



BDG SYNTHESIS

Certificate of Analysis

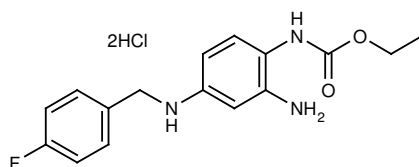
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
29 February 2016

Name: Retigabine Dihydrochloride

CAS Number: 150812-13-8

Structure:



Molecular Weight: $C_{16}H_{18}FN_3O_2 \cdot 2HCl = 376.25$

Lot Number: BDG 6766.1

Appearance: Pale purple, crystalline solid

Purity By HPLC: 98.2 %

Re-test Date: 29 February 2017

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
Light:	protect from strong sunlight.
Caution:	only experienced laboratory personnel should handle the material.

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Residual Solvents: traces (under 0.1 % w/w) of diethyl ether and ethanol and dioxane are observed.
Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 304.1458. $C_{16}H_{19}FN_3O_2$ $[M+H]^+$ requires m/z 304.1461. The deviation of 1.0 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A sharp, symmetrical peak is observed (98.2 %). Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis

	Found:	C 51.24, H 5.36, N 11.17 %
$C_{16}H_{18}FN_3O_2 \cdot 2HCl$	Requires:	C 51.07, H 5.36, N 11.17 %

The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

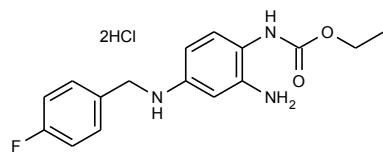
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.

