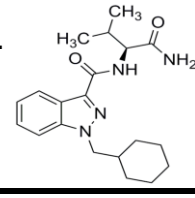
Certified Reference Material - Certificate of Analysis

AB-CHMINACA, Primary Measurement Standard

N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide

Product No.: S-108-1ML
Lot No.: FE02121802
Description of CRM: AB-CHMINACA in Methanol (Solution)
Retest Date: February 2020 See Section "Stability Assessment".
Storage: Store unopened in freezer (-10 °C to -25 °C).
Shipping: Ambient. See Section "Stability Assessment".
Chemical formula: $C_{20}H_{28}N_4O_2$
CAS No.: 1185887-21-1
Regulatory: USDEA Exempt | Canadian TK # 61-1620



Cerilliant Quality
ISO GUIDE 34
ISO/IEC 17025
ISO 13485
ISO 15194
ISO 9001
GMP/GLP

Analyte	Certified Concentration ± associated uncertainty U, u=k*u (k=2)
AB-CHMINACA	100.0 ± 0.6 µg/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 Health and safety information: Concentration is corrected for chromatographic purity, residual solvents and residual inorganics. No adjustment required before use.
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 Guide 34 and registered testing laboratory AT-1352 according to ISO/IEC 17025.

Darron Ellsworth, Quality Assurance Manager

February 22, 2019
Issue Date

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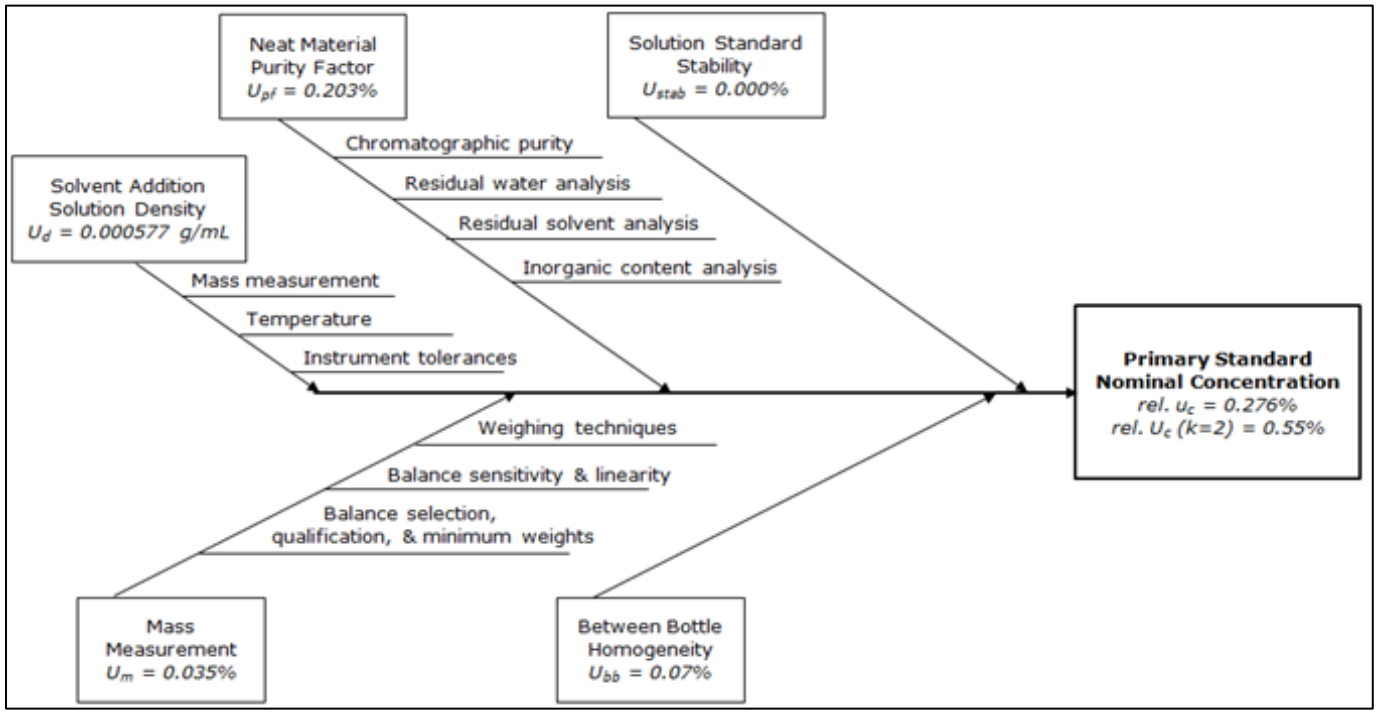
Packaging:	2 mL amber USP Type 1 glass ampoule containing not less than 1 mL of certified solution. Ampoules are overfilled to ensure a minimum of 1 mL volume can be transferred when using a 1mL Class A volumetric pipette.
Details on starting materials:	Each raw material utilized has been identified 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 Guide 34 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 Guide 34, 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 calcuated 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 areanalytically 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 50 mm	**Number of Points:**	4
Mobile Phase:	Acetonitrile:0.1% Phosphoric acid in Water (60:40)	**Linearity (r) :**	1.000
Flow Rate:	1.2 mL/min		
Wavelength:	300 nm		

