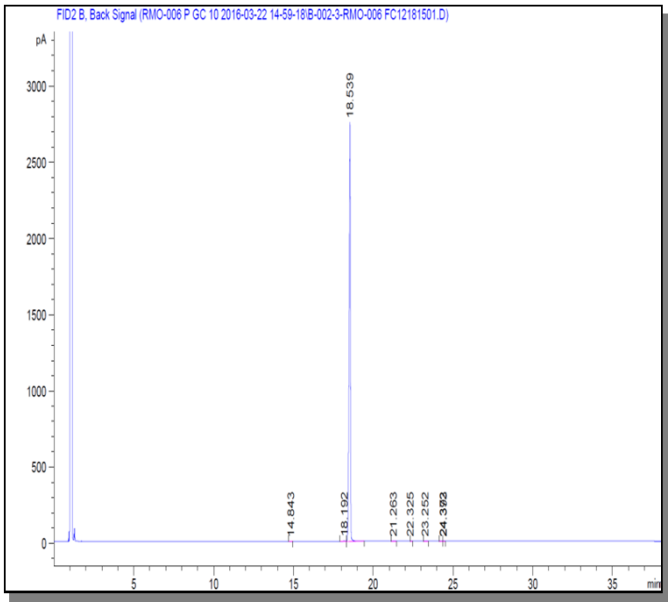
Sample Name: FC12181501

Acquired: February 24, 2020

Peak #	Ret Time	Area %
1	3.52	99.73
2	3.94	0.01
3	4.10	0.01
4	4.54	0.10
5	4.93	0.04
6	5.02	0.02
7	5.30	0.01
8	5.78	0.03
9	6.05	0.01
10	6.20	0.02
11	6.24	0.01

Spectral and Physical Data (cont.)

GC/FID

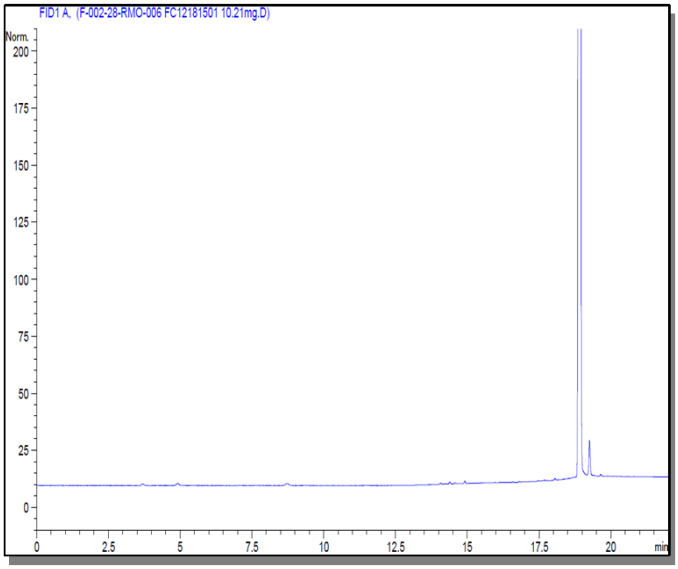


Column: DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC12181501
Acquired: March 22, 2016

Peak #	Ret Time	Area %
1	14.84	0.00
2	18.19	0.11
3	18.54	99.85
4	21.26	0.01
5	22.33	0.00
6	23.25	0.01
7	24.37	0.01
8	24.39	0.00

Residual Solvent Analysis by GC/FID Headspace



Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C hold 12 min to 220°C at 40°C/min hold 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

Sample Name: FC12181501
Acquired: February 21, 2020

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

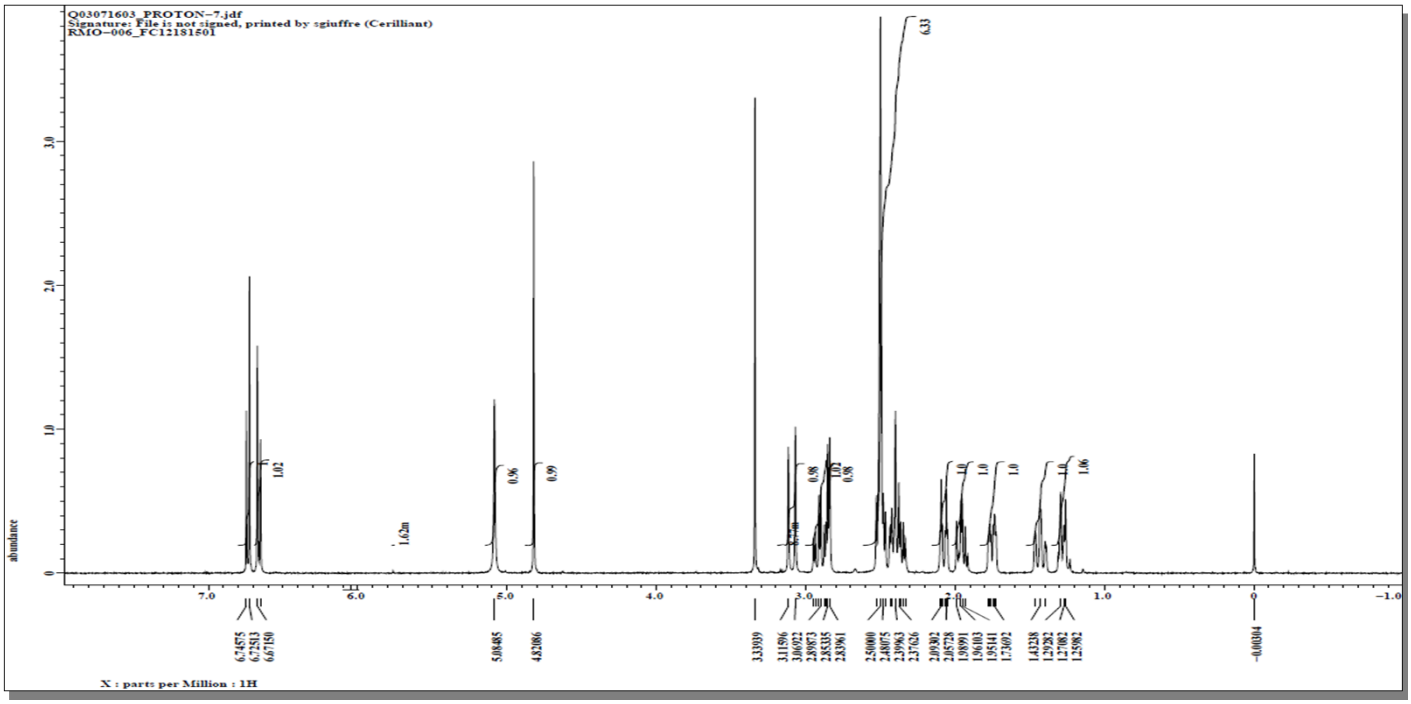
ND - None Detected

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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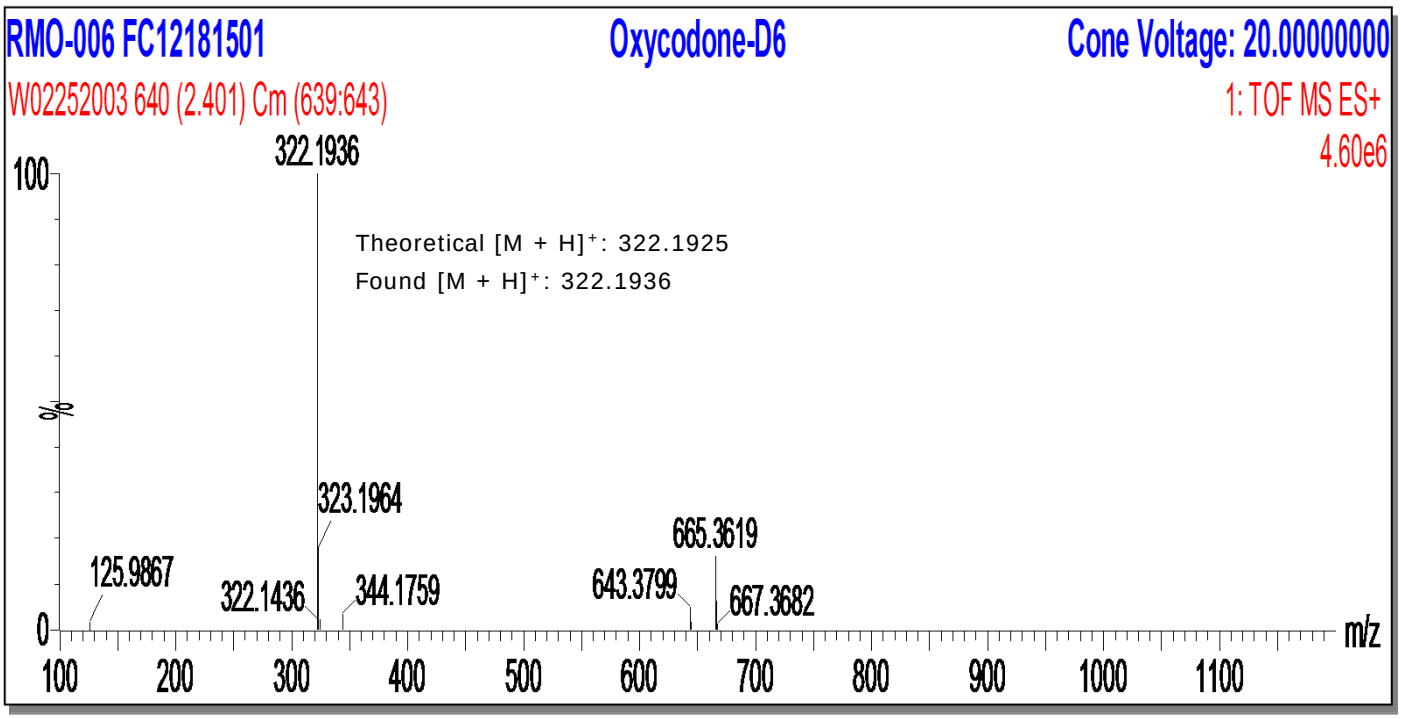
Spectral and Physical Data (cont.)

