BDG SYNTHESIS

Certificate of Analysis

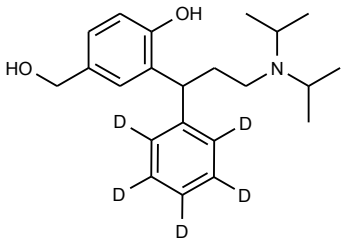
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
2 February 2015

Name: **5-Hydroxymethyltolterodine-d_5**

CAS Number: 200801-70-3 (unlabelled)

Structure:



Molecular Weight: $C_{22}H_{26}D_5NO_2$ = 346.52

Lot Number: BDG 5188.2

Appearance: White, crystalline solid

Corrected Purity: 98.8 % (HPLC) - 0.4 % (diethyl ether) = 98.4 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 2 February 2020

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.

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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 site of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of diethyl ether (0.4 % *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 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* 369.2587. $C_{22}H_{26}D_5NNaO_2$ $[M+Na]^+$ requires *m/z* 369.2561. The deviation of 7.0 ppm is somewhat outside normally accepted limits for the establishment of identity by HRMS, and the mass spectral data should be considered in conjunction with other identity criteria. No signal for d_0 material was seen (detection limit about 0.5 %).

HPLC

A sharp, slightly tailing peak is observed (98.8 %). 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 76.31, H 7.72, D 2.97, N 4.01 %
$C_{22}H_{26}D_5NO_2$	Requires:	C 76.25, H 7.56, D 2.91, N 4.04 %

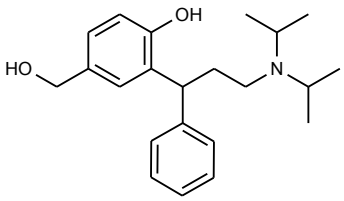
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

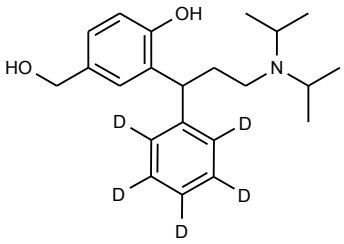
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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 5-Hydroxymethyltolterodine (top) and 5-Hydroxymethyltolterodine-d_5 (bottom) in DMSO-d_6

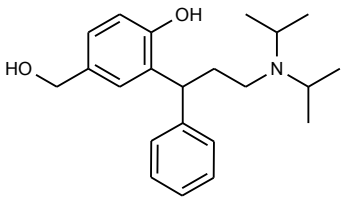


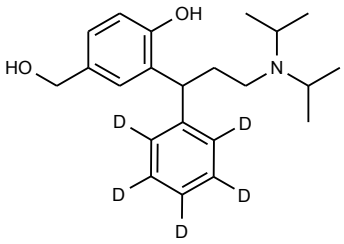


Lot Number: BDG 5188.2

BDG SYNTHESIS

Carbon-13 NMR Spectrum of 5-Hydroxymethyltolterodine (top) and 5-Hydroxymethyltolterodine-d_5 (bottom) in DMSO-d_6





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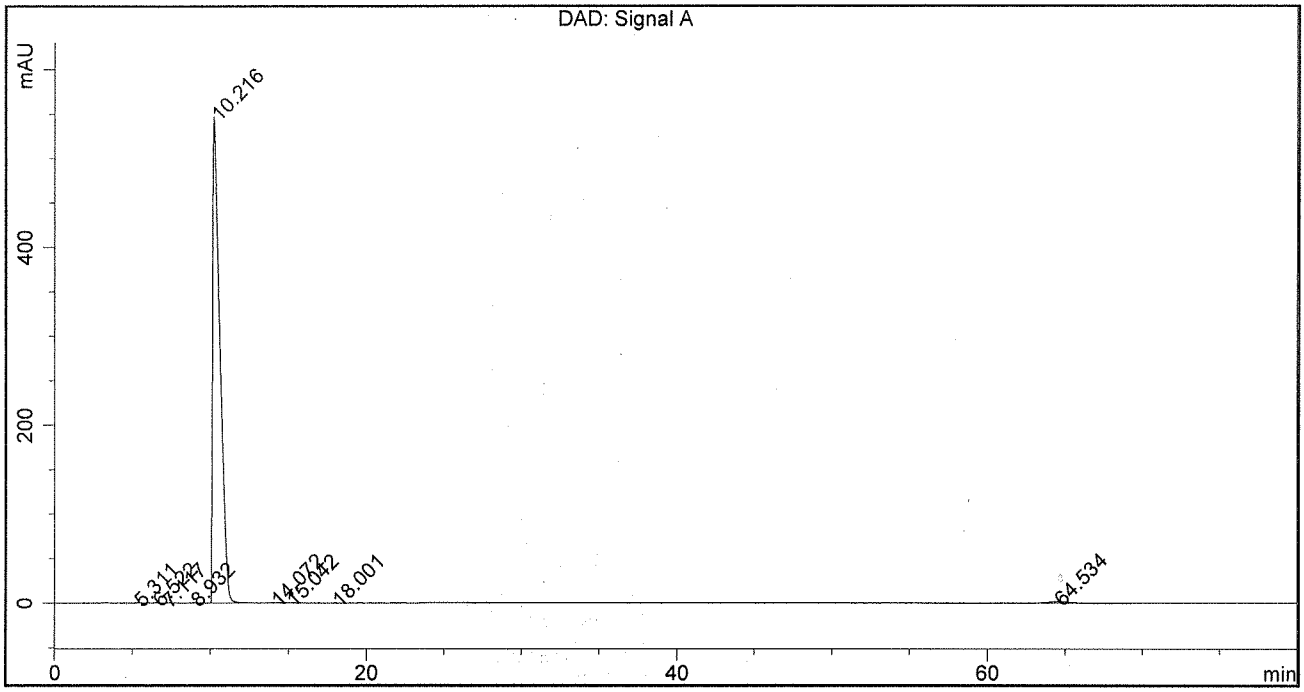
BDG - Analysis of 5-Hydroxymethyltolterodine-d5

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 78:22 10 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Flow Rate : 1.0 mL/min
Column Temperature : 30 C
Sample Solvent : Mobile Phase
Injection Volume : 10 uL
Detection : UV at 225 nm

Sample Name	BDG 5188.2	Instrument	AnalyticalLC01
Acquisition	02/02/2015, 21:26:00	Method (rev.)	LC10445b (6)
Sequence	BDG_02Feb2015d - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.31 min	0.3096	4.4152	0.1984 min	0.025 %
2	6.52 min	0.5205	5.7281	0.1724 min	0.032 %
3	7.12 min	0.3216	3.5634	0.1572 min	0.020 %
4	8.93 min	0.4561	6.0431	0.1746 min	0.034 %
5	10.22 min	546.6658	17535.9213	0.4542 min	98.812 %
6	14.07 min	0.4154	11.0033	0.3250 min	0.062 %
7	15.04 min	0.4236	14.3791	0.4201 min	0.081 %
8	18.00 min	0.2554	2.9240	0.1656 min	0.016 %
9	64.53 min	1.7257	162.7432	1.1162 min	0.917 %