		Verified Concentration (µg/mL)	**%RSD - Homogeneity**
Standard Solution	**Lot Number**	**Actual Results**	**Actual Results**
New Lot	FE02121802	99.8	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.

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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:	AB-CHMINACA	**Chemical Formula:**	$C_{20}H_{28}N_4O_2$
Material Lot:	FC06151701	**CAS Number:**	1185887-21-1
		Molecular Weight:	356.46

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 LC/MS Analysis	SP10-0107	Consistent with Structure
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]	0.57%
Residual Water Analysis by Karl Fischer Coulometry	AM1346 [2]	0.25%
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Mass Balance Purity Factor		99.10%

[1] 0.03% AB-CHMINACA metabolite-M_4 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.

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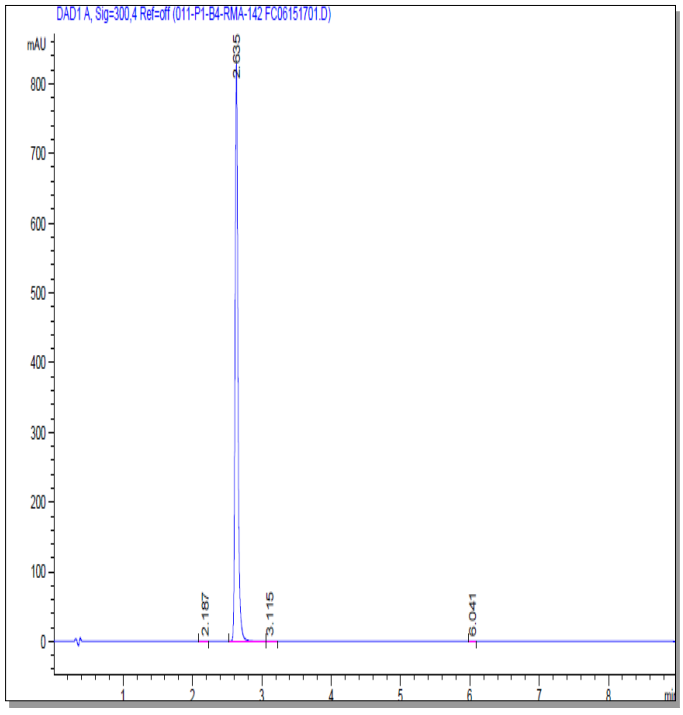
Spectral and Physical Data

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	40	60
5.0	80	20
7.0	80	20
7.1	40	60