LC / MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	February 25, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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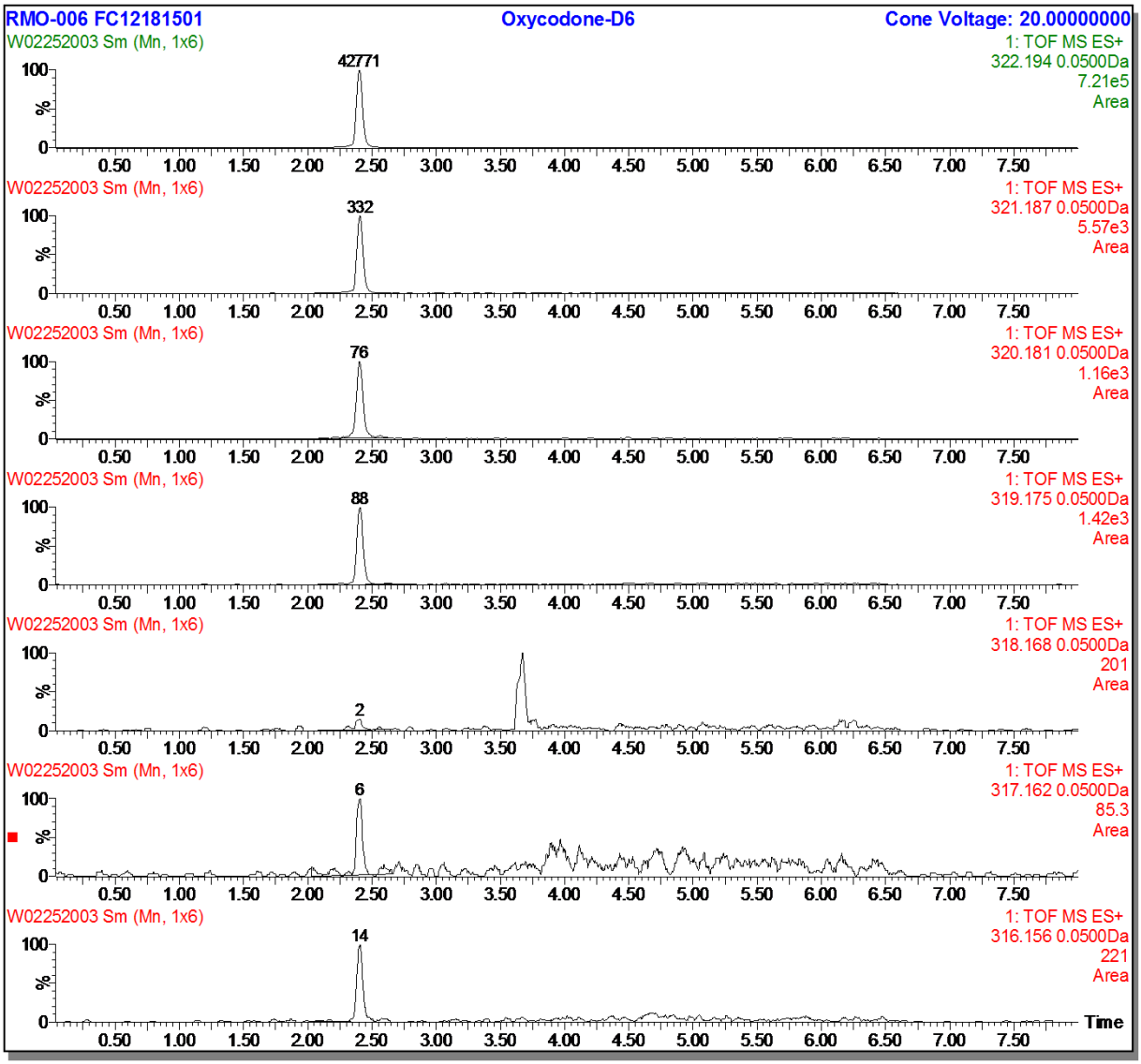
Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	316-322 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	February 25, 2020

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (O-042, Oxycodone-D_3) 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	

Transport / Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	April 13, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

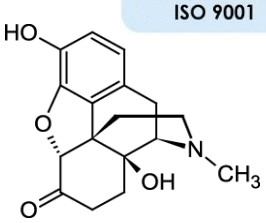
Certified Reference Material - Certificate of Analysis

Oxymorphone, Primary Measurement Standard

5α-4,5-Epoxy-3,14-dihydroxy-17-methylmorphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: O-004-1ML
Lot No.: FE01082009
Description of CRM: Oxymorphone in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{19}NO_4$
CAS No.: 76-41-5
Regulatory: USDEA Exempt | Canadian TK # 61-1416



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Oxymorphone	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

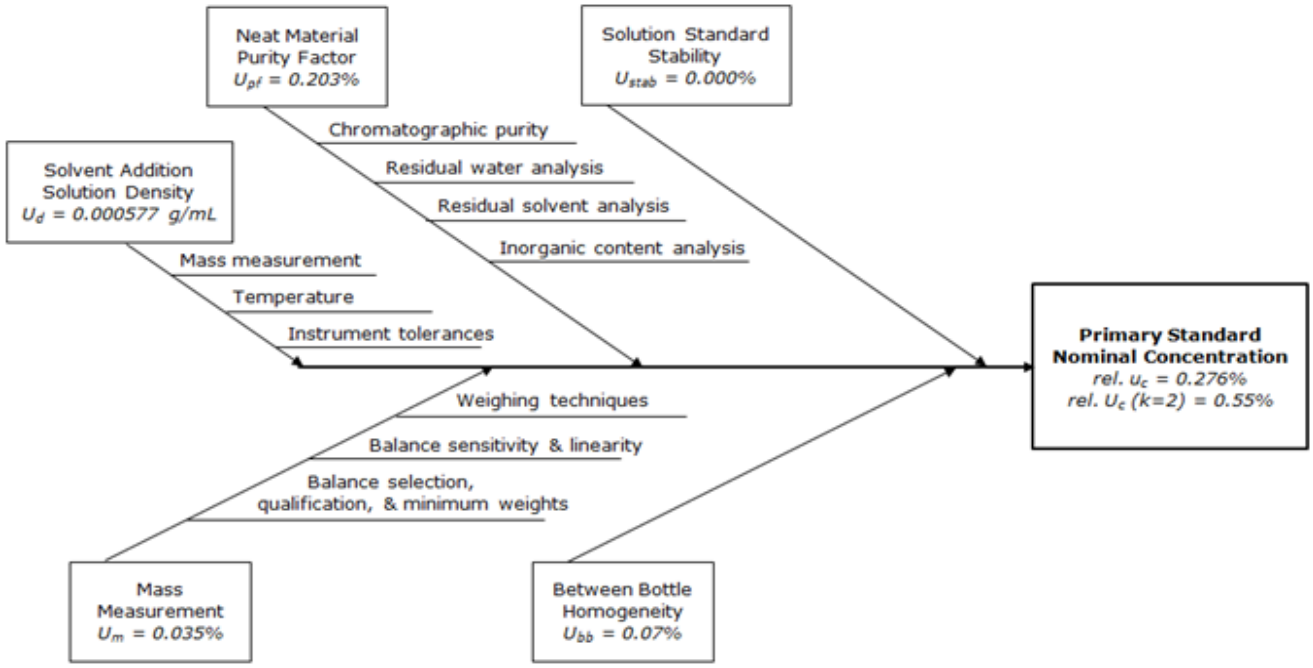
February 20, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (5:95)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082009	1.001	0.6
Previous Lot	FE03201901	0.999	0.4

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Oxymorphone	**Chemical Formula:**	$C_{17}H_{19}NO_4$
Material Lot:	FC05021701	**CAS Number:**	76-41-5
		Molecular Weight:	301.34

Material Characterization Summary

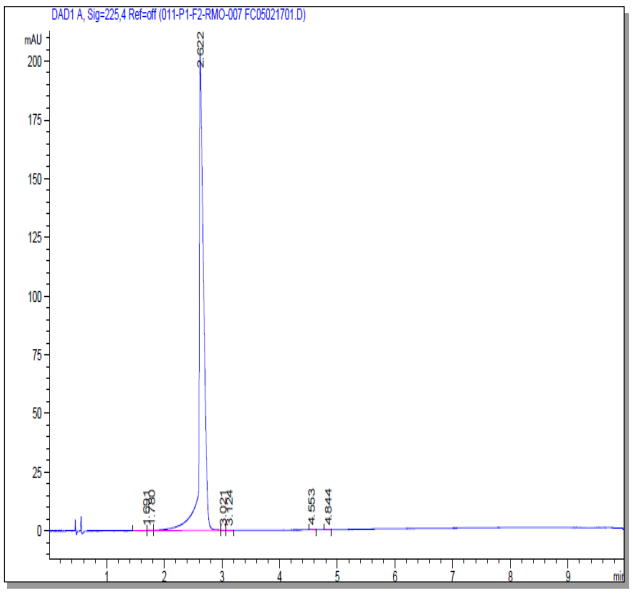
Analytical Test	**Method**	**Results**
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8%
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	> 99.9%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [1]	0.14%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [1]	Below Quantitation Limit
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.65%

[1] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Acentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
0.5	2	98
4.0	15	85
7.0	50	50
9.0	50	50
9.1	2	98

Flow Rate: 1.0 mL/min

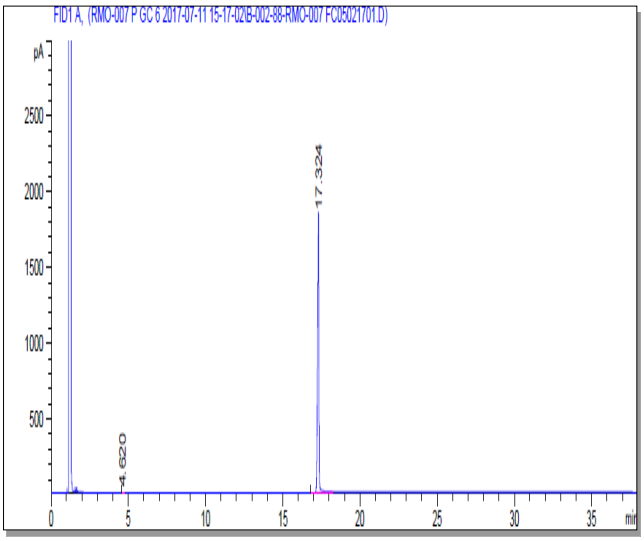
Wavelength: 225 nm

Sample Name: FC05021701

Acquired: August 02, 2017

Peak #	Ret Time	Area %
1	1.69	0.09
2	1.78	0.12
3	2.62	99.66
4	3.02	0.04
5	3.12	0.03
6	4.55	0.06
7	4.84	0.02

GC/FID



Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness

Temp Program: 40°C to 200°C at 40°C/min
200°C to 280°C at 5°C/min
hold 18 min

Injector Temp: Cool-on-Column

Detector Temp: 325°C

Sample Name: FC05021701

Acquired: July 11, 2017

Peak #	Ret Time	Area %
1	4.62	0.06
2	17.32	99.94

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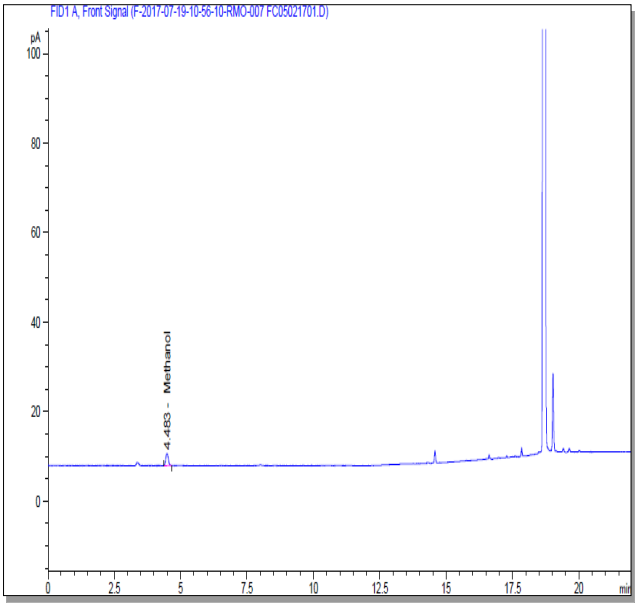
Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace

