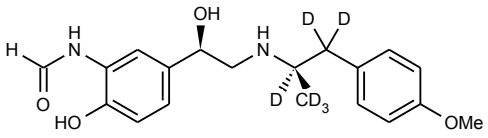
BDG SYNTHESIS

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 July 2012

Name:	**Formoterol-d_6**
CAS Number:	73573-87-2 (unlabelled)
Structure:	
Molecular Weight:	$C_{19}H_{18}D_6N_2O_4$ = 350.44
Lot Number:	BDG 12551.2
Appearance:	Beige, amorphous solid
Corrected Purity:	97.3 % (HPLC) - 2.5 % (ethyl acetate) - 0.7 % (methanol) - 6.7 % (water) = 87.4 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	24 July 2017
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.

Mailing:
BDG Synthesis Limited
PO Box 38627, Wellington Mail Centre,
Wellington 5045, New Zealand.

Shipping:
BDG Synthesis Limited
Gracefield Research Centre, Building F,
69 Gracefield Rd, Lower Hutt 5010, New Zealand.

Phone: + 64 4 569 0520
Fax: + 64 4 569 0521

info@bdg.co.nz
www.bdg.co.nz

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 the spectrum of unlabelled material, indicating clean deuteration.
Residual Solvents: small amounts of methanol (0.7 % *w/w*) and ethyl acetate (2.5 % *w/w*) 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* 351.2189. $C_{19}H_{19}D_6N_2O_4$ $[M+H]^+$ requires *m/z* 351.2191. The deviation of 0.6 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 %) The sample contains approximately 50% d_7 material, with the extra deuterium concentrated on the carbonyl carbon.

HPLC

A sharp, symmetrical peak is observed (97.3 %). 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 60.81, H 5.31, D 3.07, N 7.30 %
$C_{19}H_{18}D_6N_2O_4 \cdot 1.4H_2O$	Requires:	C 60.75, H 5.58, D 3.22, N 7.46 %, H_2O 6.71 %
$C_{19}H_{18}D_6N_2O_4$	Requires:	C 65.12, H 5.18, D 3.45, N 7.99 %

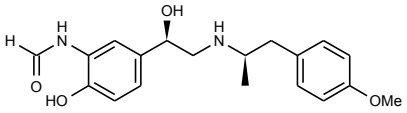
The elemental analyses fall substantially outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we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

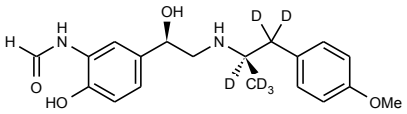
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