Flow Rate: 0.6 mL/min

Wavelength: 300 nm

Sample Name: FC06151701

Acquired: February 16, 2018

Peak #	Ret Time	Area %
1	2.19	0.03
2	2.64	99.92
3	3.12	0.04
4	6.04	0.01

Peak 1 has been identified as AB-CHMINACA metabolite-M_4

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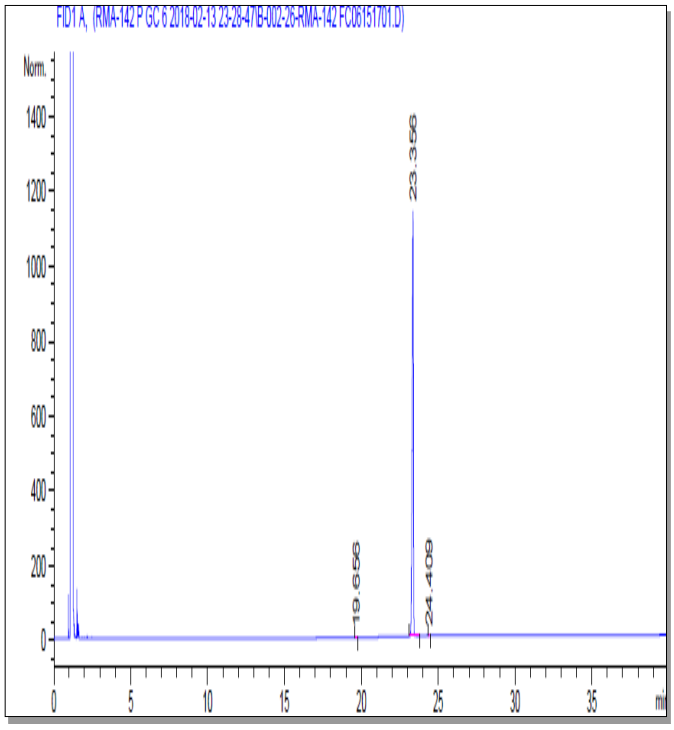
Spectral and Physical Data (cont.)

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 300°C at 5°C/min hold 16 min
Injector Temp:	Cool-on-Column
Detector Temp:	325°C
Sample Name:	FC06151701
Acquired:	February 14, 2018

Peak #	Ret Time	Area %
1	19.66	0.05
2	23.36	99.95
3	24.41	0.01

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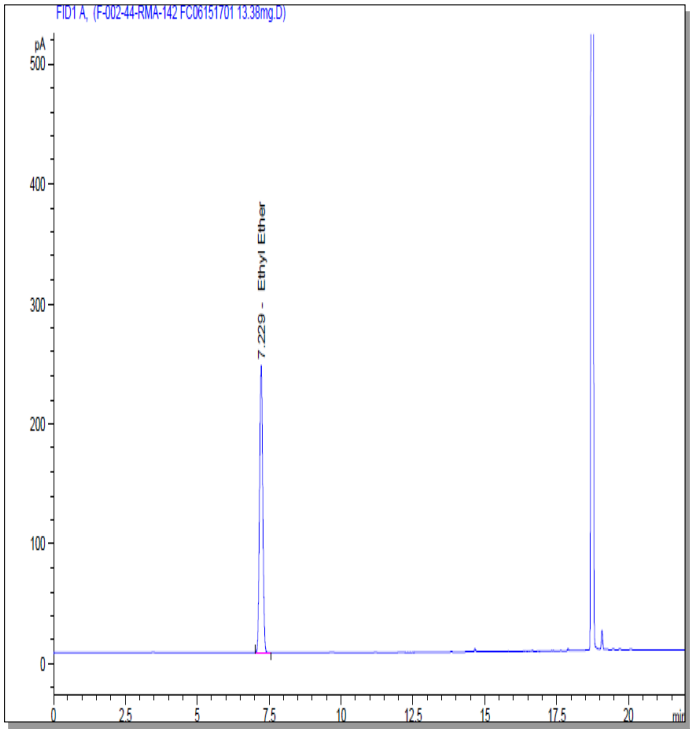
Spectral and Physical Data (cont.)

