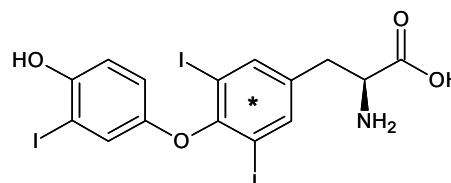


Certificate of Analysis

3,3',5-Triiodo-L-thyronine-¹³C₆ (T3-¹³C₆)

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

Catalog Number:	T-077
Solution Lot:	FN091912-01
Retest Date:	November 2014
Solvent:	0.1N NH ₃ in Methanol
Volume per Ampule:	Not less than 1 mL
Storage:	Store unopened in freezer.
Shipping:	Ship cold. See Stability Section.
Intended Use:	For R&D/ analytical purposes only. Not suitable for human or animal consumption.
Safety:	Flammable, Poison



- ♦ Retest Date - stability studies ongoing. Certificate of Analysis will be updated upon completion of retest.
- ♦ Ampules are overfilled to ensure a minimum 1 mL volume fill. We advise laboratories to use measured volumes of this standard solution before diluting to the desired concentration.

Component	Solution Purity	Certified Concentration
3,3',5-Triiodo-L-thyronine- ¹³ C ₆ (T3- ¹³ C ₆)	98.5% *	100.0 ± 0.6 µg/mL
<ul style="list-style-type: none"> ♦ Uncertainty of the concentration is expressed as an expanded uncertainty in accordance with ISO 17025 and Guide 34 at the approximate 95% confidence interval using a coverage factor of k = 2 and has been calculated by statistical analysis of our production system and incorporates uncertainty of the purity factor, material density, and balance and weighing technique. ♦ This standard is prepared gravimetrically and mass results are reported on the conventional basis for weighing in air. Concentration is calculated based on: the actual measured mass; Purity Factor of the analyte(s); measured mass of the solution; and the density of the pure diluent at 20C. ♦ Concentration is corrected for chromatographic purity, residual water, residual solvents and residual inorganics. * No thyroid hormone impurities (rT3, T2, T1, and T4) were detected during standard solution purity analysis by LC/MS. 		

Solution Standard Verification and Homogeneity

Standard Solution	Lot Number	Verified Concentration (µg/mL)		%RSD - Homogeneity	
		Actual Results	Acceptance Criteria	Actual Results	Acceptance Criteria
New Lot	FN091912-01	98.1	± 3%	0.1	≤ 3%
<ul style="list-style-type: none"> ♦ Concentration is verified through multiple analyses and is calculated as the average of multiple analyses compared to an independently prepared calibration solution. ♦ Homogeneity of the New Lot is ensured through rigorous production process controls statistically analyzed to evaluate risk and verified by analysis. The % RSD of samples pulled from across the lot demonstrate homogeneity of the New Lot. 					

Traceability

<ul style="list-style-type: none"> ♦ Gravimetrically prepared using qualified balances calibrated semi-annually by Mettler Toledo using NIST traceable weights. Calibration verification performed weekly and prior to each use utilizing NIST traceable weights. Each balance has been assigned a minimum weighing by Mettler Toledo taking into consideration the balance and installed environmental conditions to ensure weighing complies with USP tolerances of no more than 0.1% relative error. ♦ Concentration is verified against an independently prepared calibration solution gravimetrically prepared using balances calibrated to NIST. ♦ In addition, each neat material utilized has been identified and thoroughly characterized through the use of multiple analytical techniques. Spectral data is provided on subsequent pages of the COA.
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Cerilliant certifies that this standard meets the specifications stated in this certificate and warrants this product to meet the stated acceptance criteria through the expiration/retest date when stored unopened as recommended. Product should be used shortly after opening to avoid concentration changes due to evaporation. Warranty does not apply to ampoules stored after opening.