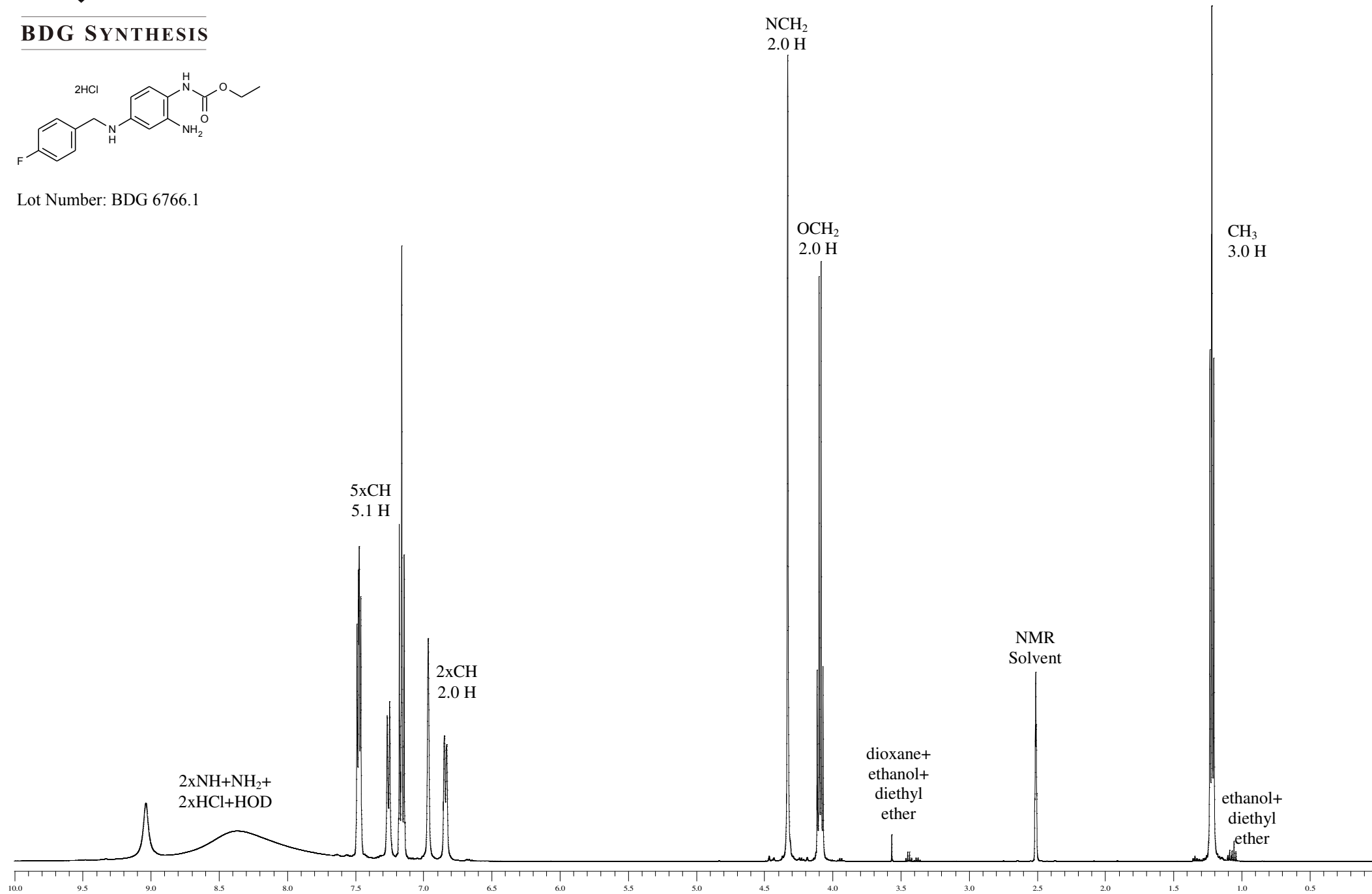


Proton NMR Spectrum of Retigabine Dihydrochloride in DMSO-d₆

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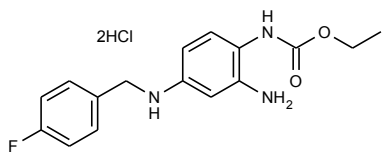
Lot Number: BDG 6766.1