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:	FC06151701
Acquired:	February 02, 2018

Peak	Compound	Area	Weight %
1	Ethyl Ether	1878.64	0.57
2	NMP	NA	NA
Total			**0.57**

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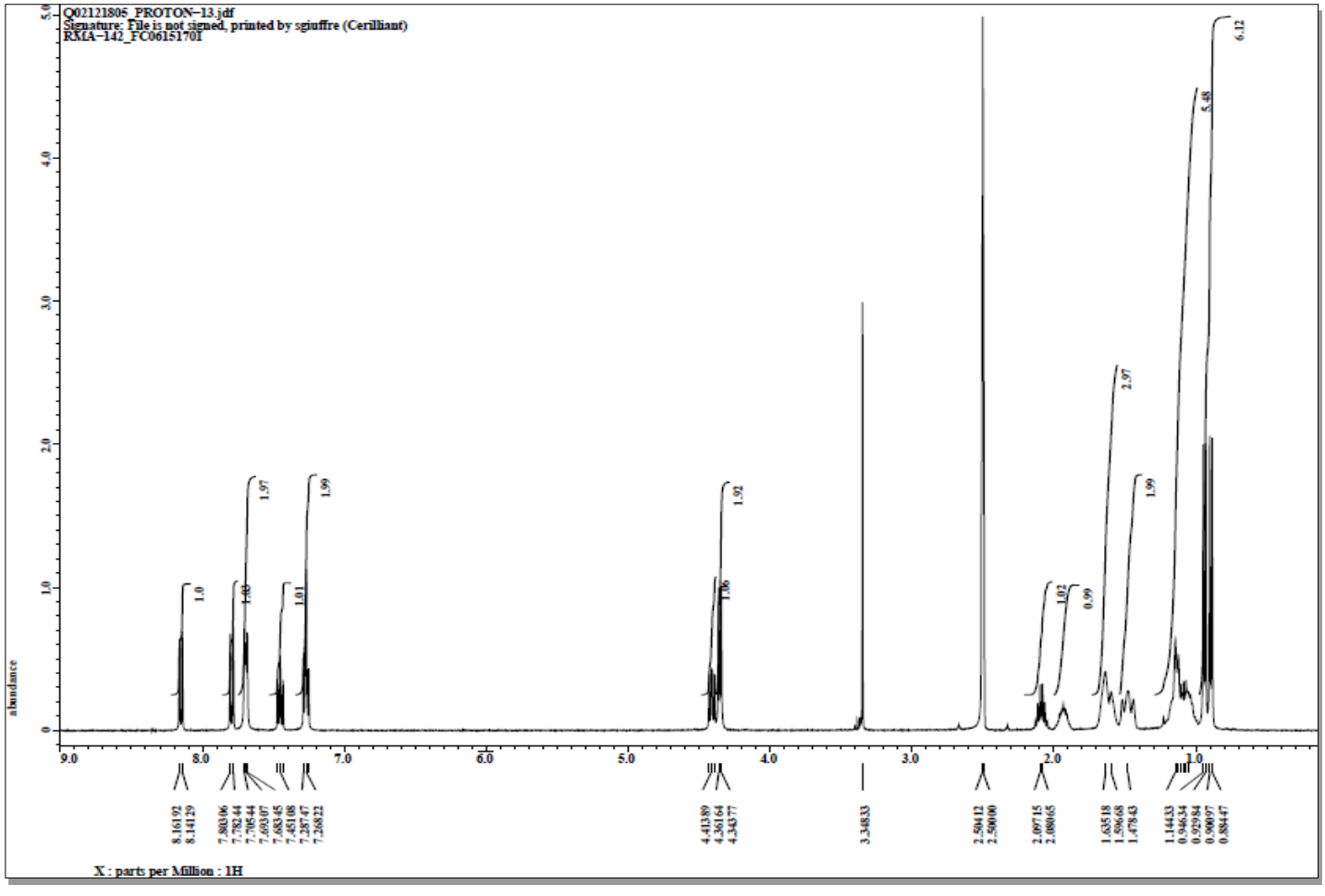
Spectral and Physical Data (cont.)