Darron Ellsworth, Quality Assurance Manager

April 23, 2014

Date

Standard Solution Assay Parameters

Analysis Method: HPLC/PDA
Column: Acquity UPLC BEH C18 1.7 μ 2.1 x 50 mm
Mobile Phase: A: Acetonitrile B: 0.1 % H₃PO₄
Gradient Program:

Time	% A	% B
0.00	30	70
1.00	90	10
1.25	30	70

Flow Rate: 1.0 mL/min
Wavelength: 230 nm

Calibration Curve

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

Neat Material Data

Compound Name: 3,3',5-Triiodo-L-thyronine-¹³C₆ (T3-¹³C₆)
Compound Lot: FN061912-01
Chemical Formula: ¹³C₆H₉I₃NO₄
CAS Number: 1213431-76-5
Molecular Weight: 656.93

Neat Material Characterization Summary

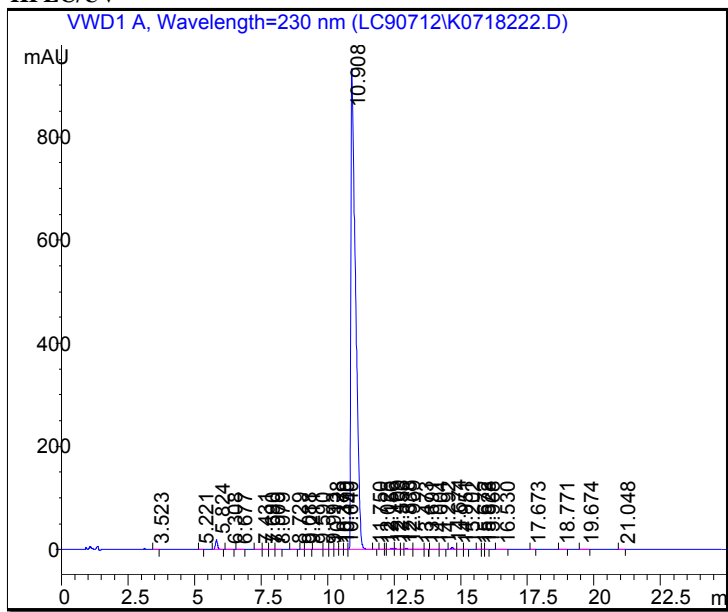
Analytical Test	Method	Results
Primary Chromatographic Purity by HPLC/UV Analysis	SP10-0102	98.3%
Secondary Chromatographic Purity by LC/MS Analysis	SP10-0107	98.4%
Identity by LC/MS Analysis	SP10-0107	Consistent with Structure
Isotopic Purity by LC/MS SIM Analysis	SP10-0107	0.022% ¹³ C ₀ vs ¹³ C ₆
		0.021% ¹³ C ₀ 0.004% ¹³ C ₄
		0.001% ¹³ C ₁ 2.436% ¹³ C ₅
		0.000% ¹³ C ₂ to ¹³ C ₃ 97.537% ¹³ C ₆
Identity by ¹ H-NMR Analysis	USP <761>, SP10-0116	Consistent with Structure
Residual Solvent by ¹ H-NMR Analysis	USP <761>, SP10-0116	1.31% Acetic acid
Residual Solvent Analysis by GC/FID Headspace	AM1087 ¹	0.19%
Residual Water Analysis by Karl Fischer Coulometry	USP <921>, SP10-0103	1.27%
Inorganic Content by Microash Analysis	SP10-0135	< 0.2%
Purity Factor		95.53%

- ♦ Primary purity is calculated as the average of two independently performed analyses utilizing two different methods. Acceptance criteria requires the purity values to be within 0.5% of each other.
- ♦ The primary chromatographic purity value is used to calculate the Purity Factor.
- ♦ A secondary chromatographic purity method is utilized as a control.
- ♦ Purity Factor = [(100 - wt% residual solvent - wt% residual water - wt% residual inorganics) x Chromatographic Purity/100].
- ♦ Purity factor does not include adjustment for chiral and/or isotopic purity.

