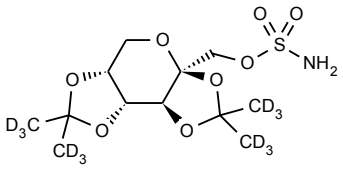
BDG SYNTHESIS

Certificate of Analysis

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

Barry Dent

Barry R. Dent, PhD, Director
21 June 2013

Name:	**Topiramate-d_{12}**
CAS Number:	97240-79-4 (unlabelled)
Structure:	
Molecular Weight:	$C_{12}H_9D_{12}NO_8S$ = 351.44
Lot Number:	BDG 7144.2
Appearance:	White, crystalline solid
Purity By HPLC:	99.7 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	21 June 2018

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:	store in an amber vial and protect from bright light.
Caution:	only experienced laboratory personnel should handle the material.

Mailing:
BDG Synthesis Limited
PO Box 38627, Wellington Mail Centre,
Wellington 5045, New Zealand.

Shipping:
BDG Synthesis Limited
Gracefield Research Centre, Building F,
69 Gracefield Rd, Lower Hutt 5010, New Zealand.

Phone: + 64 4 569 0520
Fax: + 64 4 569 0521

info@bdg.co.nz
www.bdg.co.nz

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: signals at the sites of deuteration are greatly diminished, compared with the spectrum of unlabelled material, but nevertheless inidicate that about 5 % of the total deuterium has been lost during the synthesis.
Residual Solvents: no residual solvents 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.
Isotopic Labelling: signals at the sites of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration. A 5 % loss of deuterium is unlikely to be detected in the carbon-13 NMR spectrum.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 374.1624. $C_{12}H_9D_{12}NNaO_8S$ $[M+Na]^+$ requires *m/z* 374.1633. The deviation of 2.5 ppm is within normally accepted limits for the establishment of identity by HRMS. The molecular ion region of the spectrum shows progressively smaller signals at *m/z* 373, 372, 371 and baseline signals at 370, 369 and 368; no further signal are observed below 368. This indicates that the loss of deuterium has been on a statistical basis. Outside of this envelope of isotopomers, a minor signal at *m/z* 362 is observed, which is not believed to be due to the presence of d_0 material.

HPLC

A sharp, symmetrical peak is observed (99.7 %). 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 41.28, H 2.58, D 6.88, N 3.97 %
$C_{12}H_9D_{12}NO_8S$	Requires:	C 41.01, H 2.58, D 6.88, N 3.99 %

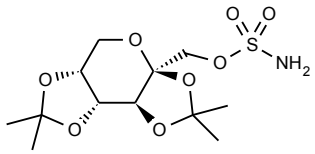
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

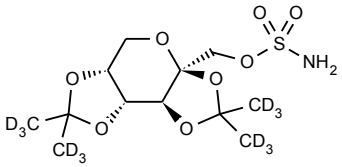
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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.

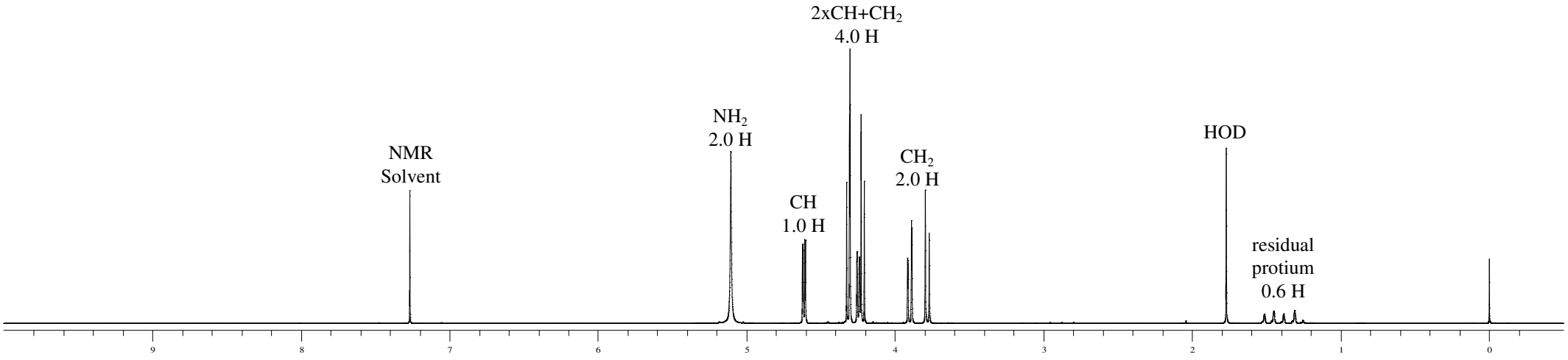
BDG SYNTHESIS

Proton NMR Spectrum of Topiramate (top) and Topiramate-d_{12} (bottom) in $CDCl_3$



