BDG SYNTHESIS

Certificate of Analysis

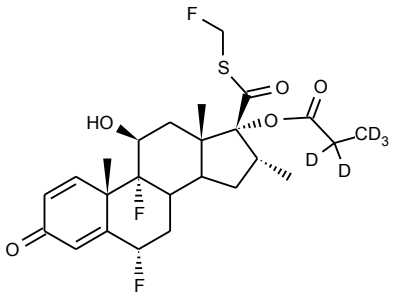
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
28 January 2013

Name: **Fluticasone Propionate-d_5**

CAS Number: 80474-14-2 (unlabelled)

Structure:



Molecular Weight: $C_{25}H_{26}D_5F_3O_5S$ = 505.60

Lot Number: BDG 2425.3

Appearance: White, crystalline solid

Corrected Purity: 93.7 % (HPLC) - 0.3 % (ethyl acetate) = 93.4 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 28 January 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.

Mailing:
BDG Synthesis 2014 Limited
PO Box 38627, Wellington Mail Centre,
Wellington 5045, New Zealand.

Shipping:
BDG Synthesis 2014 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 absent, compared with what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of ethyl acetate (0.3 % *w/w*) is observed.
Impurities: a small amount of a precursor with the fluoromethyl substituent of fluticasone propionate-d_5 replaced by chloromethyl (1.6 % w/w) is observed (the methylene is visible as a peak at δ 5.2, all of the other resonances being superimposable with those of fluticasone propionate-d_5).

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 (FAB+)

Found *m/z* 506.2242. $C_{25}H_{27}D_5F_3O_5S$ $[M+H]^+$ requires *m/z* 506.2236. The deviation of 1.1 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 (93.7 %). 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 59.56, H 5.06, D 1.95, F 11.06 %
$C_{25}H_{26}D_5F_3O_5S$	Requires:	C 59.39, H 5.18, D 1.99, F 11.27 %

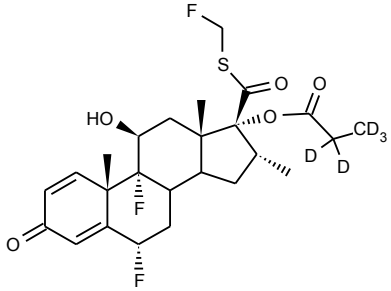
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

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

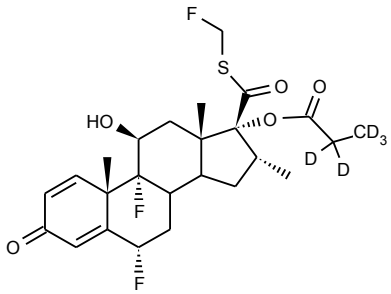
Proton NMR Spectrum of Fluticasone Propionate-d_5 in DMSO-d_6



Lot Number: BDG 2425.3

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Fluticasone Propionate-d_5 in DMSO-d_6