¹ Validated analytical method.

Spectral and Physical Data

HPLC/UV



Column: Discovery HS C18 3μ, 4.6 x 150 mm
Mobile Phase: A: Acetonitrile
 B: 0.07% Phosphoric acid
Gradient Program:

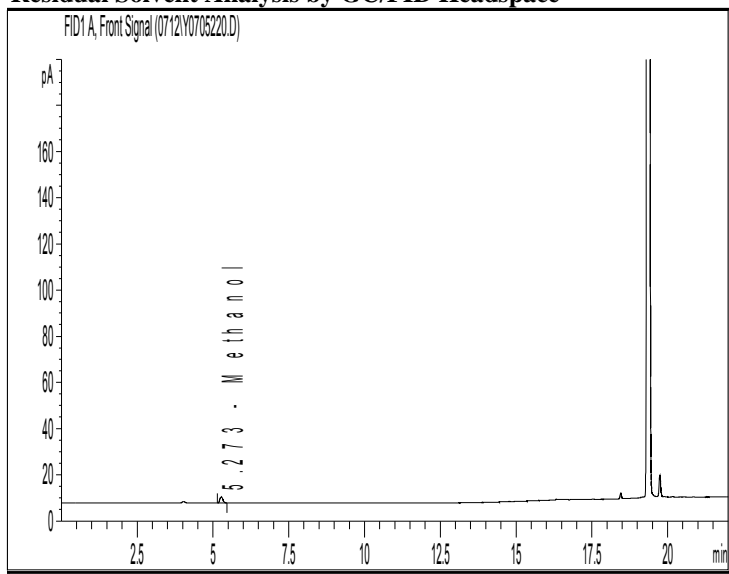
Time (mins)	%A	%B
0.0	25	75
2.0	25	75
12.0	35	65
20.0	50	50
25.0	50	50
25.1	25	75

Flow Rate: 1.5 mL/min
Wavelength: 230 nm
Data File Name: S:\HPLC\HPLC9\20120\LC90712\K0718222.D
Operator: GLR
Instrument: LC#9
Sample Name: FN061912-01
Method File: AM1379.M
Acquired: July 20, 2012 12:22 AM

Peak #	Ret Time	Area	Height	Area %	Peak #	Ret Time	Area	Height	Area %
1	3.52	0.40	0.08	0.00	22	12.16	0.12	0.31	0.00
2	5.22	0.22	0.04	0.00	23	12.41	15.04	2.18	0.13
3	5.82	105.00	18.26	0.90	24	12.56	9.51	1.34	0.08
4	6.31	0.50	0.05	0.00	25	12.84	1.10	0.20	0.01
5	6.68	0.09	0.02	0.00	26	12.97	12.29	1.90	0.11
6	7.43	0.30	0.03	0.00	27	13.47	0.83	0.08	0.01
7	4.69	0.30	0.03	0.00	28	13.69	0.18	0.03	0.00
8	7.91	0.85	0.14	0.01	29	14.00	0.44	0.03	0.04
9	8.08	0.20	0.03	0.00	30	14.29	0.36	0.05	0.00
10	8.73	5.19	0.89	0.04	31	14.67	22.80	3.91	0.20
11	9.09	0.30	0.05	0.00	32	14.95	0.49	0.04	0.00
12	9.21	0.56	0.07	0.00	33	15.20	0.38	0.06	0.00
13	9.59	0.84	0.09	0.01	34	15.67	0.65	0.12	0.01
14	9.99	0.24	0.03	0.00	35	15.83	0.08	0.02	0.00
15	10.13	0.71	0.08	0.01	36	15.97	0.17	0.04	0.00
16	10.38	2.59	0.46	0.02	37	16.53	0.32	0.04	0.00
17	10.49	6.61	0.98	0.06	38	17.67	0.16	0.03	0.00
18	10.64	2.53	0.37	0.02	39	18.77	0.39	0.05	0.00
19	10.91	11439.40	933.57	98.31	40	19.67	0.59	0.05	0.01
20	11.75	0.81	0.18	0.01	41	21.05	0.47	0.08	0.00
21	12.03	1.51	0.27	0.01					

Spectral and Physical Data (cont.)

