BDG SYNTHESIS

Certificate of Analysis

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

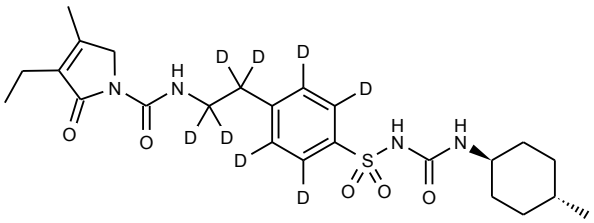
Barry Dent

Barry R. Dent, PhD, Director
10 July 2013

Name: **Glimepiride-d_8**

CAS Number: 93479-97-1 (unlabelled)

Structure:



Molecular Weight: $C_{24}H_{26}D_8N_4O_5S$ = 498.67

Lot Number: BDG 7655.1

Appearance: White powder

Corrected Purity: 98.3 % (HPLC) - 0.7 % (water) = 97.6 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 10 July 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:	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. A small amount of aromatic H/D exchange is observed.
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 the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI-)

Found *m/z* 497.2697. $C_{24}H_{25}D_8N_4O_5S$ $[M-H]^-$ requires *m/z* 497.2697. The deviation of 0.2 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 sharp, symmetrical peak is observed (98.3 %). 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 57.06, H 5.27, D 3.25, N 11.18 %
$C_{24}H_{26}D_8N_4O_5S{\cdot}0.2H_2O$	Requires:	C 57.39, H 5.30, D 3.21, N 11.15 %, H_2O 0.72 %
$C_{24}H_{26}D_8N_4O_5S$	Requires:	C 57.81, H 5.26, D 3.23, N 11.24 %

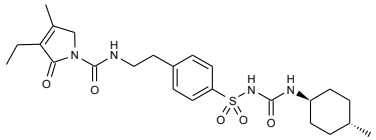
The elemental analyses fall slightly outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend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

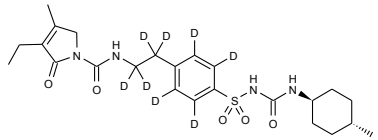
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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 Glimepiride (top) and Glimepiride-d_8 (bottom) in DMSO-d_6

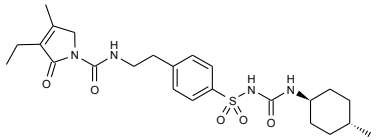


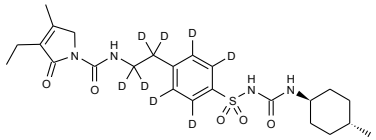


Lot Number: BDG 7655.1

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Glimepiride (top) and Glimepiride-d_8 (bottom) in DMSO-d_6





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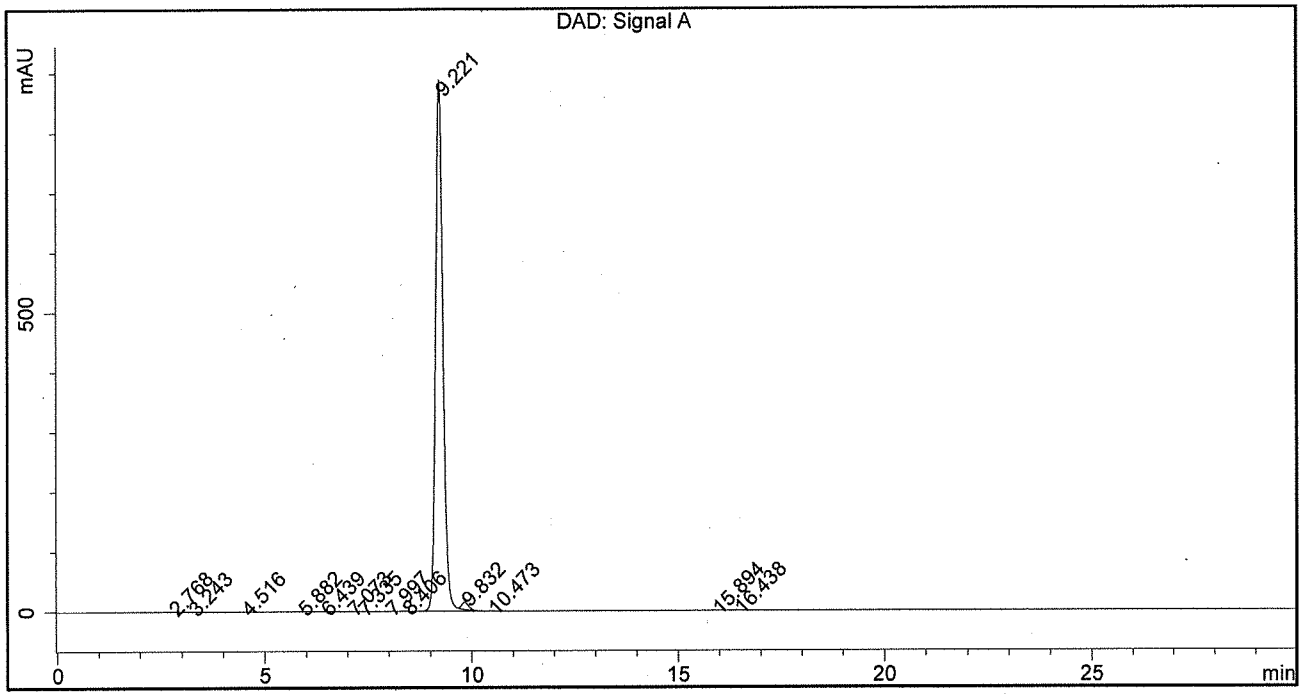
BDG - Analysis of Glimepiride-d8

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 40:60 10 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 230 nm

Sample Name	BDG 7655.1	Instrument	AnalyticalLC01
Acquisition	10/07/2013, 19:03:02	Method (rev.)	LC10296b (3)
Sequence	BDG_10Jul2013c - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	2.77 min	0.5372	2.8544	0.0800 min	0.025 %
2	3.24 min	0.2153	1.5441	0.1057 min	0.014 %
3	4.52 min	0.2119	1.8946	0.1203 min	0.017 %
4	5.88 min	0.2844	2.8135	0.1454 min	0.025 %
5	6.44 min	0.2078	2.0233	0.1356 min	0.018 %
6	7.07 min	0.2932	3.0974	0.1373 min	0.027 %
7	7.33 min	0.2470	4.1335	0.2132 min	0.037 %
8	8.00 min	0.3133	3.5236	0.1652 min	0.031 %
9	8.41 min	0.4810	7.9907	0.2418 min	0.071 %
10	9.22 min	888.1718	11099.5254	0.1918 min	98.321 %
11	9.83 min	12.2272	139.5686	0.1792 min	1.236 %
12	10.47 min	0.2293	2.9153	0.1663 min	0.026 %
13	15.89 min	0.3649	6.8978	0.2525 min	0.061 %
14	16.44 min	0.4312	10.2723	0.2940 min	0.091 %