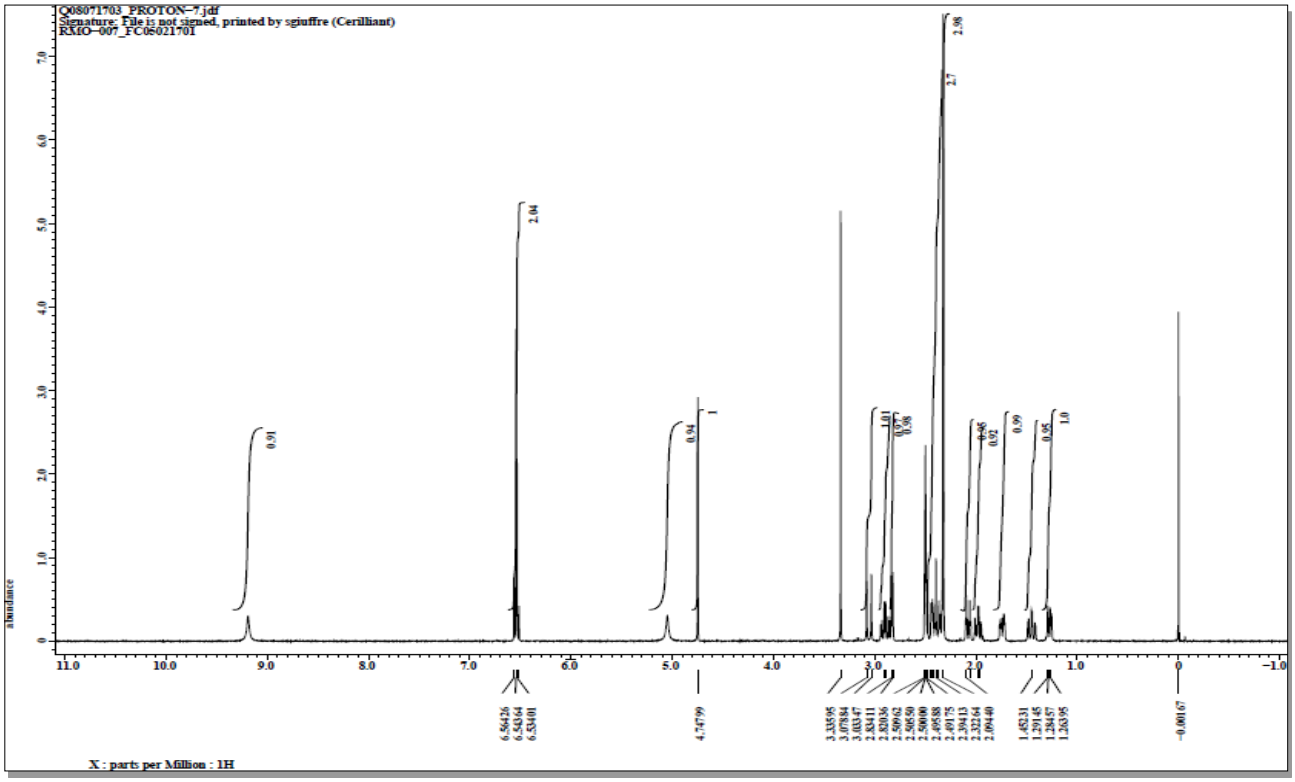


Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC05021701
Acquired:	July 19, 2017

Peak	Compound	Area	Weight %
1	Methanol	18.15	0.14
2	NMP	NA	NA
Total			**0.14**

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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Spectral and Physical Data (cont.)

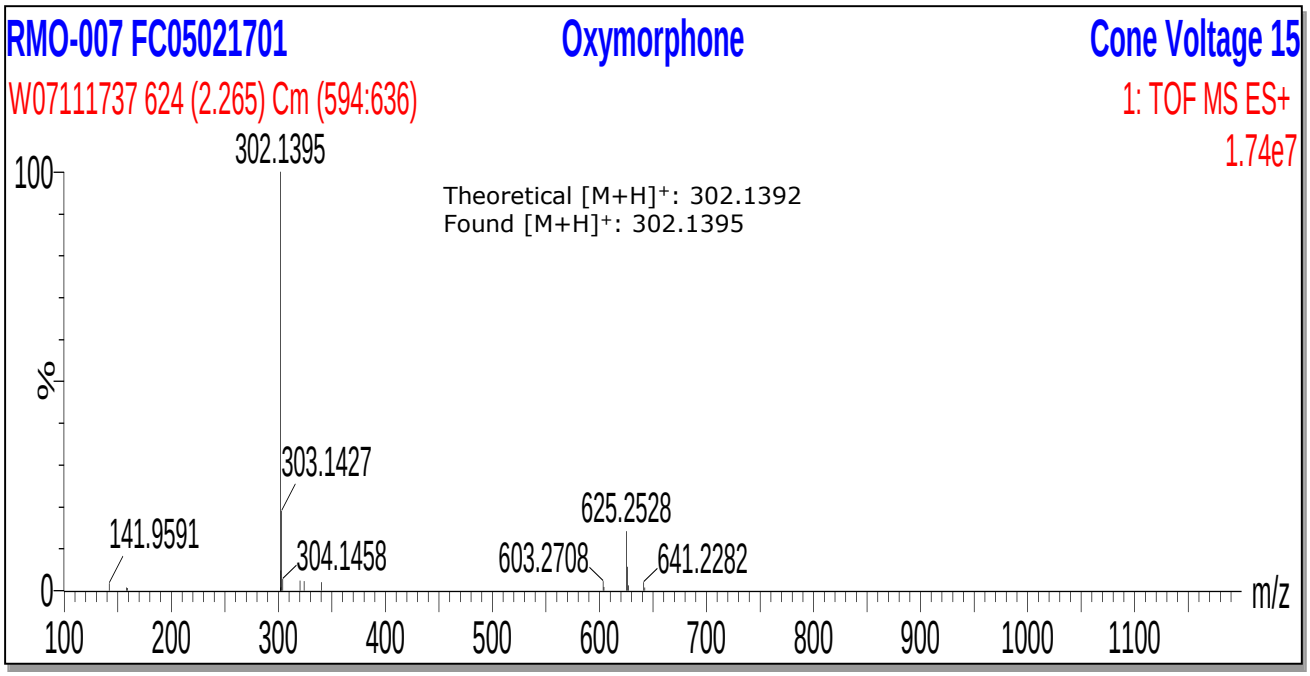
LC/MS

Column: Ascentis Express C18, 2.7 µm, 3.0 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: 100 - 1200 amu
Ionization: Electrospray, Positive Ion
Instrument: Waters XEVO G2 QTOF
Acquired: July 11, 2017



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 stability findings for a related product (O-003, Oxymorphone-D_3) 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 20, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

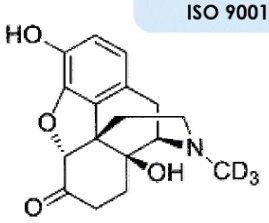
Certified Reference Material - Certificate of Analysis

Oxymorphone-D_3, Primary Measurement Standard

(5α-4,5-Epoxy-3,14-dihydroxy-17-trideuteromethylmorphinan-6-one

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: O-019-1ML
Lot No.: FE01082010
Description of CRM: Oxymorphone-D_3 in Methanol (Solution)
Expiration Date: January 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{17}H_{16}D_3NO_4$
CAS No.: 145225-03-2
Regulatory: USDEA Exempt | Canadian TK # 61-1421



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
Oxymorphone-D_3	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

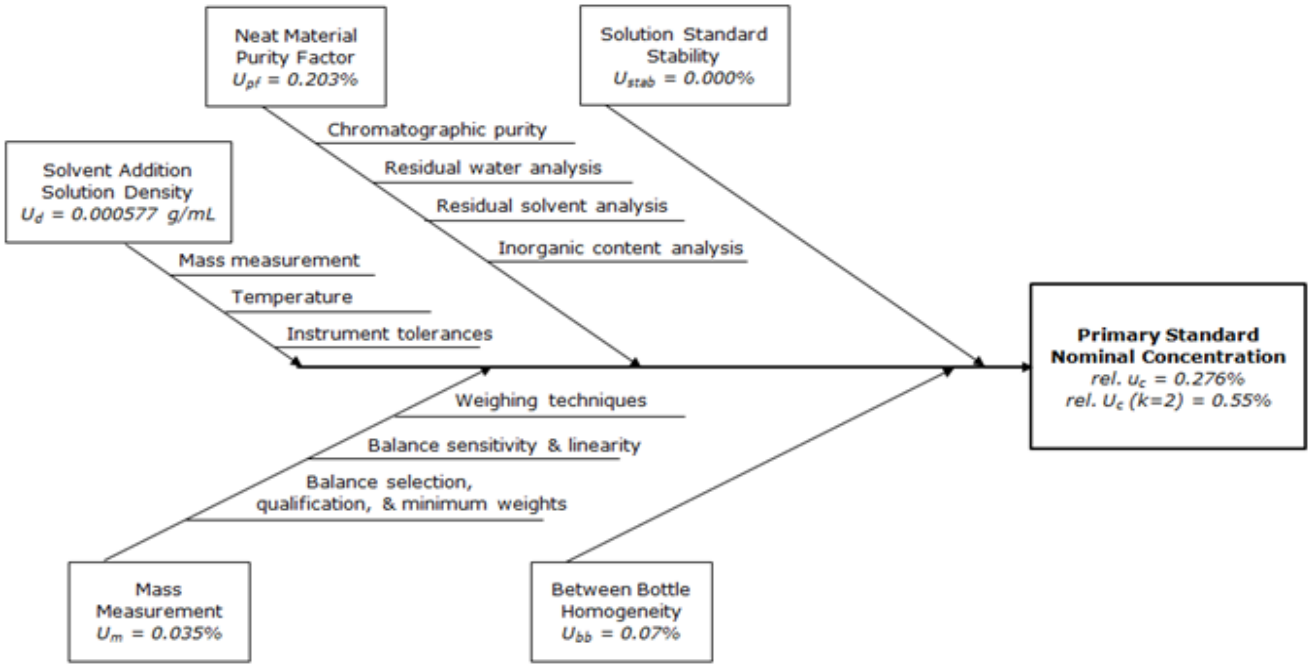
February 18, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.
Certificate of Origin:	Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (5:95)	**Linearity (r) :**	1.000
Flow Rate:	1.5 mL/min		
Wavelength:	225 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE01082010	0.992	0.5
Previous Lot	FE07311802	0.998	0.3

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	Oxymorphone-D_3	**Chemical Formula:**	$C_{17}H_{16}D_3NO_4$
Material Lot:	FC03151801	**CAS Number:**	145225-03-2
		Molecular Weight:	304.36

Material Characterization Summary

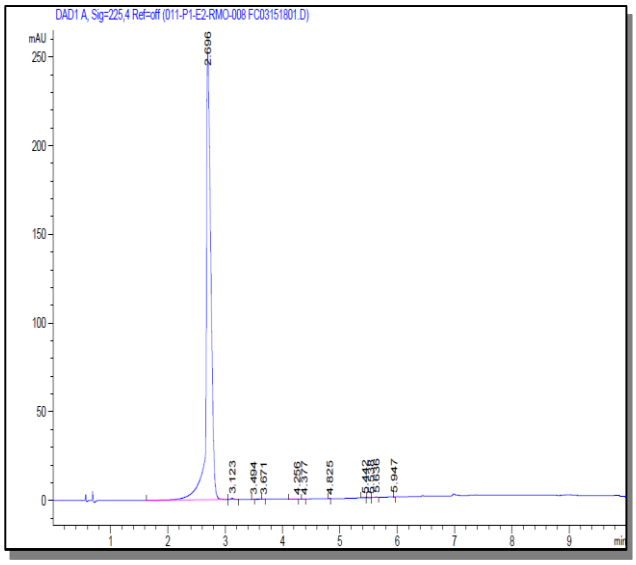
Analytical Test	**Method**	**Results**	
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	99.8% [1]	
Secondary Chromatographic Purity by GC/FID Analysis	SP10-0101	99.4%	
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure	
Isotopic Purity and Distribution by LC/MS SIM Analysis	SP10-0107	0.17% D_0 vs D_3	
		0.16% D_0	0.24% D_2
		0.05% D_1	99.55% D_3
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure	
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	None Detected	
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	Below Quantitation Limit	
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%	
Mass Balance Purity Factor		99.79%	

[1] 0.02% Noroxymorphone detected by HPLC/UV analysis.
[2] Validated analytical method