Residual Solvent Analysis by GC/FID Headspace



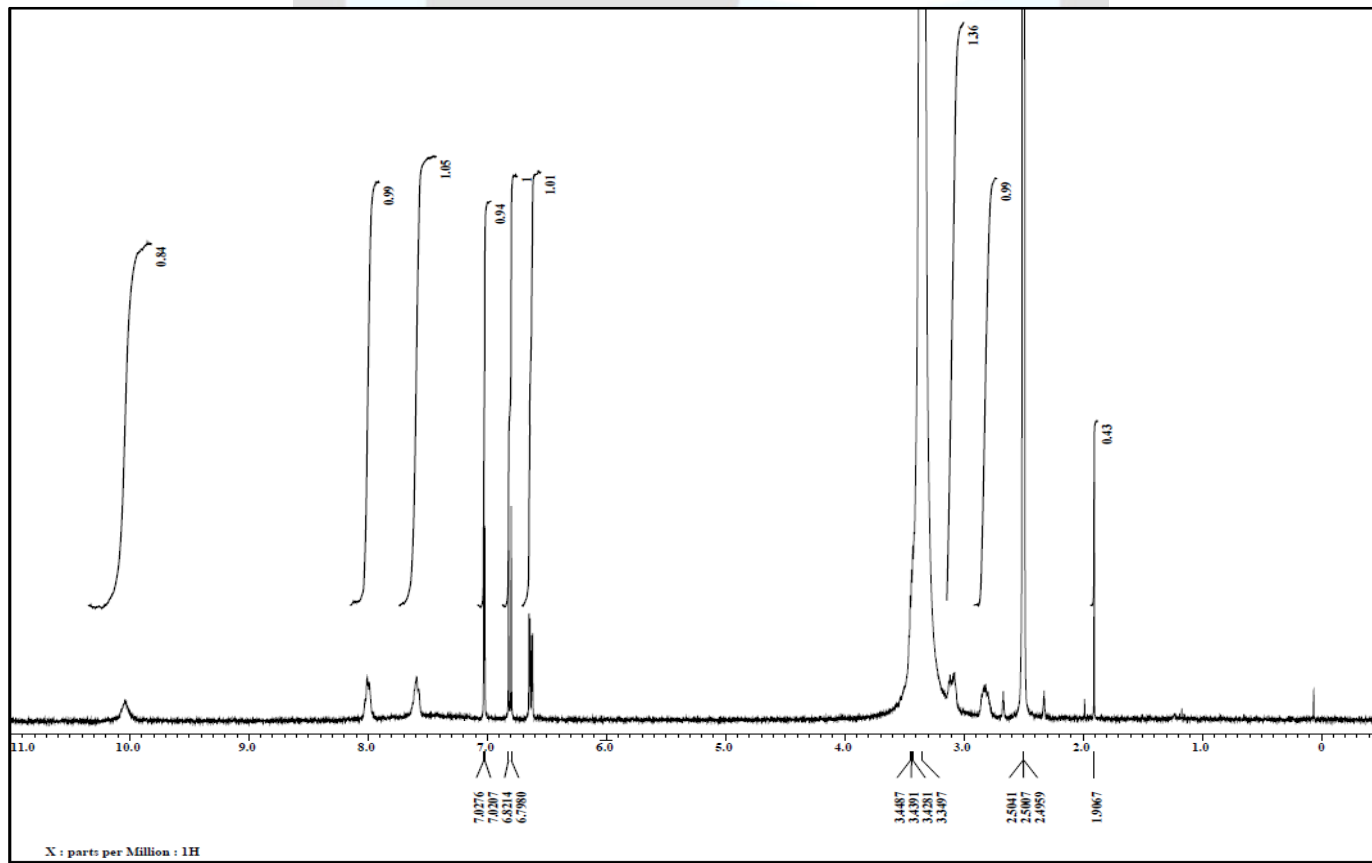
Column: DB-ALC1 30 m x 0.53 mm, 3 µm film thickness
Temp Program: 40°C (12 min) to 220°C at 40°C/min (5.5 min)
Carrier Gas: Helium
Flow Rate: 2.0 mL/min
Detector Heater Temp: 250°C
Injector: Headspace Sampler
HS Oven Temp: 60°C
Vial Equilibration: 10 minutes