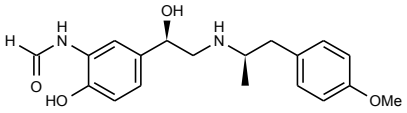


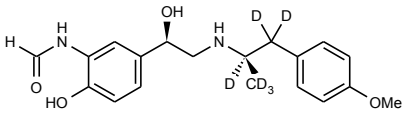


Lot Number: BDG 12551.2

BDG SYNTHESIS

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



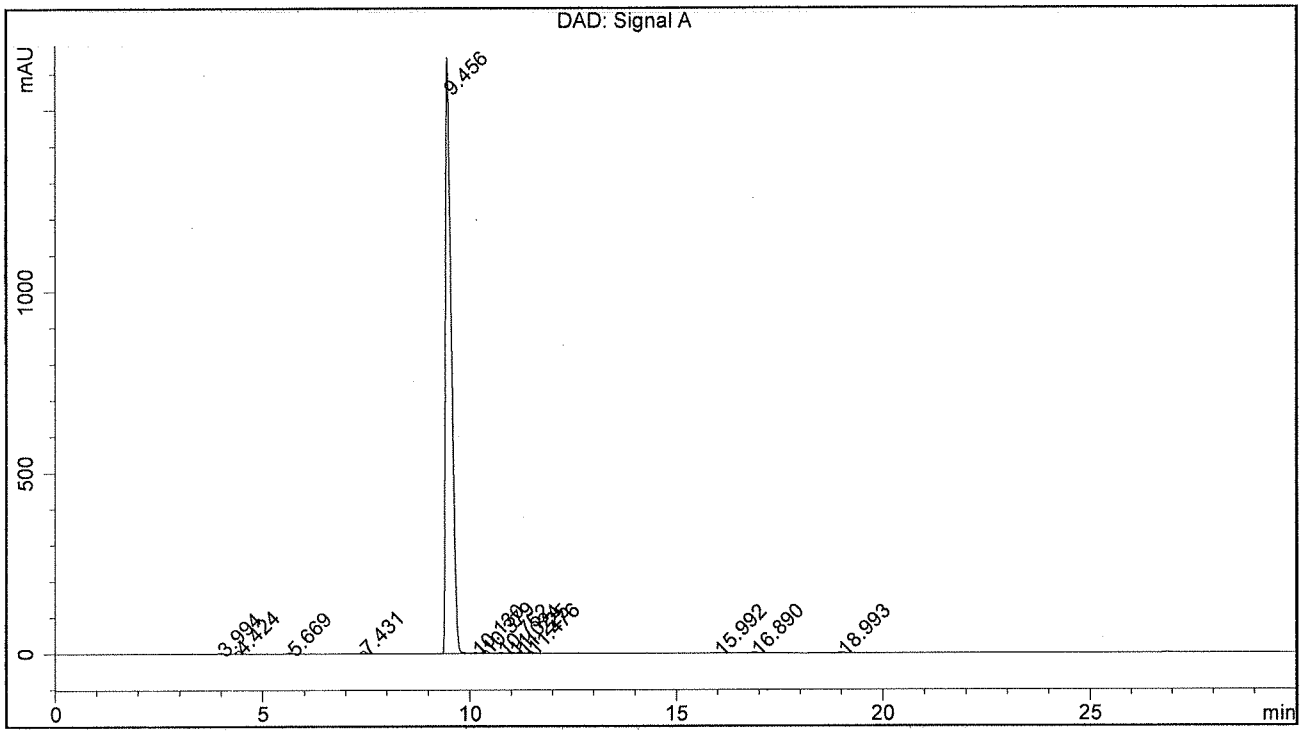


Lot Number: BDG 12551.2

BDG - Analysis of Formoterol-d6

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 90:10 20 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Mobile Phase B : 40:60 20 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Gradient (A:B) : T0=100:0, T25=0:100, T30=0:100, T32=100:0, T35=100:0
Flow Rate : 1.0 mL/min . . . . . Sample Solvent : Initial Mobile Phase
Column Temperature : 20C . . . . . Injection Volume : 10 uL . . . . . Detection : UV at 242 nm

Sample Name	BDG 12551.2	Instrument	AnalyticalLC01
Acquisition	24/07/2012, 19:06:18	Method (rev.)	LC10526a (4)
Sequence	BDG_24Jul2012f - Reprocessed	Vial Position	52
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.99 min	2.2907	21.3863	0.1369 min	0.128 %
2	4.42 min	7.6476	61.6294	0.1220 min	0.368 %
3	5.67 min	3.0605	23.1121	0.1161 min	0.138 %
4	7.43 min	7.3259	51.0879	0.1054 min	0.305 %
5	9.46 min	1644.4671	16301.6666	0.1497 min	97.309 %
6	10.13 min	2.7259	22.0285	0.1183 min	0.131 %
7	10.38 min	8.3088	72.9971	0.1305 min	0.436 %
8	10.75 min	2.7783	23.8889	0.1223 min	0.143 %
9	11.02 min	3.1904	22.5903	0.1046 min	0.135 %
10	11.23 min	4.1080	40.2890	0.1404 min	0.240 %
11	11.48 min	5.2284	46.6381	0.1281 min	0.278 %
12	15.99 min	1.6878	19.6590	0.1659 min	0.117 %
13	16.89 min	3.1187	23.0578	0.1143 min	0.138 %
14	18.99 min	2.5826	22.4109	0.1312 min	0.134 %