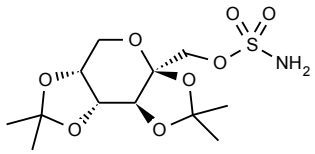


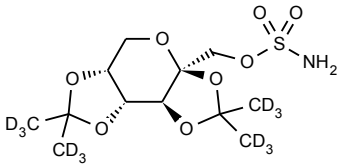
Lot Number: BDG 7144.2



BDG SYNTHESIS

Carbon-13 NMR Spectrum of Topiramate (top) and Topiramate-d_{12} (bottom) in $CDCl_3$



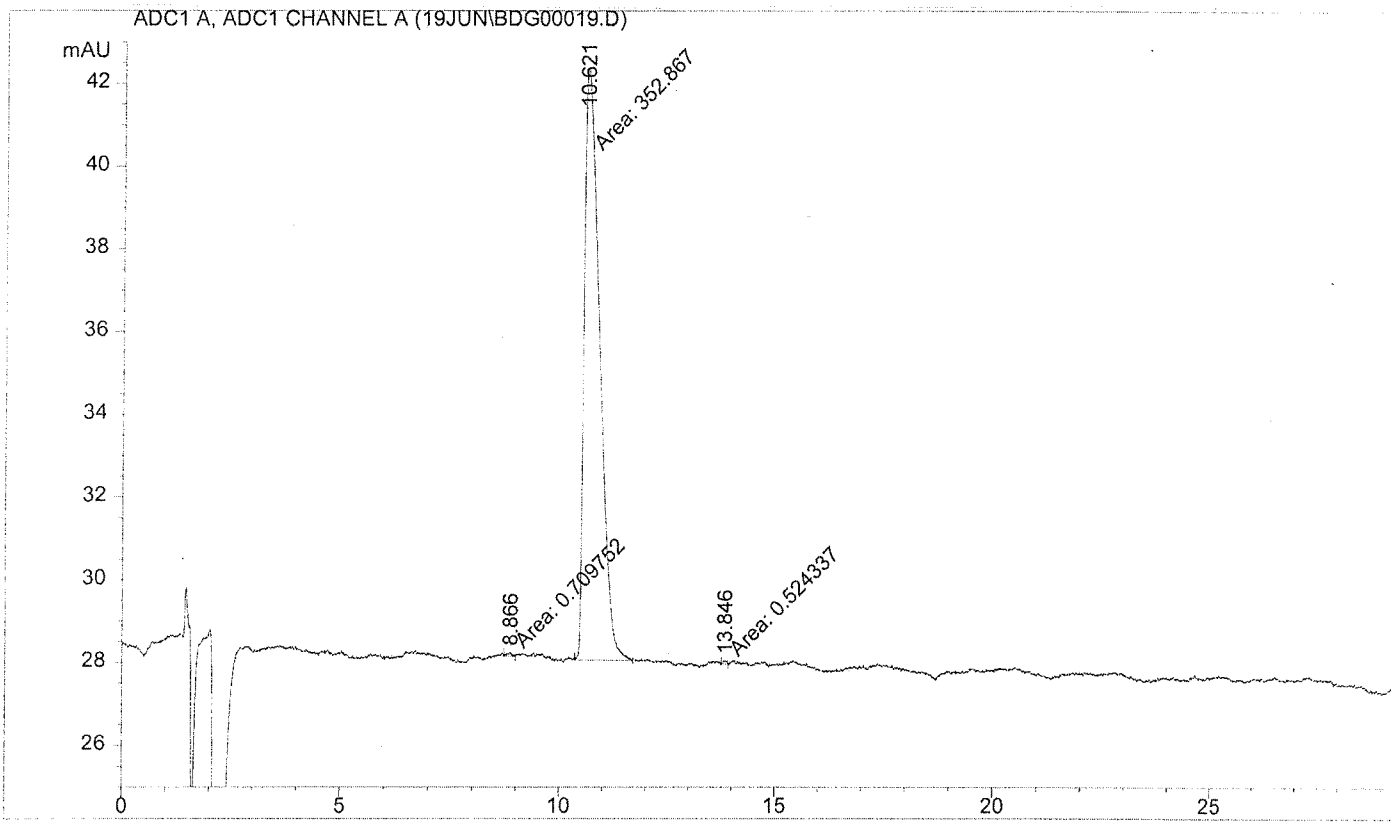


Lot Number: BDG 7144.2

BDG - Analysis of Topiramate-d12

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C8 RP 4 x 3 mm
Mobile Phase : 73:27 10mM Potassium Dihydrogen Phosphate pH=2.3 : Acetonitrile
Flow Rate : 1.5 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 35C
Injection Volume : 40 uL
Detection : RI

Sample Name	BDG 7144.2	Instrument	AnalyticalLC01
Acquisition	21/06/2013, 11:25:44	Method (rev.)	LC10069b (9)
Sequence	BDG_21Jun2013a - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1




```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: ADC1 A, ADC1 CHANNEL A

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.866 MM    0.1054 7.09752e-1 1.12201e-1   0.2004
   2  10.621 MM    0.4099  352.86710   14.34604  99.6515
   3  13.846 MM    0.0867 5.24337e-1 1.00851e-1   0.1481

Totals :                  354.10118   14.55909

 Results obtained with enhanced integrator!
================================================================================
                          *** End of Report ***
```