Data File Name: S:\GC\GC-HS11\2012\0712\Y0705220.D
Operator: RPC
Instrument: GC#11
Sample Name: FN061912-01
Acquired: July 5, 2012 8:24 PM

Peak	Compound	Area	Weight %
1	Methanol	17.92297	0.19
2	NMP	NA	NA
Total			0.19

¹H NMR

Instrument: JEOL ECS 400
Solvent: DMSO-D₆

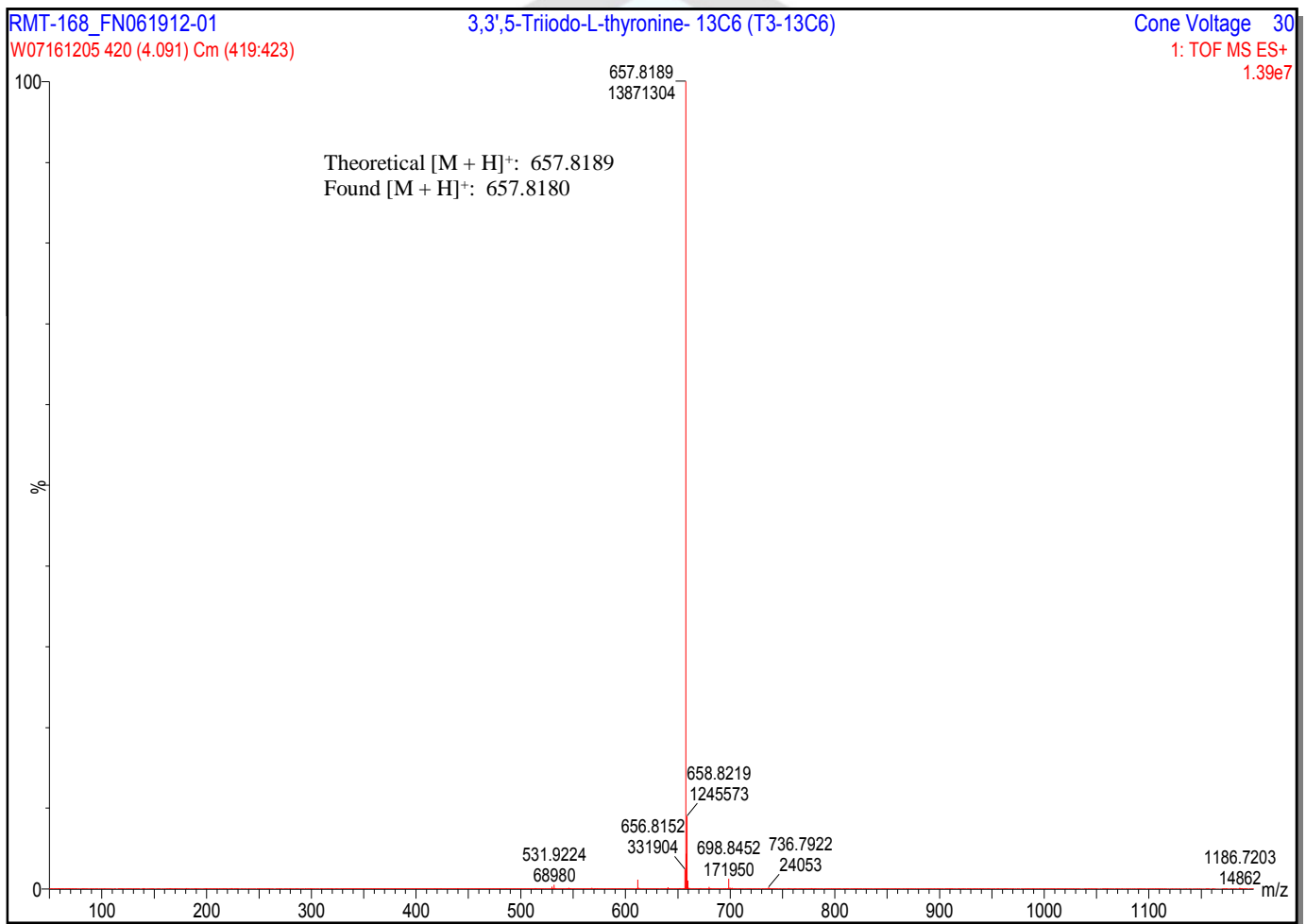


Spectral and Physical Data (cont.)

LC/MS

Column: Acquity BEH 1.7 μ C₁₈, 2.1 x 50 mm
Mobile Phase: 0.1% Ammonium acetate in Water::Acetonitrile
(90::10 to 60::40 at 5 mins, to 90::10 at 6.1 mins,
hold 1.9 mins)
Flow Rate: 0.4 mL/min
Scan Range: 50-1200 amu
Ionization: Electrospray, Positive Ion

Data File Name: W07161205
Operator: BBM
Instrument: Waters XEVO G2 QTOF
Sample Name: FN061912-01
Method File: 19-46C1A
Acquired: July 16, 2012 12:00 AM