- 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 purity method was selected to optimize resolution of impurities while minimizing degradation of the analyte. Secondary purity methods with orthogonal detector capabilities from the primary purity method are used as controls to confirm an accurate purity value.
- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- A secondary chromatographic purity method is utilized as a control.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



Column: Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm

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

Gradient:

Time (min)	% A	% B
0.0	2	98
0.5	2	98
4.0	15	85
7.0	50	50
9.0	50	50
9.1	2	98

Flow Rate: 0.8 mL/min

Wavelength: 225 nm

Sample Name: FC03151801

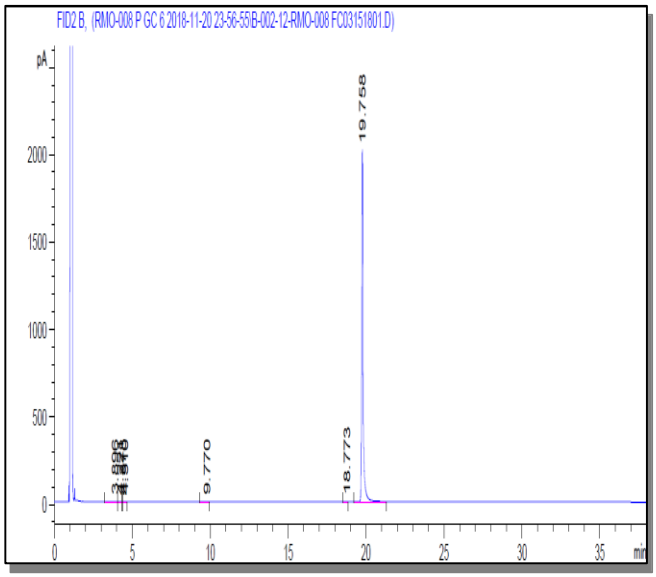
Acquired: December 05, 2018

Peak #	Ret Time	Area %
1	2.70	99.72
2	3.12	0.17
3	3.49	0.01
4	3.67	0.01
5	4.26	0.02
6	4.38	0.01
7	4.83	0.00
8	5.44	0.01
9	5.54	0.01
10	5.64	0.05
11	5.95	0.00

Peak #5 has been identified as Noroxymorphone

Spectral and Physical Data (cont.)

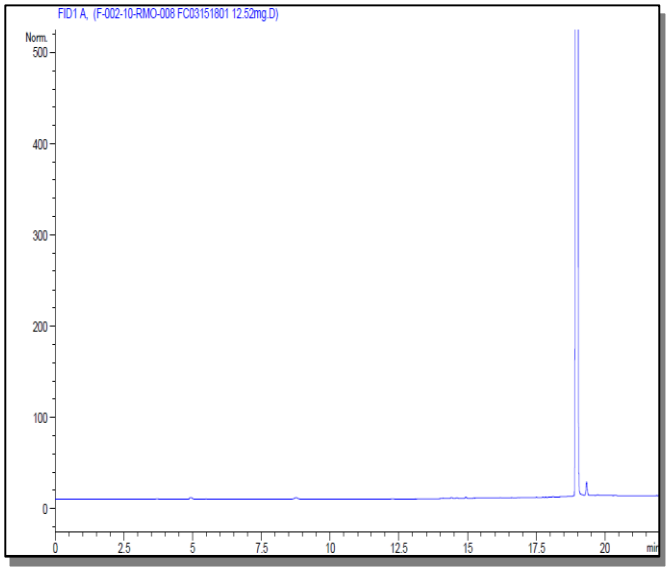
GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	40°C to 200°C at 40°C/min 200°C to 280°C at 5°C/min hold 18 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC03151801
Acquired:	November 21, 2018

Peak #	Ret Time	Area %
1	3.90	0.31
2	4.22	0.12
3	4.38	0.02
4	4.51	0.07
5	9.77	0.03
6	18.77	0.02
7	19.76	99.43

Residual Solvent Analysis by GC/FID Headspace



Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 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
Sample Name:	FC03151801
Acquired:	November 20, 2018

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

ND - None Detected

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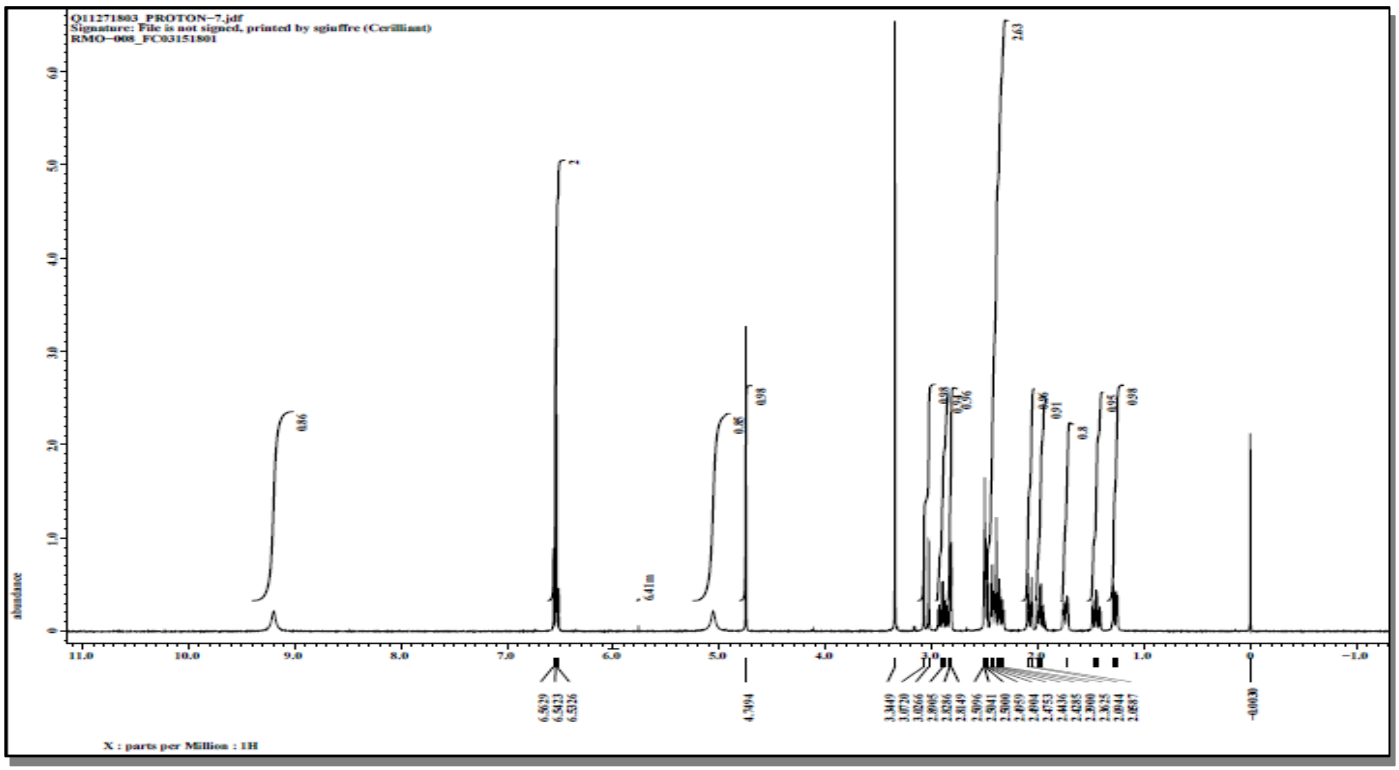
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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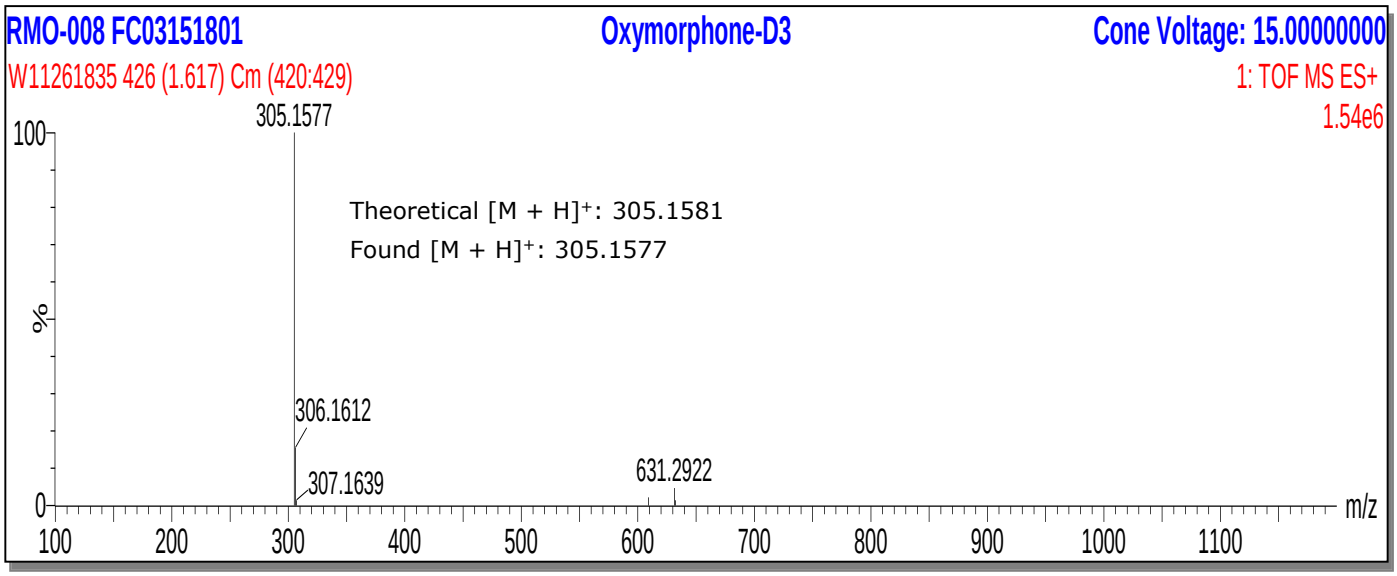
Spectral and Physical Data (cont.)