^{1}H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D_6



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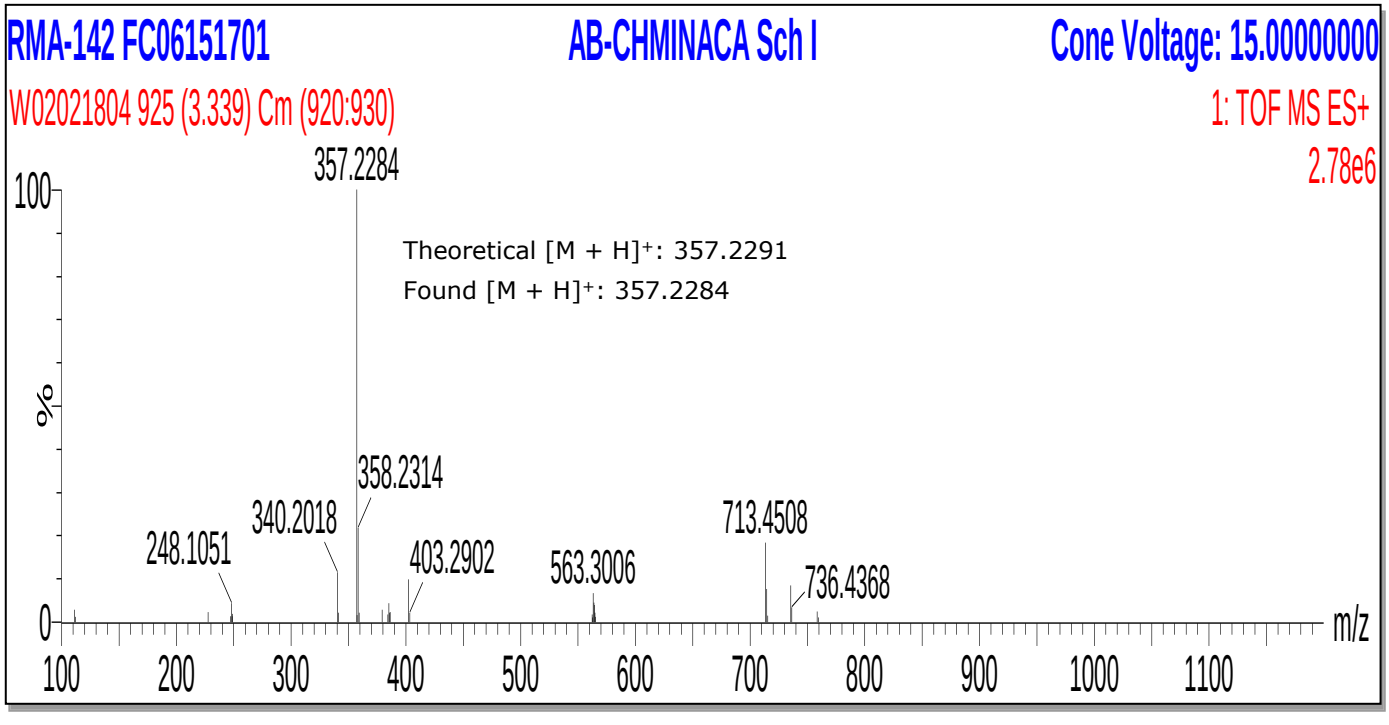
Spectral and Physical Data (cont.)

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:**	February 02, 2018

Time (min)	% A	% B
0.0	70	30
0.5	70	30
4.0	20	80
5.8	20	80
6.0	70	30
8.0	70	30



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Spectral and Physical Data (cont.)

