



## BDG SYNTHESIS

### Certificate of Analysis

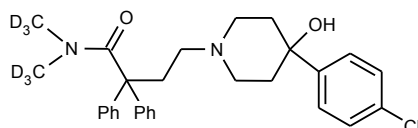
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

*Barry Dent*

Barry R. Dent, PhD, Director  
24 November 2004

**Name:** Loperamide- $d_6$   
**CAS Number:** 53179-11-6 (unlabelled)

**Structure:**



**Molecular Weight:**  $C_{29}H_{27}D_6ClN_2O_2 = 483.07$

**Lot Number:** BDG 4660

**Appearance:** White, crystalline solid

**Corrected Purity:** 99.0 % (HPLC) - 1.1 % (2-propanol) - 1.8 % (water) = 96.1 %

**Isotopic Purity:** Under 0.5 %  $d_0$

**Re-test Date:** 24 November 2009

**Storage and Handling:**

Temperature:	ambient laboratory temperature; may be refrigerated.
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.

Isotopic Labelling: signals at the sites of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: a small amount of 2-propanol (1.1 % w/w) is 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 site of deuteration are obscured by the signal for the NMR solvent.

### High-resolution Mass Spectrum (ESI+)

Found  $m/z$  483.2693.  $C_{29}H_{28}D_6ClN_2O_2$   $[M+H]^+$  requires  $m/z$  483.2685. The deviation of 1.6 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for  $d_0$  material was seen (detection limit about 0.5 %).

### HPLC

A sharp, symmetrical peak is observed (99.0 %). 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 70.63, H 5.78, D 2.57, N 5.56 %
$C_{29}H_{27}D_6ClN_2O_2 \cdot 0.5 H_2O$	Requires:	C 70.78, H 5.74, D 2.46, N 5.69 %, $H_2O$ 1.83 %
$C_{29}H_{27}D_6ClN_2O_2$	Requires:	C 72.10, H 5.63, D 2.50, N 5.80 %

The elemental analyses fall substantially outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the "best-fit" hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend that the "best-fit" water content be used when determining corrected purity.

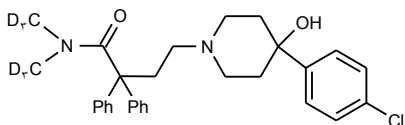
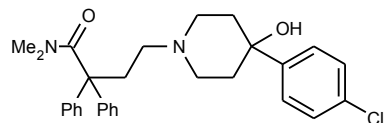
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

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.