LC/MS

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	100-1200 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	November 26, 2018

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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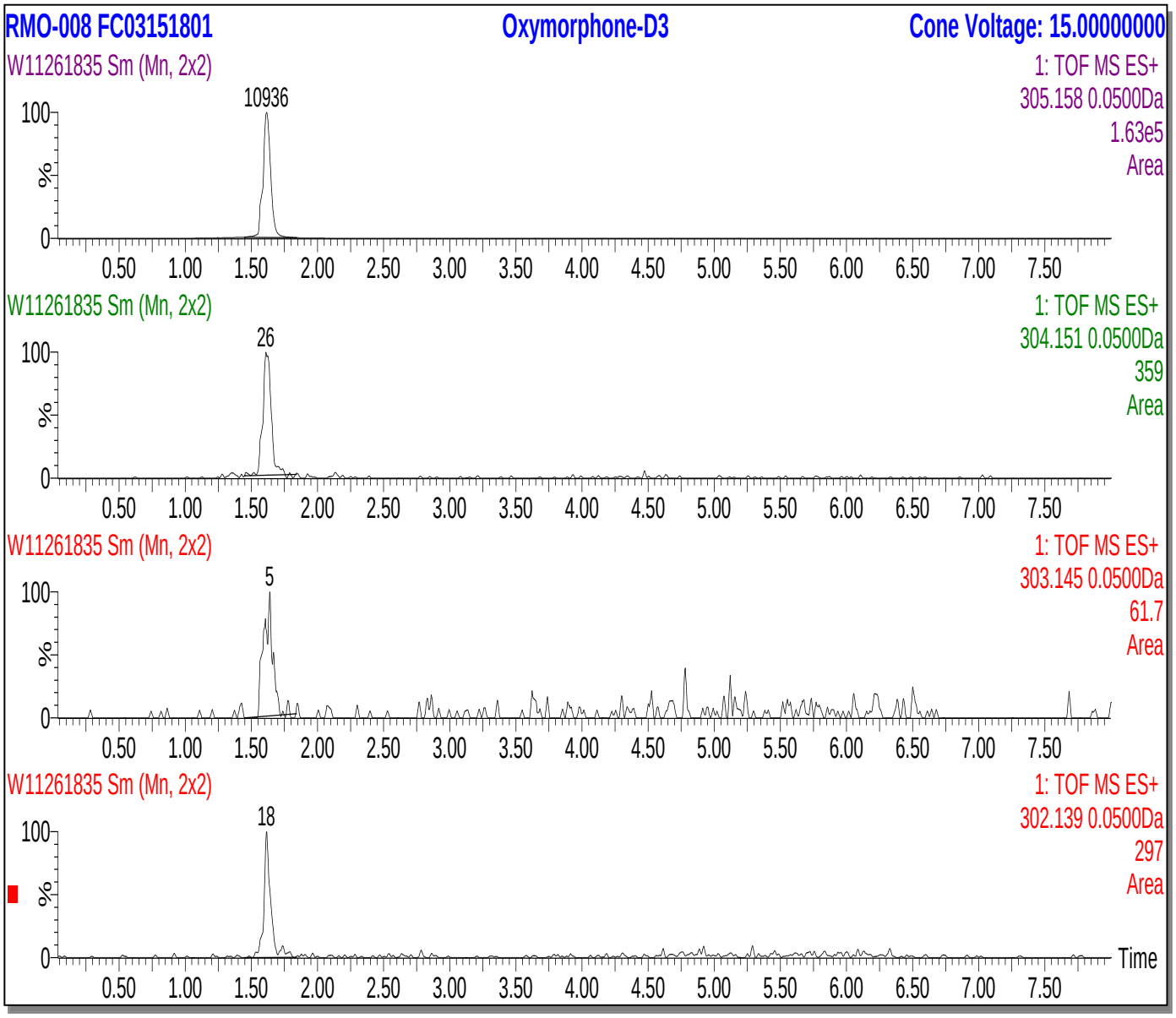
Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM

Column:	Ascentis Express C18, 2.7 µm, 3.0 x 50 mm	**Flow Rate:**	0.4 mL/min
Mobile Phase:	A: 0.1% Formic acid in Water B: Acetonitrile	**Scan Range:**	302-305 amu
		Ionization:	Electrospray, Positive Ion
		Instrument:	Waters XEVO G2 QTOF
Gradient:		**Acquired:**	November 26, 2018

Time (min)	% A	% B
0.0	98	2
0.5	98	2
4.0	70	30
5.8	70	30
6.0	98	2
8.0	98	2



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	February 18, 2020	Initial version.

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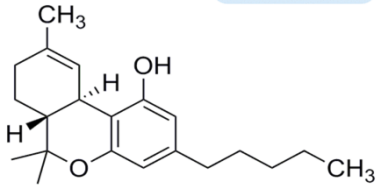
Certified Reference Material - Certificate of Analysis

(-)-Δ^9-THC, Primary Measurement Standard

(6aR,10aR)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6H-dibenzo[b,d]pyran-1-ol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: T-005-1ML
Lot No.: FE02072002
Description of CRM: (-)-Δ^9-THC in Methanol (Solution)
Expiration Date: February 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{21}H_{30}O_2$
CAS No.: 1972-08-3
Regulatory: USDEA Exempt | Canadian TK # 61-1540



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(-)-Δ^9-THC	1.000 ± 0.006 mg/mL

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

May 01, 2020
Issue Date

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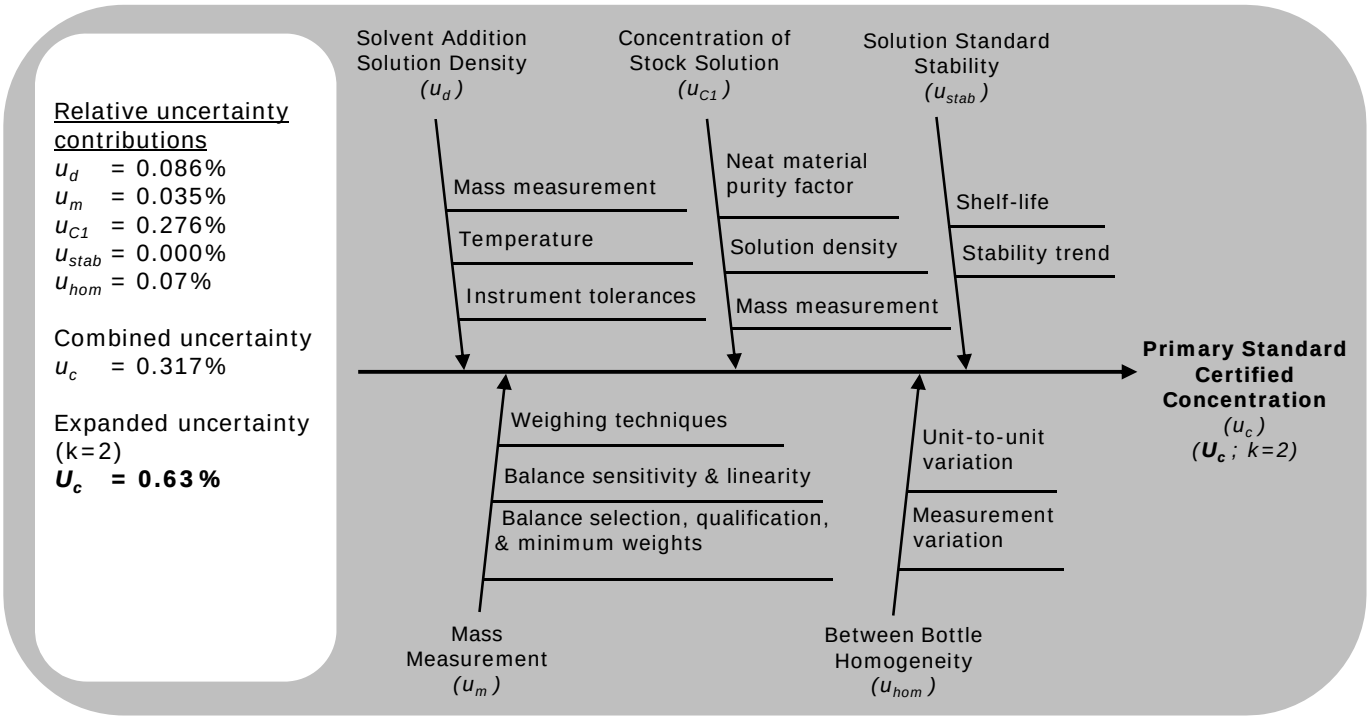
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Luna C18 (2), 3 µm, 4.6 x 150 mm	**Number of Points:**	4
Mobile Phase:	Methanol:Water:Tetrahydrofuran (71:24:5)	**Linearity (r) :**	1.000
Flow Rate:	1.0 mL/min		
Wavelength:	228 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02072002	0.986	0.5
Previous Lot	FE08221804	0.948	0.1

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Standard Solution	**Lot Number**	**Verified Concentration against USP Standard HPLC Analysis**
New Lot	FE02072002	1.018

- Concentration is verified against an independently prepared calibration solution using USP Standard 1651621 Lot R045H0

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Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(-)-Δ^9-THC	**Chemical Formula:**	$C_{21}H_{30}O_2$
Material Lot:	FC02181901	**CAS Number:**	1972-08-3
		Molecular Weight:	314.46

Material Characterization Summary

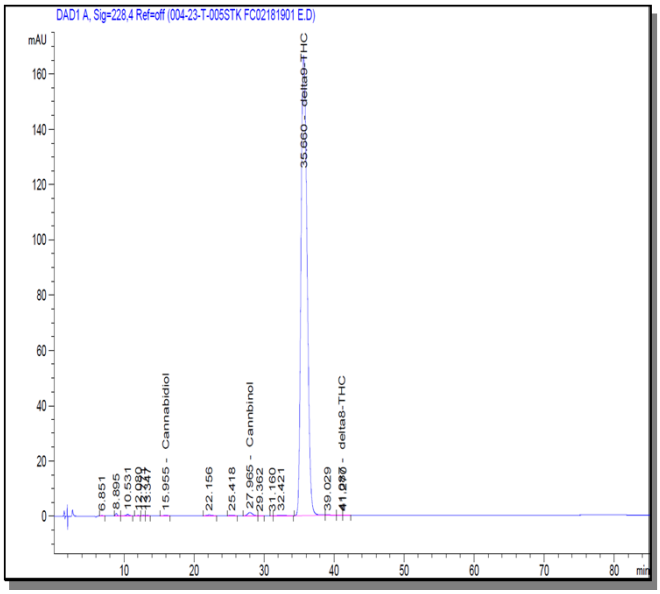
Analytical Test	**Method**	**Results**
Chromatographic Purity by HPLC/UV Analysis	AM1280	99.0% [1]
exo-THC Determination by GC/FID Analysis	AM1266	0.1%
Identity by GC/MS Analysis	SP10-0105	Consistent with Structure
Identity by ^{1}H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	AM1087 [2]	0.22%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	0.32%
Mass Balance Purity Factor		98.51%

[1] Purity value adjusted for known impurities as shown on the trace below.
[2] Validated analytical method

- The chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC / UV



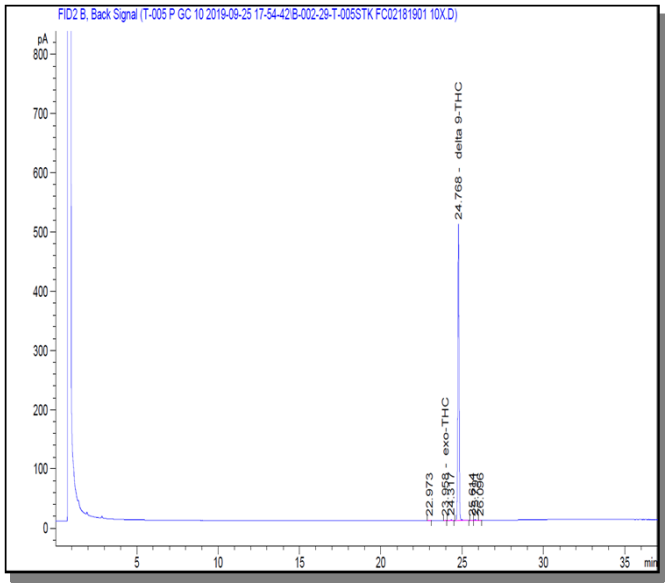
Column: Luna C18, 3 µm, 4.6 x 150 mm
Mobile Phase: Methanol:Water:Tetrahydrofuran (71:24:5)
Flow Rate: 1.0 mL/min
Wavelength: 228 nm

Sample Name: FC02181901
Acquired: September 23, 2019

Peak #	Ret Time	Area %	
1	6.85	0.02	
2	8.90	0.14	
3	10.53	0.13	
4	12.08	0.01	
5	12.77	0.02	
6	13.35	0.02	
7	15.96	0.05	Cannabidiol
8	22.16	0.09	
9	25.42	0.04	
10	27.97	0.51	Cannabinol
11	29.36	0.00	
12	31.16	0.00	
13	32.42	0.10	
14	35.66	98.72	(-)-Δ^9-THC
15	39.03	0.09	
16	41.09	0.02	(-)-Δ^8-THC
17	41.27	0.02	

Spectral and Physical Data (cont.)