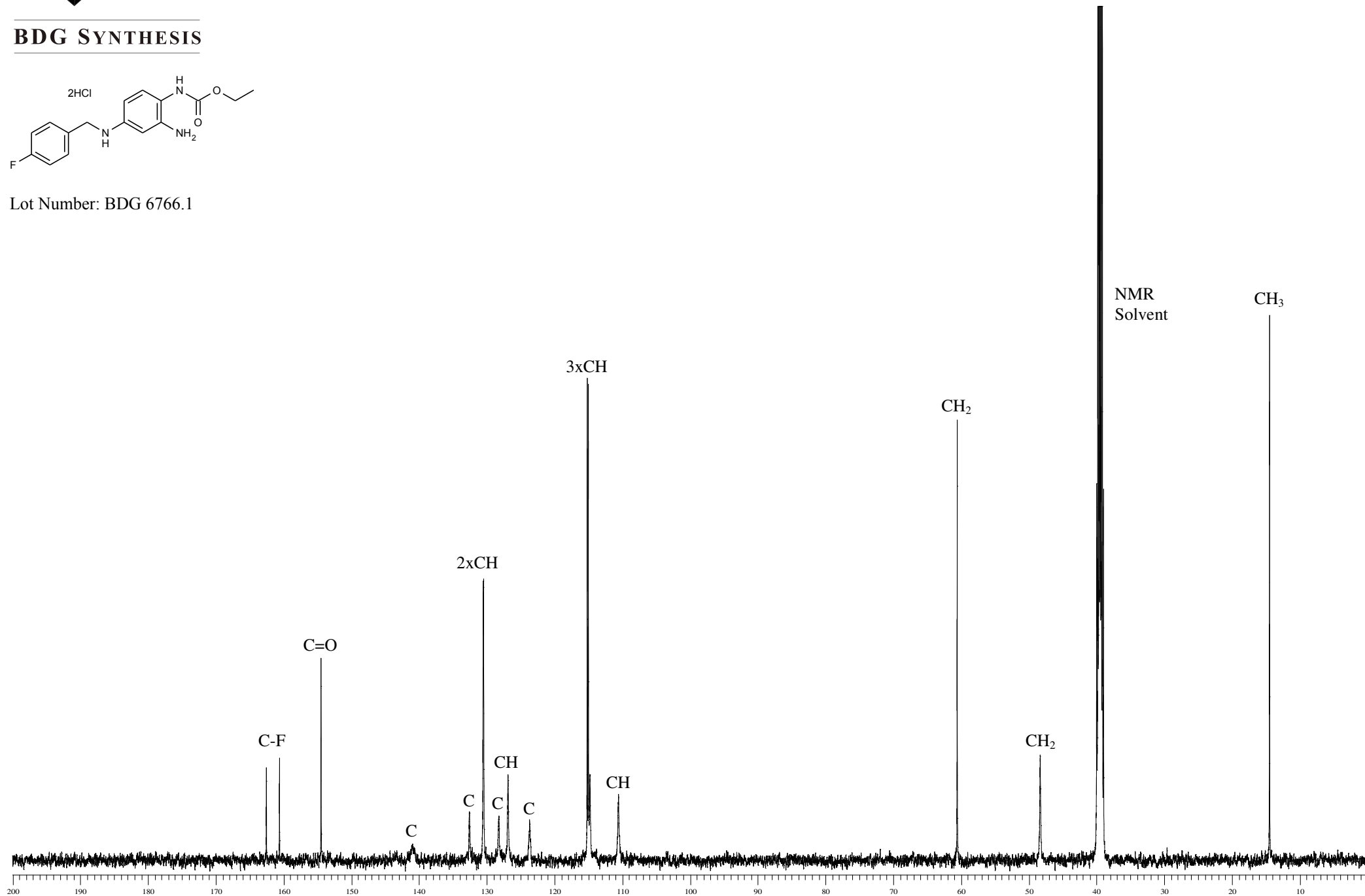


Carbon-13 NMR Spectrum of Retigabine Dihydrochloride in DMSO-d₆

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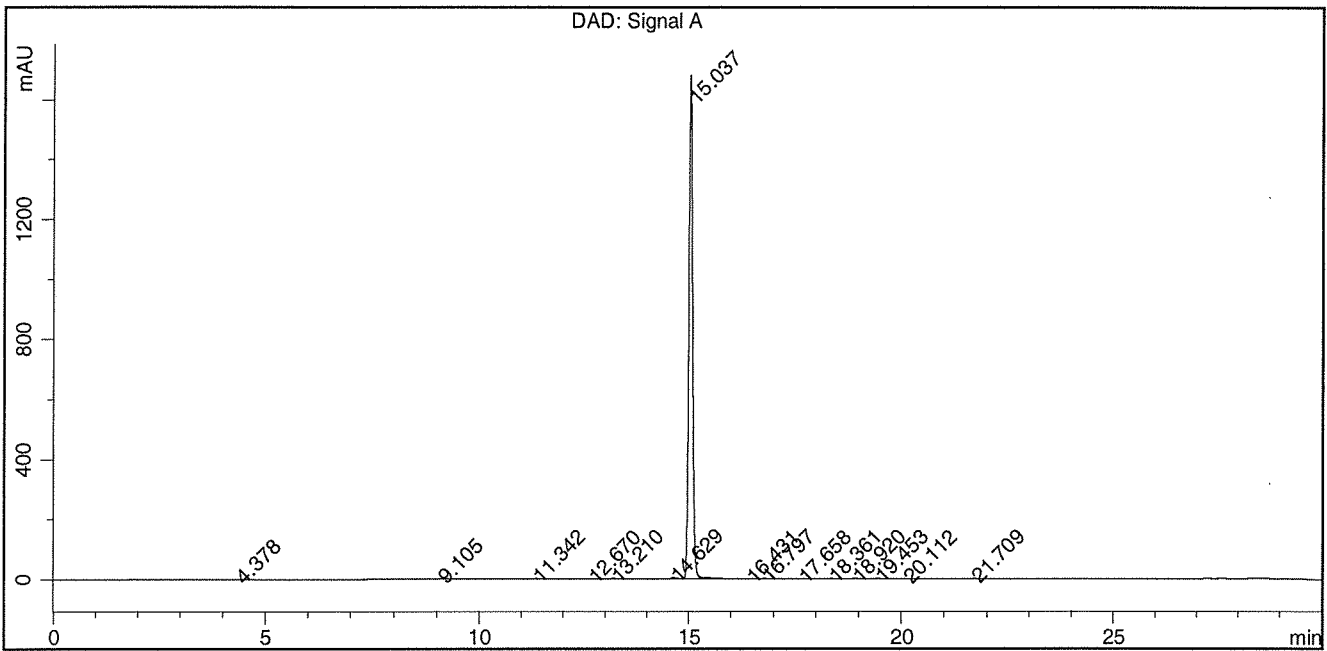
Lot Number: BDG 6766.1



BDG - Analysis of Retigabine Dihydrochloride

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase A : 75:25 10 mM diPotassium Hydrogen Phosphate pH=7.0 : Acetonitrile
 Mobile Phase B : 25:75 10 mM diPotassium Hydrogen Phosphate pH=7.0 : Acetonitrile
 Gradient : T0=100:0, T20=0:100, T25=0:100, T26=100:0, T30=100:0
 Flow Rate : 1.0 mL/min Column Temperature : 30 C. Injection Volume : 10 uL
 Sample Solvent : 70:30 Water : Acetonitrile Detection : UV at 247 nm

Sample Name	BDG 6766.1	Instrument	AnalyticalLC01
Acquisition	29/02/2016, 12:29:02	Method (rev.)	LC10671a (7)
Sequence	BDG_29Feb2016b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	4.38 min	1.0746	6.8076	0.0959 min	0.064 %
2	9.11 min	0.6573	5.1596	0.1116 min	0.049 %
3	11.34 min	1.9485	13.6595	0.1018 min	0.129 %
4	12.67 min	0.7097	6.9115	0.1356 min	0.065 %
5	13.21 min	2.2658	22.5028	0.1399 min	0.212 %
6	14.63 min	4.3700	45.9620	0.1507 min	0.433 %
7	15.04 min	1680.9965	10416.0532	0.0943 min	98.229 %
8	16.43 min	0.5781	8.1787	0.1870 min	0.077 %
9	16.80 min	1.7106	16.5079	0.1366 min	0.156 %
10	17.66 min	0.6985	5.4542	0.1111 min	0.051 %
11	18.36 min	1.2704	9.0528	0.1071 min	0.085 %
12	18.92 min	2.0650	20.0748	0.1394 min	0.189 %
13	19.45 min	1.6743	14.8380	0.1294 min	0.140 %
14	20.11 min	0.6639	6.4461	0.1333 min	0.061 %
15	21.71 min	0.8480	6.1928	0.1132 min	0.058 %