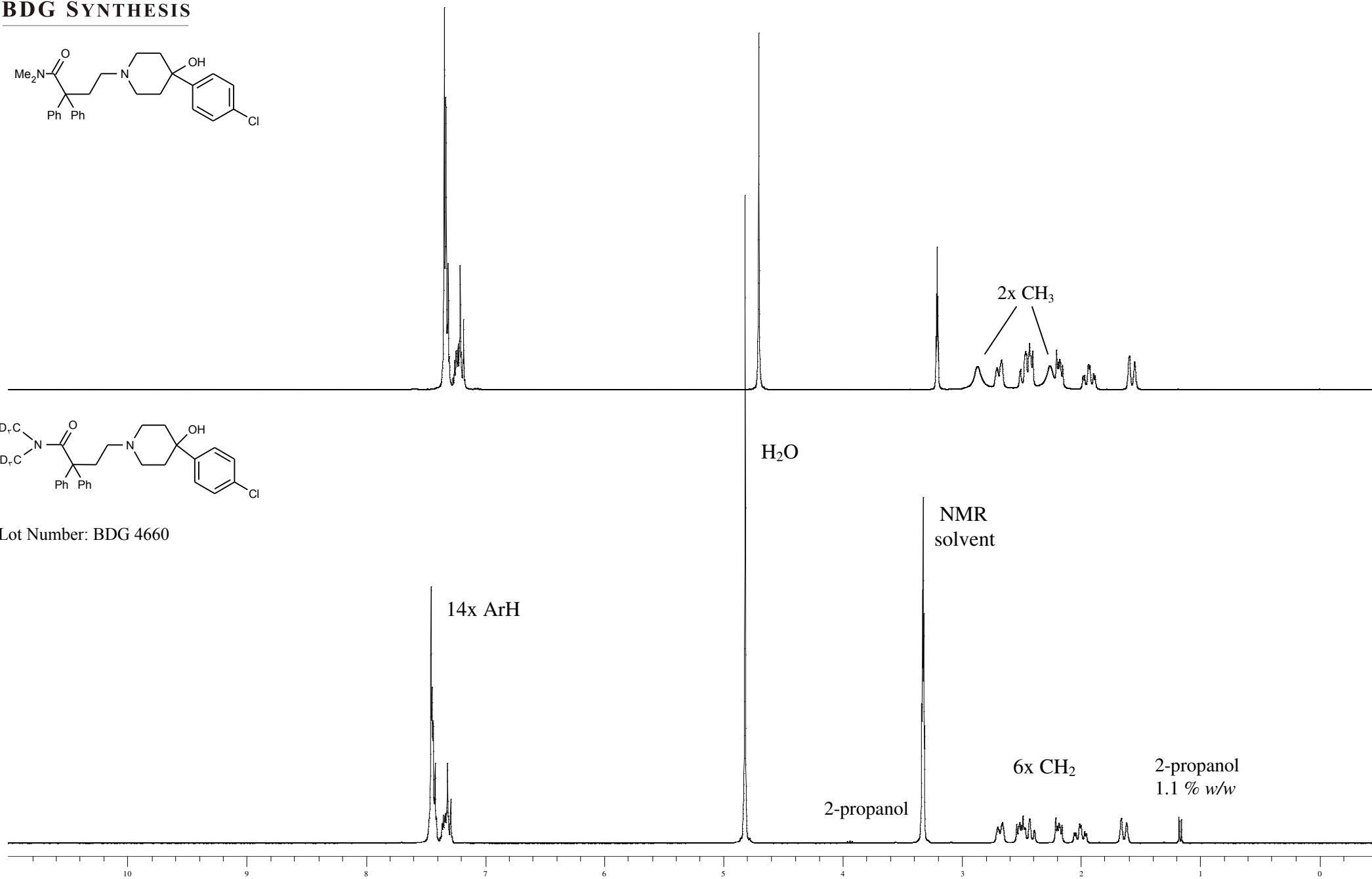


Proton NMR Spectrum of Loperamide (top) and Loperamide-d<sub>6</sub> (bottom) in Methanol-d<sub>4</sub>