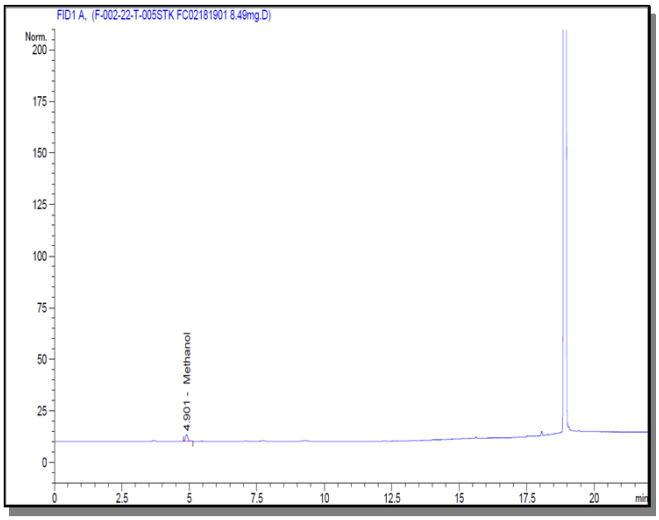
exo-THC by GC/FID



Column:	DB-35ms, 30 m x 0.53 mm ID, 1.0 µm film thickness
Temp Program:	60°C to 200°C at 10°C/min 200°C to 280°C at 5°C/min hold 7 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC02181901
Acquired:	September 25, 2019

Peak #	Ret Time	Area %	
1	22.97	0.03	
2	23.96	0.05	exo-THC
3	24.32	0.20	
4	24.77	99.44	(-)-Δ^9-THC
5	25.61	0.04	
6	25.79	0.20	
7	26.10	0.03	

Residual Solvent Analysis by GC/FID Headspace



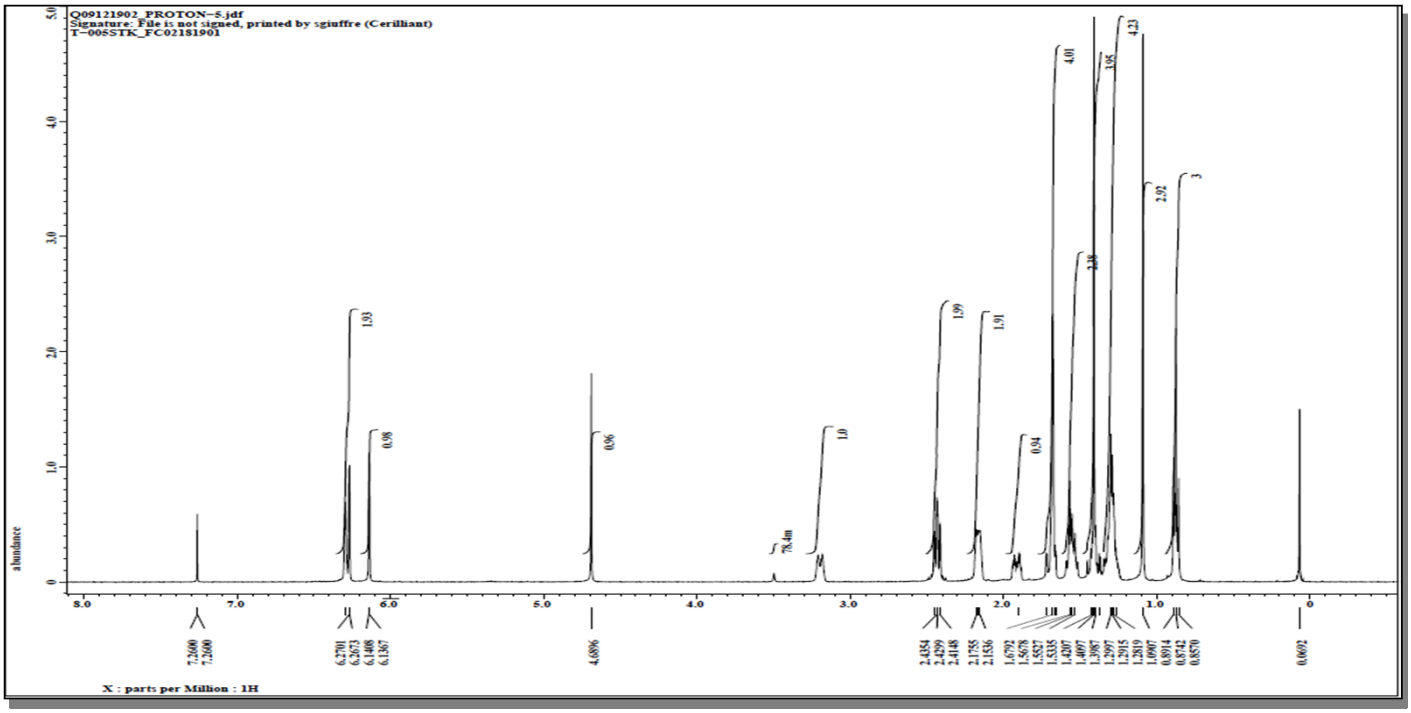
Column:	DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program:	40°C hold 12 min to 220°C at 40°C/min hold 5.5 min
Carrier Gas:	Helium
Flow Rate:	2.0 mL/min
Detector Heater Temp:	250°C
Injector:	Headspace Sampler
HS Oven Temp:	60°C
Vial Equilibration:	10 minutes
Sample Name:	FC02181901
Acquired:	September 13, 2019

Peak	Compound	Area	Weight %
1	Methanol	20.94	0.22
2	NMP	NA	NA
Total			**0.22**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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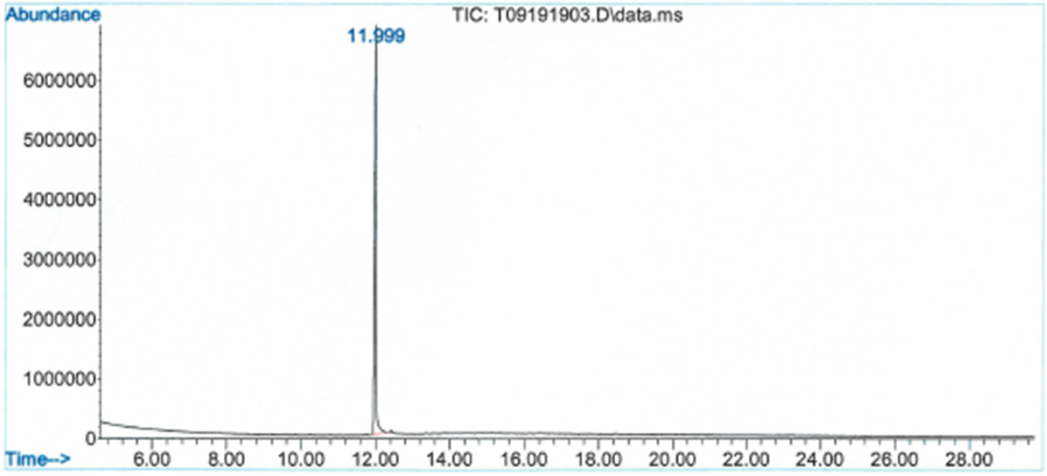
Spectral and Physical Data (cont.)

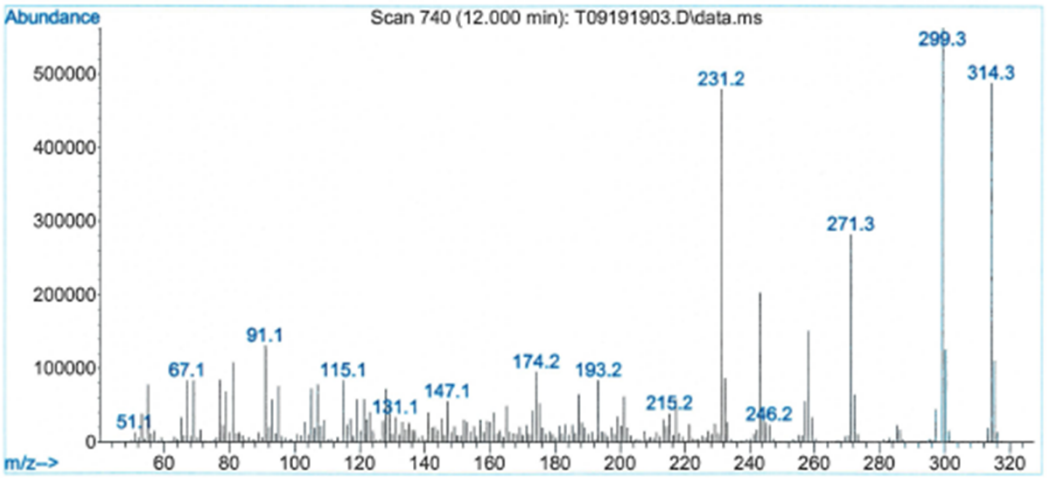
GC / MS

```
Compound Name        : (-)-delta9-THC
Lot Number           : FC02181901
Instrument           : Agilent GCMS
Operator             : ECM(SGIUFFRE)
Date Reported        : Thu Sep 19 09:33:31 2019
Column Type          : DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program        : 50°C to 200°C@40°C/min, 200°C to 300°C@10°C/min, 16min hold
Injector Temp.       : Cool on-column
Carrier Gas          : Helium
Flow Rate (mL\min)   : 0.80 mL/min
Transfer Line Temp.  : 280°C
Scan Range           : 50-500
```

Total Ion Chromatogram



Mass Spectrum



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Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	May 01, 2020	Initial version.

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

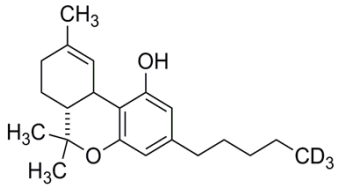
Certified Reference Material - Certificate of Analysis

(-)-Δ^9-THC-D_3, Primary Measurement Standard

(6aR,10aR)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-(pentyl-5,5,5-d $_3$)-6H-dibenzo[b,d]pyran-1-ol

Cerilliant Quality
ISO 17034
ISO/IEC 17025
ISO 13485
ISO 14001
ISO 9001

Product No.: T-011-1ML
Lot No.: FE02042012
Description of CRM: (-)-Δ^9-THC-D_3 in Methanol (Solution)
Expiration Date: May 2025 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{21}H_{27}D_3O_2$
CAS No.: 81586-39-2
Regulatory: USDEA Exempt | Canadian TK # 61-1546



Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
(-)-Δ^9-THC-D_3	**1.000 ± 0.006 mg/mL**

Metrological traceability: Traceable to the SI and higher order standards from NIST through an unbroken chain of comparisons. See "Details on metrological traceability" on page 2.

Measurement method: The certified value is calculated from high precision weighing of thoroughly characterized starting material. See "Details about certification process" on page 2.

Intended use: This Certified Reference Material is suitable for the in vitro identification, calibration, and quantification of the analyte(s) in analytical and R&D applications. Not suitable for human or animal consumption.

Minimum sample size: 1 µL for quantitative applications

Instructions for handling and correct use: Concentration is corrected for chromatographic purity, residual water, residual solvents, and residual inorganics. No adjustment required before use.
Users should quantitatively transfer desired volume using established good laboratory practices to spike into matrix or to dilute to the desired concentration. Each ampoule is intended for one-time use.
For MS Applications, we advise laboratories not to mix lots during a single sequence.

Health and safety information: Danger. Please refer to the Safety Data Sheet for detailed information about the nature of any hazard and appropriate precautions to be taken.