GC/MS

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Compound Name          : AB-CHMINACA
  t Number             : FC06151701
Instrument             : Agilent GCMS
Operator               : ECM(SGIUFFRE)
Date Reported          : Fri Feb 02 10:33:29 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
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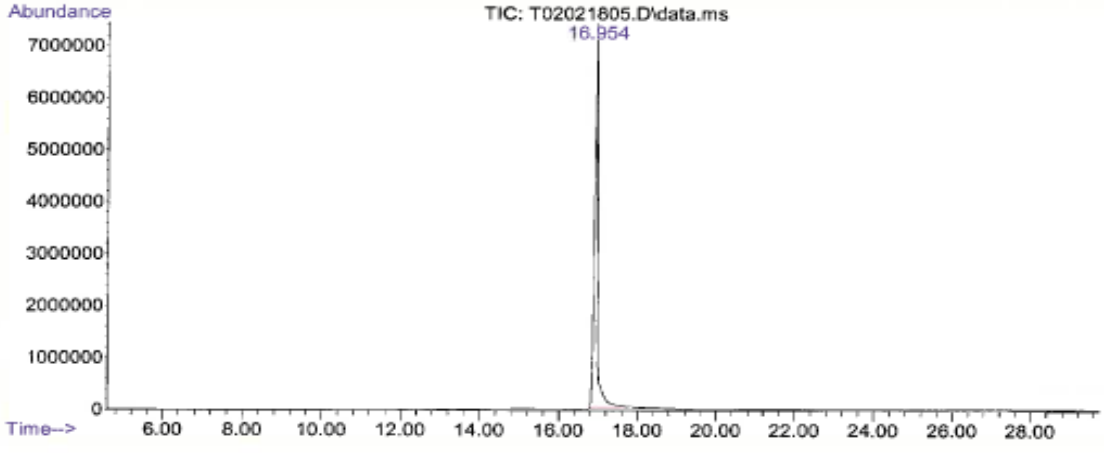
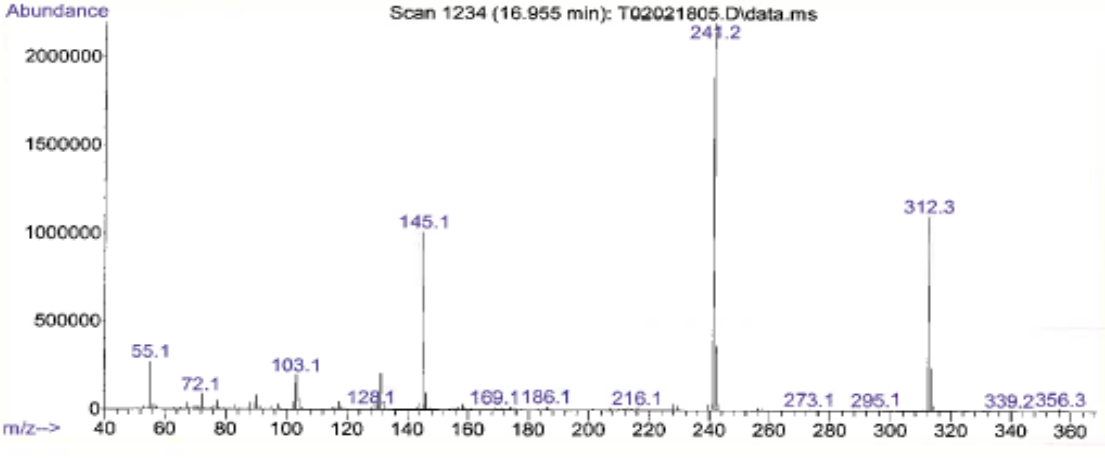
Total Ion Chromatogram



Mass Spectrum



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Stability

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

Short Term Stability: *A summary of accelerated stability findings for 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 11 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 16, 2018	Initial version
01	April 10, 2018	Revised Short Term Stability section to reflect 4 week data.
02	February 22, 2019	Updated Retest Date from May 2019 to February 2020.
		Added Long Term Stability Section.

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