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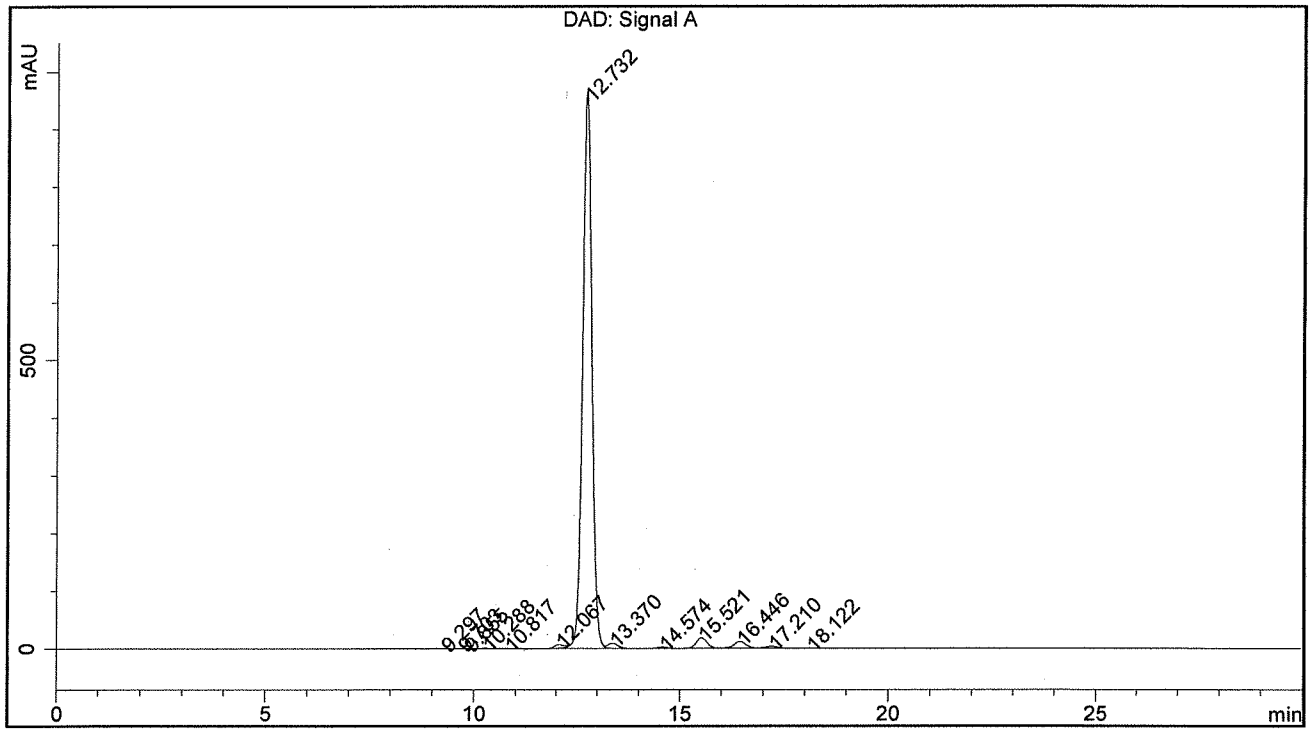
BDG - Analysis of Fluticasone propionate-d5

Column : Phenomenex Luna C18 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 4 x 3 mm
Mobile Phase : 40:60 Water : Acetonitrile
Flow Rate : 1.0 mL/min
Sample Solvent : 40:60 Water : Acetonitrile
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 239 nm

Sample Name	BDG 2425.3	**Instrument**	AnalyticalLC01
Acquisition	28/01/2013, 11:36:07	**Method (rev.)**	LC10240b (6)
Sequence	BDG_28Jan2013a - Reprocessed	**Vial Position**	1
Operator	solvation010\cerityadmin	**Injection**	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	9.30 min	0.4016	6.6808	0.2281 min	0.041 %
2	9.70 min	0.4146	4.4561	0.1614 min	0.028 %
3	9.85 min	0.4188	4.8010	0.1717 min	0.030 %
4	10.29 min	0.7627	10.2978	0.2055 min	0.064 %
5	10.82 min	0.5969	8.4649	0.2194 min	0.053 %
6	12.07 min	6.5310	107.7040	0.2424 min	0.668 %
7	12.73 min	965.6359	15105.4774	0.2405 min	93.740 %
8	13.37 min	8.8955	155.5227	0.2640 min	0.965 %
9	14.57 min	2.3845	41.6361	0.2637 min	0.258 %
10	15.52 min	18.1411	338.3946	0.2896 min	2.100 %
11	16.45 min	11.9644	244.6639	0.3106 min	1.518 %
12	17.21 min	3.4690	74.7660	0.3314 min	0.464 %
13	18.12 min	0.4155	11.4016	0.3642 min	0.071 %