Accreditation: Cerilliant Corp. is accredited by the US accreditation authority ANAB as registered reference material producer AR-1353 in accordance with ISO 17034 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER

Darron Ellsworth, Quality Assurance Manager

June 01, 2020
Issue Date

Cerilliant Corporation, 811 Paloma Drive, Suite A Round Rock, TX 78665, USA, Tel: 800-848-7837 / 512-238-9974

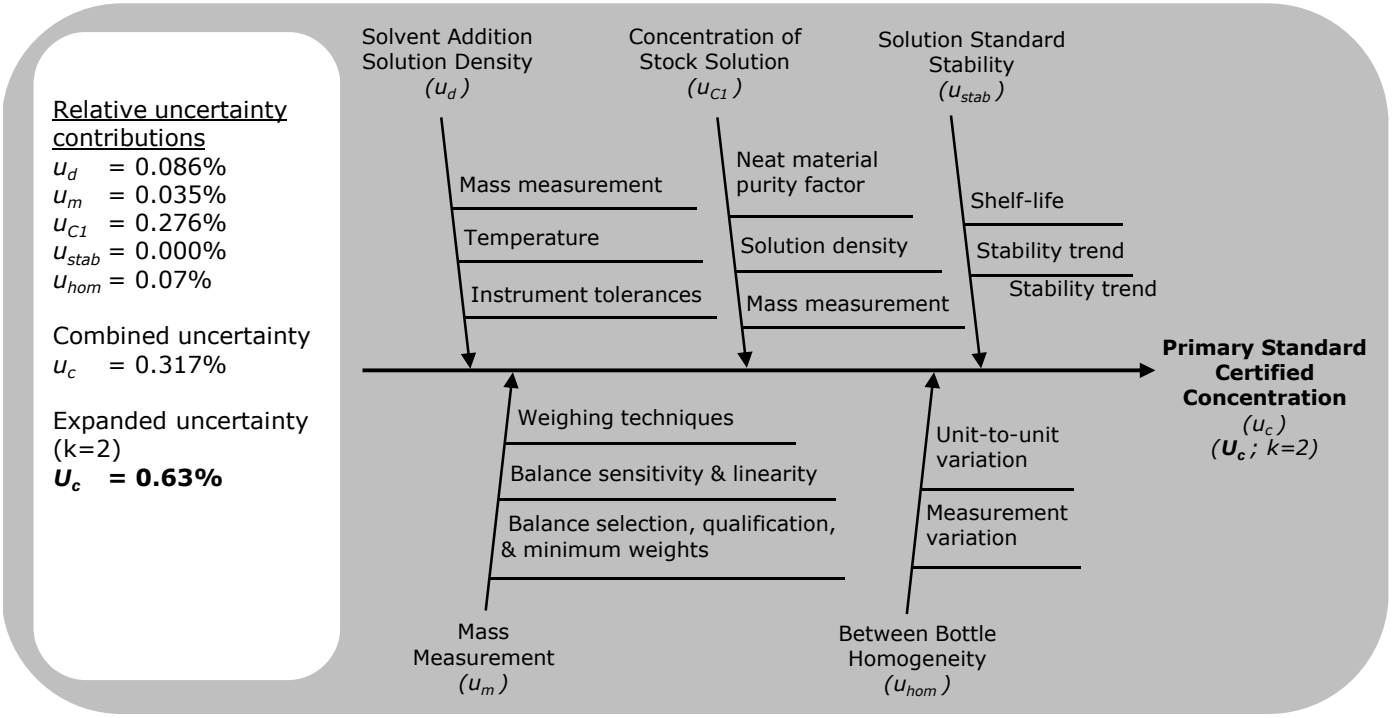
Packaging: 2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.

Details on starting materials: Each raw material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques and is assigned a Mass Balance Purity Factor. Spectral data is provided on subsequent pages of this CoA.

Certificate of Origin: Cerilliant Corporation certifies no material of animal origin (BSE/TSE) was used in the preparation of this product. This material was manufactured in the USA.

Associated uncertainty:

The uncertainty has been calculated by statistical analysis of all aspects of our production system and incorporated uncertainty of the mass balance purity factor, material density, balance, weighing technique, and homogeneity. Uncertainty components of the gravimetrically prepared Primary Standard concentration are shown in the figure below. Uncertainty is expressed as an expanded uncertainty in accordance with ISO 17034 at the approximate 95% confidence interval using a coverage factor of k=2. Uncertainty contribution from neat material homogeneity was established to be negligible through establishment of process controls and verification of the control process. Stability uncertainty was determined to be negligible by regression analysis.



Details on metrological traceability:

- This standard has been gravimetrically prepared using balances that have been fully qualified and calibrated to ISO 17025 requirements. All calibrations utilize NIST traceable weights which are calibrated externally by a qualified ISO 17025 accredited calibration laboratory to NIST standards. Qualification of each balance includes the assignment of a minimum weighing by a qualified and ISO 17025 accredited calibration vendor taking into consideration the balance and installed environmental conditions to ensure compliance with USP tolerances of NMT 0.10% relative error.
- Fill volume to predetermined specifications is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- The density and material Mass Balance Purity Factor of each raw material is traceable to the SI and higher order reference materials through mass measurement and instrument qualification and calibrations.

Details about certification process:

This standard has been prepared and certified under the ISO 17034, ISO/IEC 17025, ISO 9001 and ISO 13485 standards. This standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

- Nominal concentration is calculated based on: the actual mass; Mass balance purity factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20°C.
- Fill volume is gravimetrically verified throughout the dispensing process using qualified and calibrated balances.
- Concentration is verified against an independently prepared calibration solution gravimetrically prepared.
- Additional certification information available upon request.

Solution Standard Verification

Concentration accuracy and within- and between-bottle homogeneity are analytically verified against an independently prepared calibration solution and to the prior lot.

Solution standard verification demonstrates confirmation that the specified requirements for the Primary Measurement Standard have been fulfilled and validated under ISO 13485.

Standard Solution Assay Parameters		**Calibration Curve**	
Analysis Method:	HPLC/UV	**Calibration Curve:**	Linear Regression
Column:	Ascentis Express Phenyl-Hexyl, 2.7 µm, 3.0 x 100 mm	**Number of Points:**	4
		Linearity (r) :	1.000
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (70:30)		
Flow Rate:	1.5 mL/min		
Wavelength:	228 nm		

		Verified Concentration (mg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02042012	0.996	0.1
Previous Lot	FE04231905	0.981	0.1

- Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution.
- Within-sample and between-sample homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. Multiple samples pulled from across the lot using a random stratified sampling plan were analyzed to verify homogeneity. % RSD results shown above for the New Lot demonstrate ampoule-to-ampoule homogeneity.

Analyte Certification - Mass Balance Purity Factor

Each analyte is thoroughly identified and characterized using an orthogonal approach. A mass balance purity factor is assigned incorporating chromatographic purity and residual impurities. The mass balance purity factor is utilized to calculate the weighing adjustment necessary to ensure accuracy of the solution standard concentration.

Material Name:	(-)-Δ^9-THC-D_3	**Chemical Formula:**	$C_{21}H_{27}D_3O_2$
Material Lot:	FC10041904	**CAS Number:**	81586-39-2
		Molecular Weight:	317.48

Material Characterization Summary

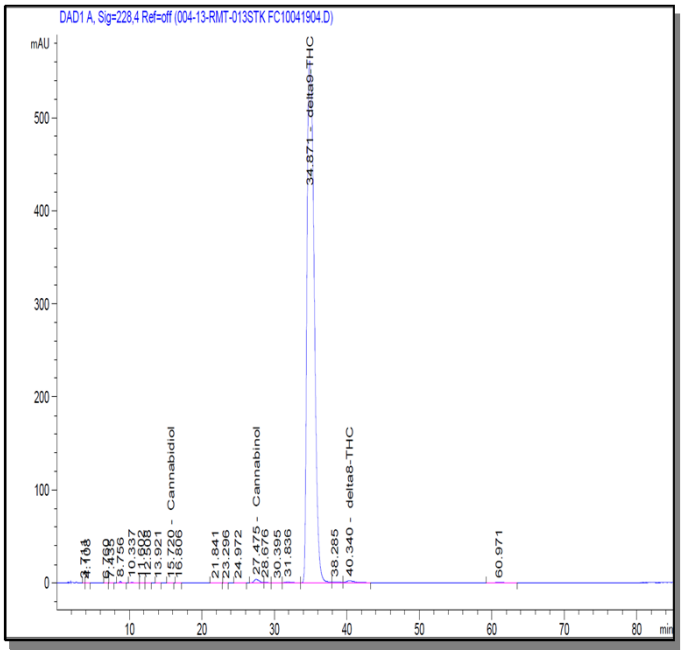
Analytical Test	**Method**	**Results**
Chromatographic Purity by HPLC/UV Analysis	20397996	98.8% [1]
exo-THC Determination by GC/FID Analysis	20397988	0.1%
Identity by GC/MS Analysis	20384214	Consistent with Structure
Identity by ^{1}H-NMR Analysis	20384224	Consistent with Structure
Residual Solvent Analysis by GC/FID Headspace	20397799 [2]	1.34%
Residual Water Analysis by Karl Fischer Coulometry	20398075 [2]	Below Quantitation Limit
Mass Balance Purity Factor		97.49%

[1] Purity value adjusted for known impurities as shown on the trace below.
[2] Validated analytical method

- The primary chromatographic purity value is used to calculate the Mass Balance Purity Factor.
- Mass Balance Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- Mass Balance Purity Factor does not include adjustment for chiral and/or isotopic purity.

Spectral and Physical Data

HPLC/UV



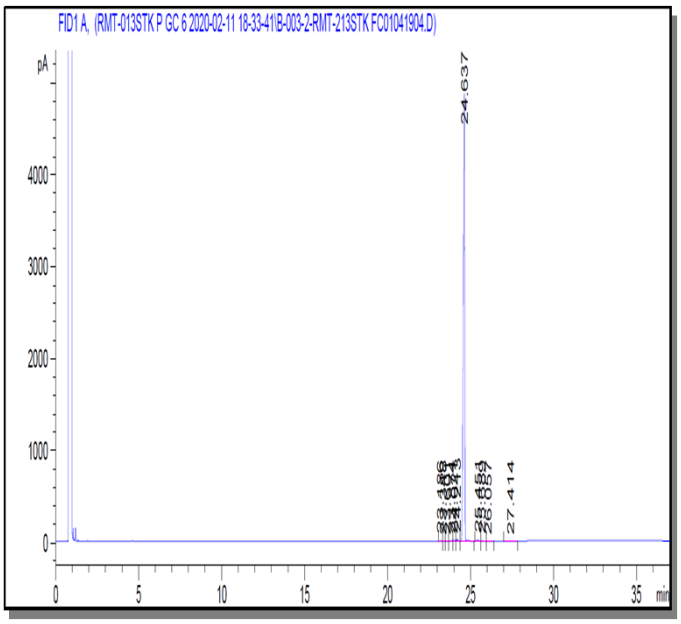
Column: Luna C18, 3 µm, 4.6 x 150 mm
Mobile Phase: Methanol:Water:Tetrahydrofuran (71:24:5)
Flow Rate: 1.0 mL/min
Wavelength: 228 nm

Sample Name: FC10041904
Acquired: February 10, 2020

Peak #	Ret Time	Area %	
1	3.71	0.00	
2	4.11	0.00	
3	6.76	0.00	
4	7.44	0.00	
5	8.76	0.07	
6	10.34	0.04	
7	11.60	0.01	
8	12.51	0.01	
9	13.92	0.00	
10	15.72	0.01	Cannabidiol
11	16.81	0.00	
12	21.84	0.02	
13	23.30	0.00	
14	24.97	0.02	
15	27.48	0.46	Cannabinol
16	28.68	0.03	
17	30.40	0.02	
18	31.84	0.13	
19	34.87	98.53	(-)-Δ^9-THC
20	38.29	0.19	
21	40.34	0.40	(-)-Δ^8-THC
22	60.97	0.04	