**BDG SYNTHESIS**



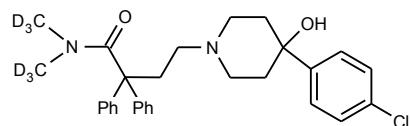
Lot Number: BDG 4660



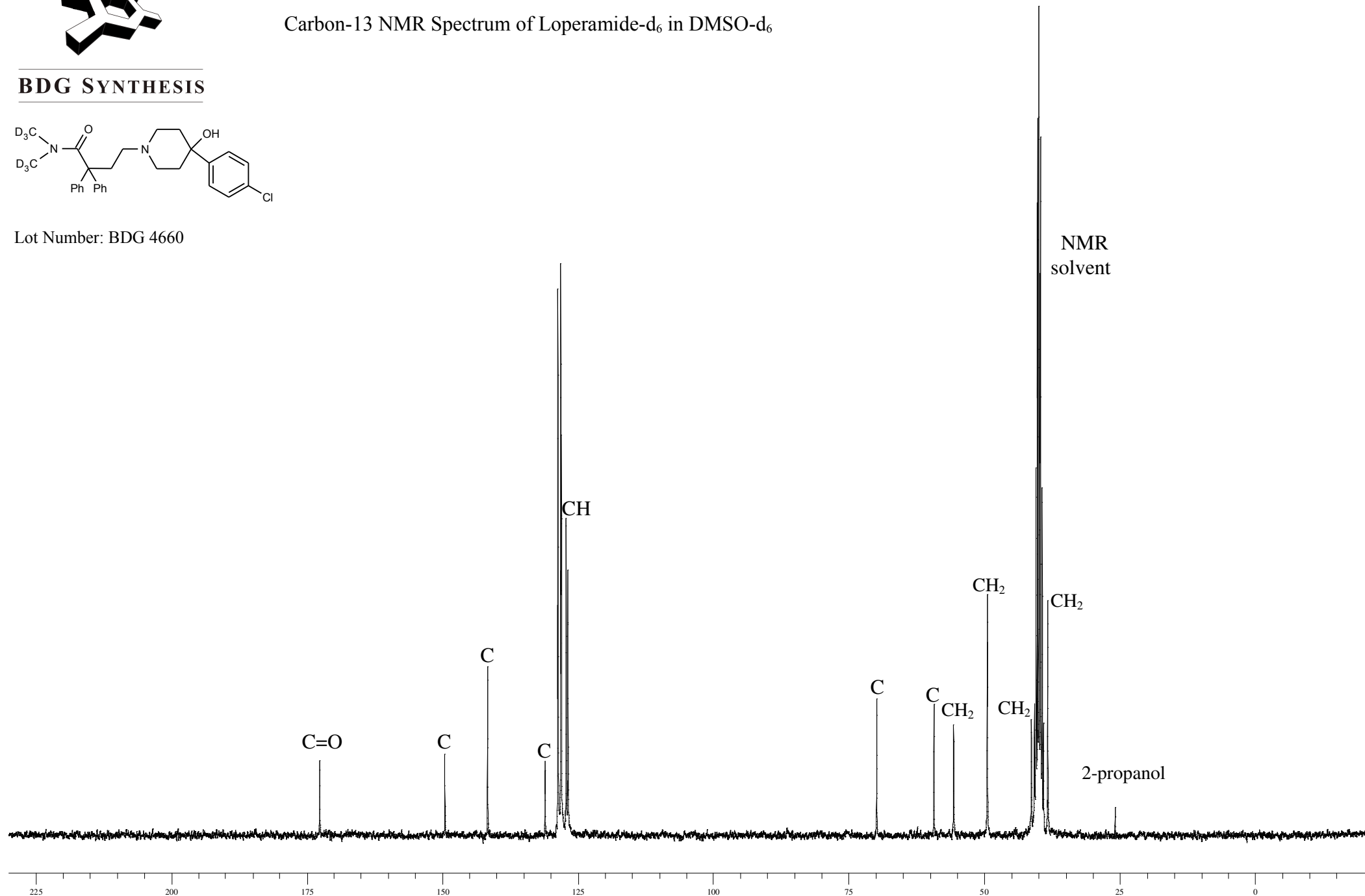


# Carbon-13 NMR Spectrum of Loperamide-d<sub>6</sub> in DMSO-d<sub>6</sub>

## BDG SYNTHESIS



Lot Number: BDG 4660

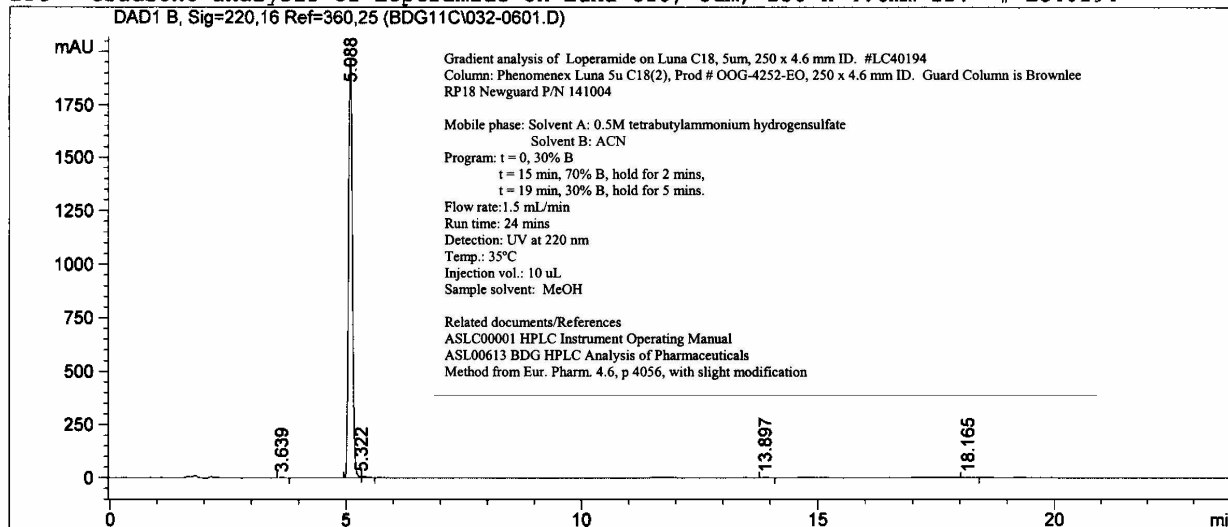


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Injection Date   : 11/23/04 7:01:13 PM           Seq. Line   :    6
Sample Name     : BDG 4660                       Location    : Vial 32
Acq. Operator   : BHHman                          Inj         :    1
                                                    Inj Volume  : 10 µl

Acq. Method     : N:\LC1100_2\1\METHODS\LC40194A.M
Last changed    : 11/23/04 4:53:33 PM by YRLman
Analysis Method : N:\LC1100_2\1\METHODS\LC40194A.M
Last changed    : 11/24/04 11:19:13 AM by YRLman
                  (modified after loading)
    
```

BDG - Gradient analysis of Loperamide on Luna C18, 5µm, 250 x 4.6mm ID. # LC40194



Area Percent Report

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Sorted By      :      Signal
Multiplier     :      1.0000
Dilution      :      1.0000
    
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Signal 1: DAD1 B, Sig=220,16 Ref=360,25

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.639	PB	0.0903	16.98806	2.90388	0.1493
2	5.088	MF	0.0952	1.12684e4	1973.21802	99.0642
3	5.322	FM	0.1261	48.99715	6.47568	0.4308
4	13.897	PB	0.1072	26.02243	3.74040	0.2288
5	18.165	PB	0.1227	14.43859	1.81704	0.1269

Totals : 1.13748e4 1988.15502

Results obtained with enhanced integrator!

\*\*\* End of Report \*\*\*