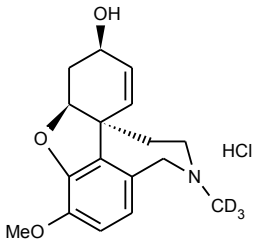
BDG SYNTHESIS

Certificate of Analysis

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

Barry Dent

Barry R. Dent, PhD, Director
26 November 2009

Name:	**Galanthamine-d_3 HCl**
CAS Number:	357-70-0 (unlabelled free base)
Structure:	
Molecular Weight:	$C_{17}H_{18}D_3NO_3 \cdot HCl$ = 326.83
Lot Number:	BDG 2767
Appearance:	Off-white, powder
Purity By HPLC:	98.0 % (HPLC) - 1.1 % (water) = 96.9 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	26 November 2014

Storage and Handling:

Temperature:	ambient laboratory temperature; may be refrigerated.
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.

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Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: the signal at the site of deuteration is still present at about 3 % of the intensity of that for unlabelled material, indicating that some H/D exchange has occurred.
Residual Solvents: no residual solvents are observed.
Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: The carbon-13 NMR spectrum of the product showed broadened and split peaks and was of limited value to assess identity and purity. This observation is common for salts. The spectrum of the derived free base was more informative and the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: the signal for the *N*-methyl carbon is a small multiplet, consistent with deuterium incorporation at this position.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 291.1773. $C_{17}H_{19}D_3NO_3$ $[M+H]^+$ (free base) requires *m/z* 291.1785. The deviation of 4.2 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 broad, slightly tailing peak is observed (98.0 %). 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 61.60, H 5.52, D 1.84, N 4.29 %
$C_{17}H_{18}D_3NO_3{\cdot}HCl{\cdot}0.2H_2O$	Requires:	C 61.79, H 5.92, D 1.83, N 4.24 %, H_2O 1.09 %
$C_{17}H_{18}D_3NO_3{\cdot}HCl$	Requires:	C 62.47, H 5.86, D 1.85, N 4.29 %

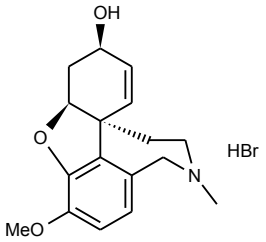
The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the "best-fit" hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend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

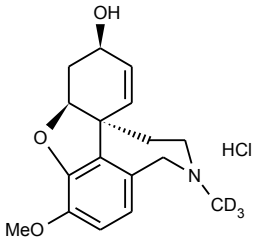
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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. 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 Galanthamine HBr (top) and Galanthamine-d_3 HCl (bottom) in D_2O

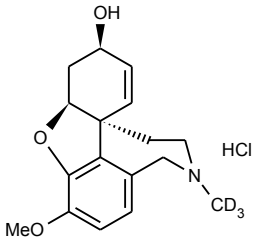




Lot Number: BDG 2767

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Galanthamine-d_3 HCl in Methanol-d_4



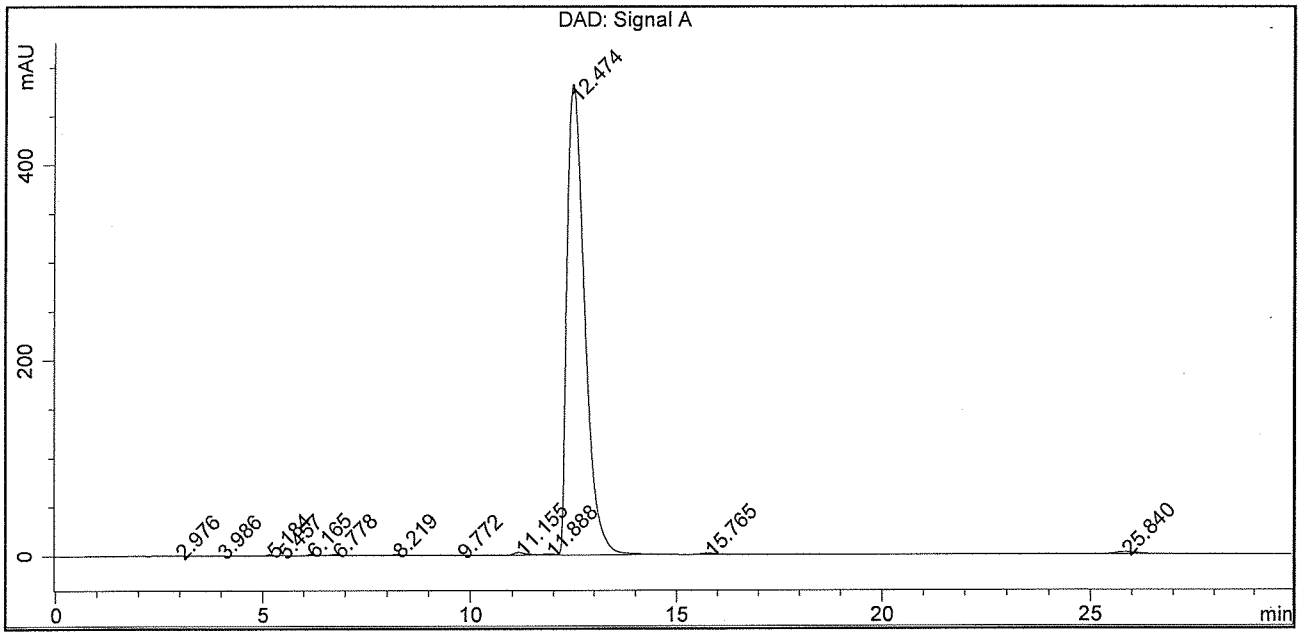
Lot Number: BDG 2767

Note: Compound converted into its free base for spectral clarity.

BDG - Analysis of Galanthamine-d3 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 60:30:10 50mM Ammonium Acetate pH=8.5 (NH4OH) : Methanol : Acetonitrile
Flow Rate : 1.0 mL/min . . . . . Column Temperature : 20C
Sample Solvent : Mobile Phase . . . . . Injection Volume : 10 uL . . . . . Detection : UV at 235 nm

Sample Name	BDG 2767	**Instrument**	AnalyticalLC01
Acquisition	26/11/2009, 11:59:02	**Method (rev.)**	LC10358a (3)
Sequence	BDG_26Nov2009a - Reprocessed	**Vial Position**	1
Operator	solvation010\cerityadmin	**Injection**	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	2.98 min	0.2872	2.3840	0.1208 min	0.016 %
2	3.99 min	0.2918	3.5330	0.1632 min	0.024 %
3	5.18 min	1.2172	11.9973	0.1490 min	0.081 %
4	5.46 min	0.1993	2.2257	0.1463 min	0.015 %
5	6.16 min	1.2756	11.3476	0.1378 min	0.077 %
6	6.78 min	1.1006	18.3527	0.2685 min	0.124 %
7	8.22 min	1.2562	21.1688	0.2426 min	0.143 %
8	9.77 min	0.2144	4.4613	0.2488 min	0.030 %
9	11.15 min	2.8733	59.4468	0.2994 min	0.401 %
10	11.89 min	1.1890	24.8753	0.2981 min	0.168 %
11	12.47 min	482.3622	14533.0366	0.4775 min	98.037 %
12	15.77 min	1.5550	43.5241	0.3845 min	0.294 %
13	25.84 min	2.1855	87.6376	0.5278 min	0.591 %