BDG SYNTHESIS

Certificate of Analysis

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

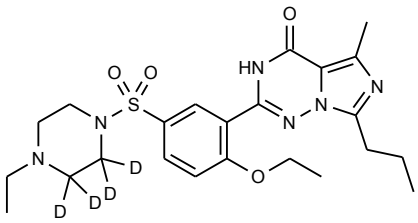
Barry Dent

Barry R. Dent, PhD, Director
4 November 2011

Name: **Vardenafil-d_4**

CAS Number: 224785-90-4 (unlabelled)

Structure:



Molecular Weight: $C_{23}H_{28}D_4N_6O_4S$ = 492.63

Lot Number: BDG 6615.1

Appearance: Off-white, crystalline solid

Corrected Purity: 96.6 % (HPLC) - 0.7 % (water) = 95.9 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 4 November 2016

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.

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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: signals at the sites of deuteration are greatly diminished, compared with what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: no residual solvents are observed.
Impurities: traces of unidentified impurities are seen in the baseline.

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 what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 247.1316, z = 2 (*m/z* 494.2633). $C_{23}H_{30}D_4N_6O_4S$ $[M+2H]^{2+}$ requires *m/z* 494.2613. The deviation of 4.8 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 somewhat broadened, symmetrical peak is observed (96.6 %). 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 55.64, H 5.67, D 1.63, N 17.11 %
$C_{23}H_{28}D_4N_6O_4S{\cdot}0.2H_2O$	Requires:	C 55.67, H 5.77, D 1.62, N 16.94 %, H_2O 0.7 %
$C_{23}H_{28}D_4N_6O_4S$	Requires:	C 56.08, H 5.73, D 1.64, N 17.06 %

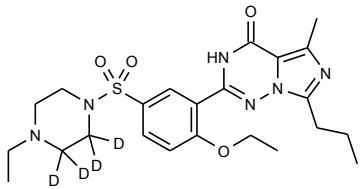
The elemental analyses fall slightly outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend 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

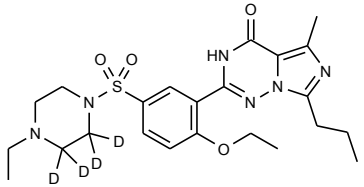
Proton NMR Spectrum of Vardenafil-d_4 in Methanol-d_4



Lot Number: BDG 6615.1

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Vardenafil-d_4 in Methanol-d_4

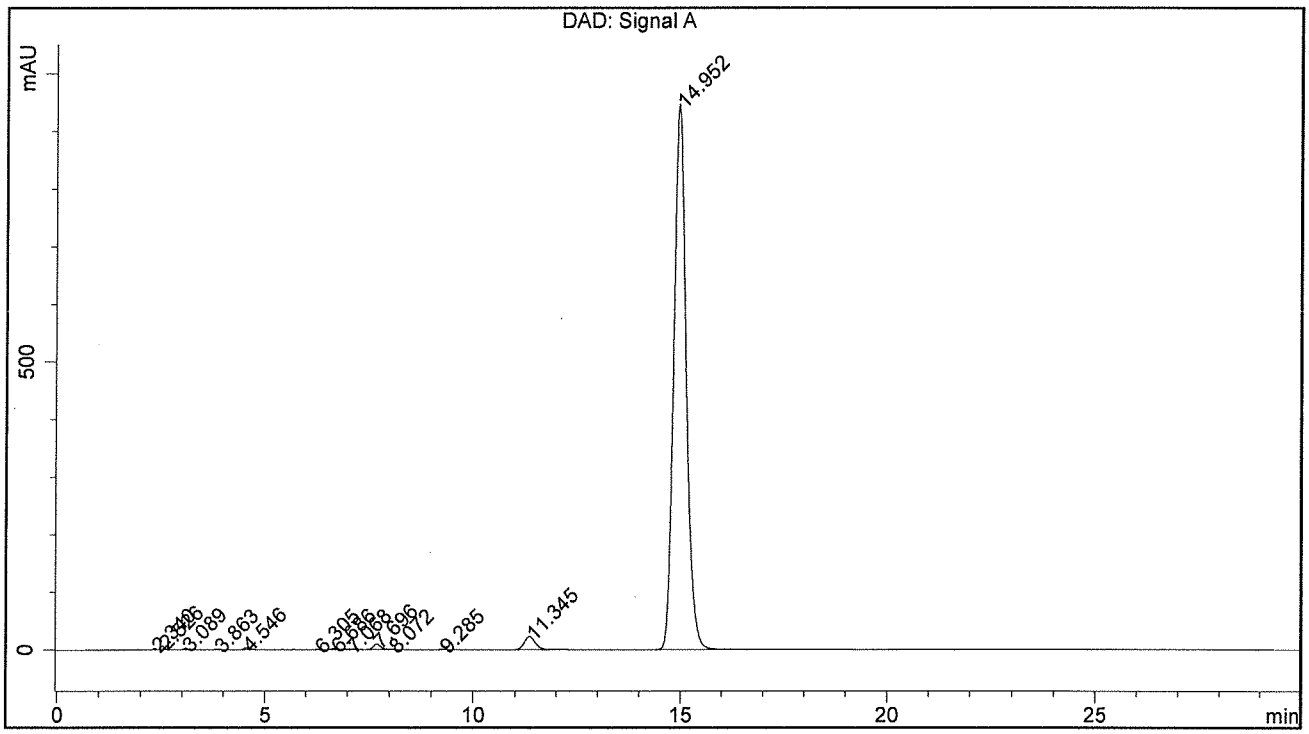


Lot Number: BDG 6615.1

BDG - Analysis of Vardenafil-d4

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 60:40 100 mM Ammonium Acetate : Acetonitrile
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 240 nm

Sample Name	BDG 6615.1	Instrument	AnalyticalLC01
Acquisition	04/11/2011, 11:35:54	Method (rev.)	LC10062c (2)
Sequence	BDG_04Nov2011a	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	2.34 min	2.3045	13.5135	0.0864 min	0.066 %
2	2.53 min	6.6801	35.3207	0.0797 min	0.172 %
3	3.09 min	2.6473	17.9136	0.0989 min	0.087 %
4	3.86 min	1.4619	13.7812	0.1380 min	0.067 %
5	4.55 min	3.1036	32.7409	0.1511 min	0.160 %
6	6.30 min	0.5075	5.4095	0.1463 min	0.026 %
7	6.69 min	1.5467	17.5055	0.1800 min	0.085 %
8	7.07 min	1.1004	16.8265	0.2104 min	0.082 %
9	7.70 min	9.3580	118.3349	0.1915 min	0.577 %
10	8.07 min	0.6021	5.7993	0.1404 min	0.028 %
11	9.28 min	0.6603	8.7800	0.1931 min	0.043 %
12	11.35 min	22.7820	418.6393	0.2804 min	2.040 %
13	14.95 min	945.6863	19819.2785	0.3205 min	96.567 %