Spectral and Physical Data (cont.)

exo-THC by GC/FID

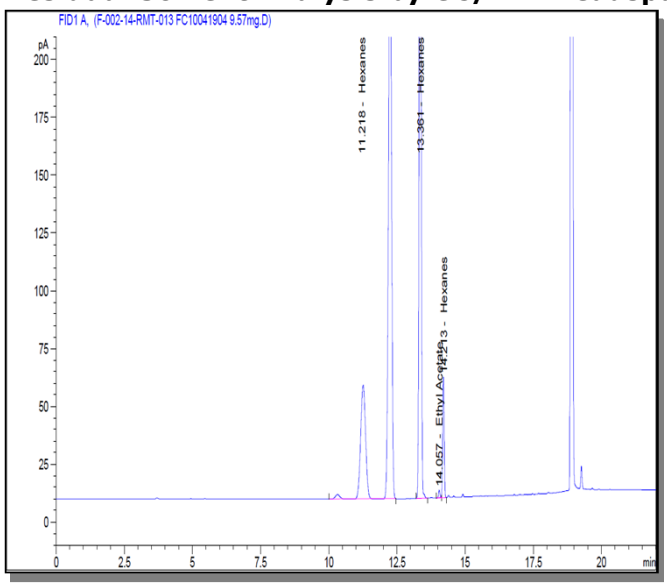


Column: DB-5ms, 30 m x 0.53 mm ID, 1.5 µm film thickness
Temp Program: 60°C to 200°C at 10°C/min 200°C to 280°C at 5°C/min hold 7 min
Injector Temp: Cool-on-Column
Detector Temp: 325°C

Sample Name: FC10041904
Acquired: February 11, 2020

Peak #	Ret Time	Area %	
1	23.19	0.06	
2	23.35	0.01	
3	23.60	0.01	
4	23.87	0.10	
5	24.02	0.15	exo-THC
6	24.21	0.37	(-)-Δ^8-THC
7	24.64	99.01	(-)-Δ^9-THC
8	25.45	0.24	
9	25.69	0.04	
10	26.06	0.01	
11	27.41	0.01	

Residual Solvent Analysis by GC/FID Headspace



Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C hold 12 min to 220°C at 40°C/min hold 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

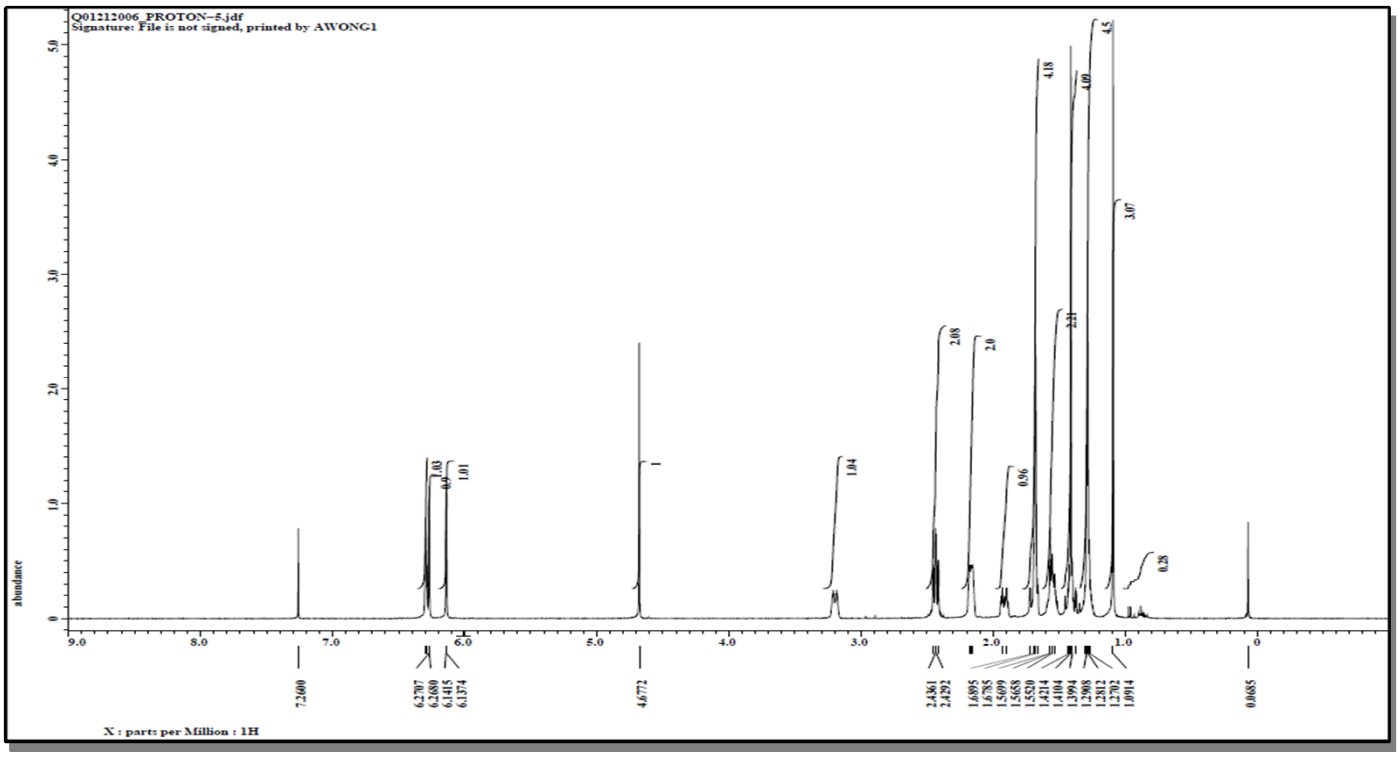
Sample Name: FC10041904
Acquired: January 31, 2020

Peak	Compound	Area	Weight %
1	Hexanes	4799.00	1.30
2	Ethyl acetate	12.19	0.04
3	NMP	NA	NA
Total			**1.34**

Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: Chloroform-D



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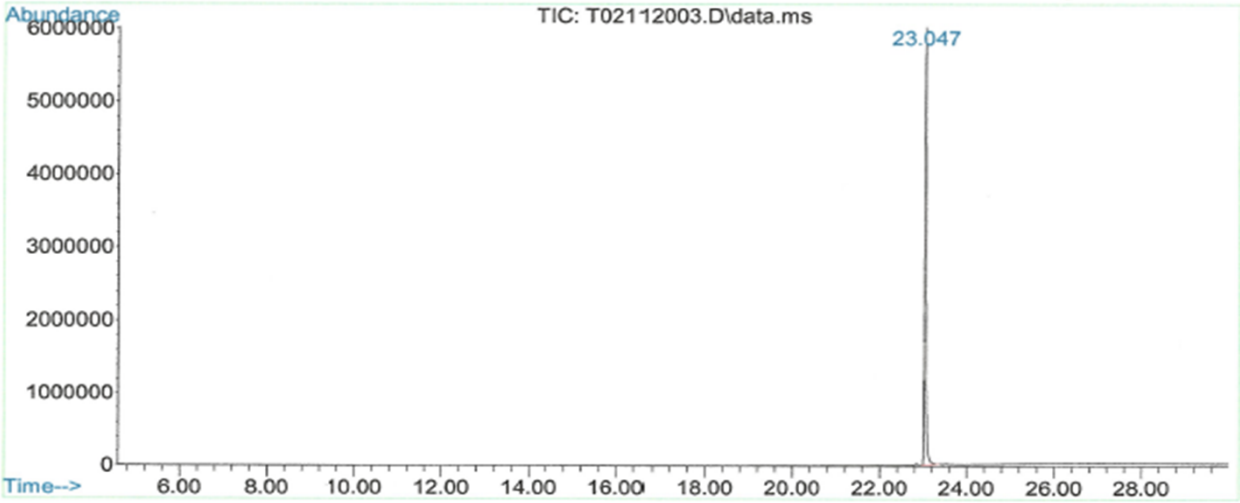
Spectral and Physical Data (cont.)

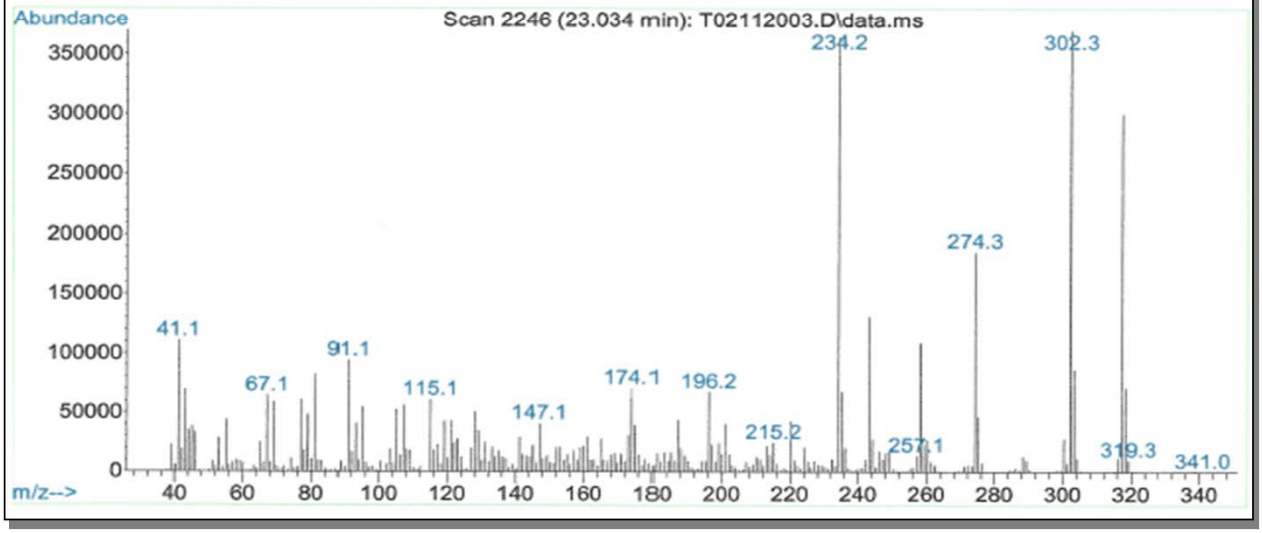
GC/MS

Compound Name	: (-)-delta9-THC-D3
Lot Number	: FC10041904
Instrument	: Agilent GCMS
Operator	: ECM(SGIUFFRE)
Date Reported	: Wed Feb 12 06:47:37 2020
Column Type	: DB-5ms, 30m x 0.25mm ID, 0.25um film thickness
Temp. Program	: 50°C to 300°C @ 10°C/min (hold for 5 min)
Injector Temp.	: Cool on-column
Carrier Gas	: Helium
Flow Rate (mL\min)	: 0.80 mL/min
Transfer Line Temp.	: 280°C
Scan Range	: 35-400

Total Ion Chromatogram



Mass Spectrum



Stability

Short term stability studies have been performed in multiple storage conditions for a period of up to four weeks. Short term data is utilized 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 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	

Transport/Shipping: *Stability studies support the transport of this product at ambient conditions.*

Long Term Stability: *Long term stability has been assessed for Freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 60 months has been established for a related product (T-003, (-)-Δ^9-THC) through real-time stability studies.*

Commutability

This standard is a solution of a pure substance in an organic solvent and is a Primary Standard. This Primary Standard is suitable for use in the preparation of calibrators and/or controls in any biological matrix. This standard is not in a biological matrix and therefore commutability to methods or standards in biological matrices does not apply.

COA Revision History

Revision No.	Date	Reason for Revision
00	June 01, 2020	Initial version.