BDG SYNTHESIS

Certificate of Analysis

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

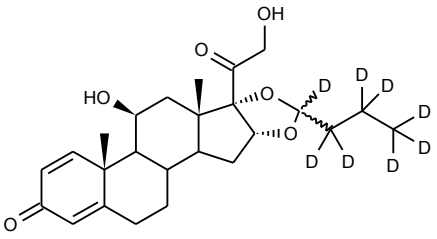
Barry Dent

Barry R. Dent, PhD, Director
5 June 2009

Name: **Budesonide-d_8**

CAS Number: 51333-22-3 (unlabelled)

Structure:



Molecular Weight: $C_{25}H_{26}D_8O_6$ = 438.58

Lot Number: BDG 4561

Appearance: White, crystalline solid

Purity By HPLC: 95.9 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 5 June 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:	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. Some of the signals are split due to the presence of unequal amounts of epimers.
Isotopic Labelling: Signals at the sites of deuteration are absent (CD_3, 0.9 ppm) or, where they coincide with signals from elsewhere within the molecule, greatly diminished (2 x CD_2, 1-2 ppm; CD, 4-5.2 ppm), compared with the spectrum of unlabelled material, indicating clean deuteration. Note: The spectrum for the unlabelled material comprises the same epimers but in a different ratio.
Residual Solvents: no residual solvents are 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* 439.2919. $C_{25}H_{27}D_8O_6$ $[M+H]^+$ requires *m/z* 439.2927. The deviation of 1.9 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

Two somewhat broadened peaks for the two epimers are observed (95.9 area % total). 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 68.65, H 6.03, D 3.71 %
$C_{25}H_{26}D_8O_6$	Requires:	C 68.46, H 5.98, D 3.67 %

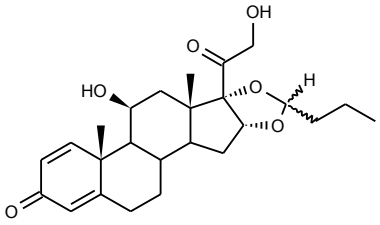
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

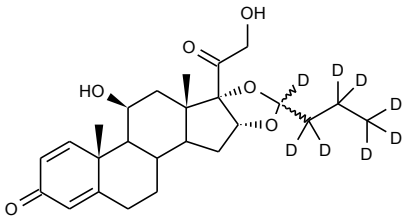
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

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 Budesonide (top) and Budesonide-d_8 (bottom) in $CDCl_3$

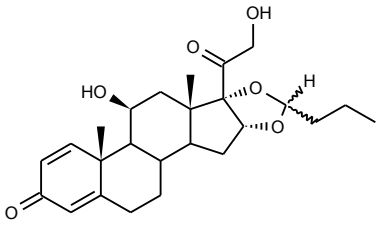


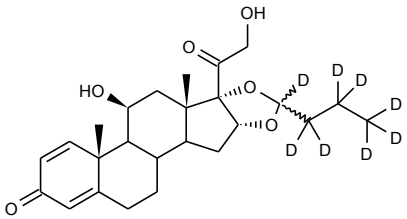


Lot Number: BDG 4561

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Budesonide (top) and Budesonide-d_8 (bottom) in $CDCl_3$





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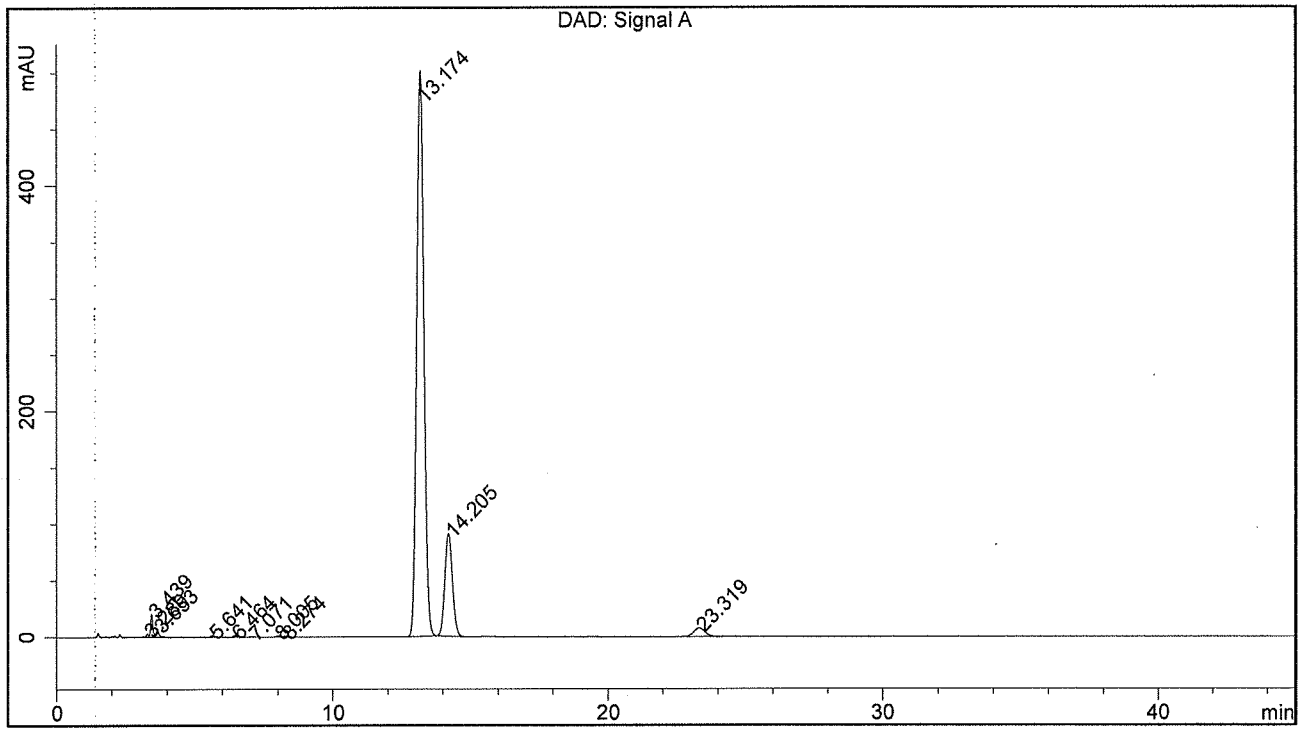
BDG - Analysis of Budesonide-d8

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 30 mM Potassium diHydrogen Phosphate pH=3.2 : Acetonitrile
Flow Rate : 1.5 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 240 nm

Sample Name	BDG 4561	Instrument	AnalyticalLC01
Acquisition	05/06/2009, 17:19:35	Method (rev.)	LC10326a (3)
Sequence	BDG_05Jun2009h	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.29 min	2.8393	14.7750	0.0767 min	0.131 %
2	3.44 min	20.1882	114.3853	0.0861 min	1.012 %
3	3.65 min	6.8720	55.4971	0.1142 min	0.491 %
4	5.64 min	1.3823	25.0849	0.2397 min	0.222 %
5	6.46 min	1.3548	13.2584	0.1502 min	0.117 %
6	7.07 min	0.6447	8.5369	0.1945 min	0.076 %
7	8.01 min	0.8058	8.8757	0.1685 min	0.079 %
8	8.27 min	0.8983	12.8983	0.1955 min	0.114 %
9	13.17 min	500.9501	9099.3216	0.2799 min	80.480 %
10	14.21 min	90.5418	1745.7477	0.3009 min	15.440 %
11	23.32 min	7.5132	207.9684	0.4309 min	1.839 %