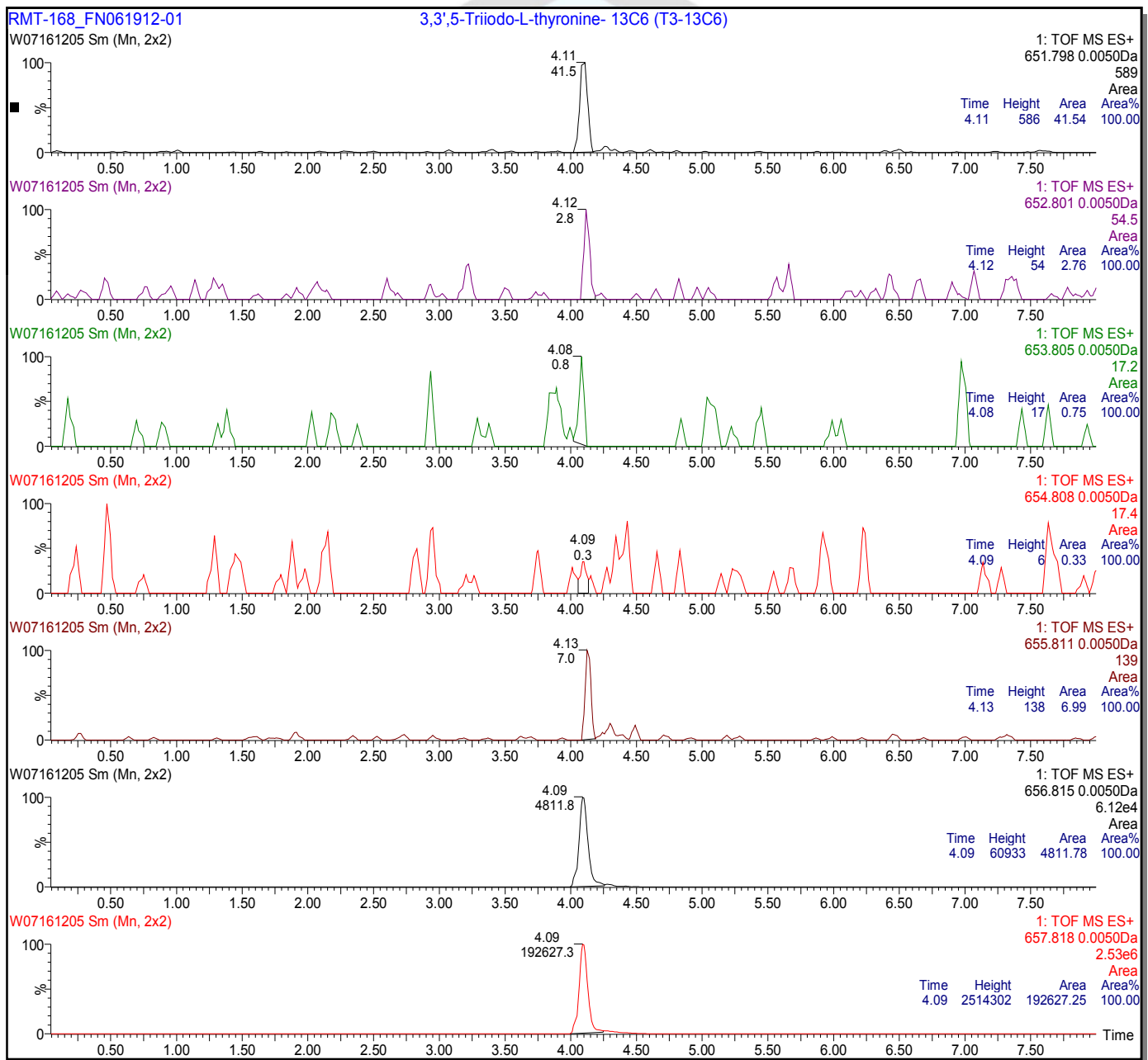


Spectral and Physical Data (cont.)

Isotopic Purity by LC/MS SIM Analysis

Column: Acquity BEH 1.7 μ C₁₈, 2.1 x 50 mm
Mobile Phase: 0.1% Ammonium acetate in Water::Acetonitrile
 (90::10 to 60::40 at 5 mins, to 90::10 at 6.1 mins,
 hold 1.9 mins)
Flow Rate: 0.4 mL/min
Scan Range: 50-1200 amu
Ionization: Electrospray, Positive Ion

Data File Name: W07161205
Operator: BBM
Instrument: Waters XEVO G2 QTOF
Sample Name: FN061912-01
Method File: 19-46C1A
Acquired: July 16, 2012 12:00 AM



Stability

Short Term Stability : A summary of accelerated stability findings for a related product (T-074, 3,3',5-Triiodo-L-thyronine (T3)) is listed below.

Storage Condition	Mean Kinetic Temperature (MKT)	Time Period
Freezer	-15°C	No decrease in purity was noted after one week.
Refrigerator	4°C	
Room Temperature	21°C	
40°C	40°C	0.64% decrease in purity after one week.

Transport/Shipping : Ship Cold.

Long Term Stability: Long term stability has been assessed for freezer storage (-10 °C to -25 °C) conditions. Stability of a minimum of 6 months has been established through real-time stability studies.

COA Revision History

Revision No.	Date	Reason for Revision
00	October 10, 2012	Initial version
01	October 15, 2012	Typographical error: corrected CAS Number from 1213431-76-5 to 1217473-60-3.
02	October 17, 2012	Added Statement regarding the absence of thyroid hormone impurities during standard solution purity analysis by LC/MS.
03	April 2, 2013	Revised Retest Date from November 2013 to November 2014.
04	September 12, 2013	Updated Long Term Stability to include 6-month real-time study.
05	April 23, 2014	Corrected CAS Number from 1217473-60-3 to 1213431-76-5. 1217473-60-3 is for the salt form and 1213431-76-5 is for the free base.