



BDG SYNTHESIS

Certificate of Analysis

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

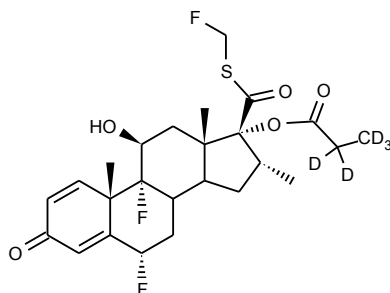
Barry Dent

Barry R. Dent, PhD, Director
3 April 2008

Name: Fluticasone Propionate-d₅

CAS Number: 80474-14-2 (unlabelled)

Structure:



Molecular Weight: C₂₅H₂₆D₅F₃O₅S = 505.60

Lot Number: BDG 2425.3

Appearance: White, crystalline solid

Corrected Purity: 93.8 % (HPLC) - 0.5 % (ethyl acetate) = 93.3 %

Isotopic Purity: Under 0.5 % d₀

Re-test Date: 3 April 2013

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.

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 (0.5 % w/w) is observed.

Impurities: a small amount of a precursor with the fluoromethyl substituent of fluticasone propionate-d₅ replaced by chloromethyl (1.7 % 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-d₅).

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. C₂₅H₂₇D₅F₃O₅S [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 d₀ material was seen (detection limit about 0.5 %).

HPLC

A somewhat broadened, symmetrical peak is observed (93.8 %). 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 59.56, H 5.06, D 1.95, F 11.06 %
C ₂₅ H ₂₆ D ₅ F ₃ O ₅ S	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).

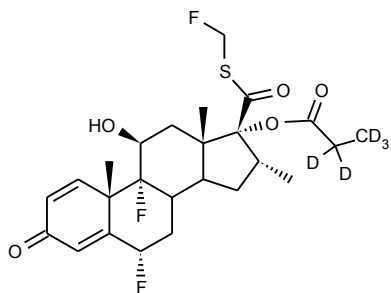
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

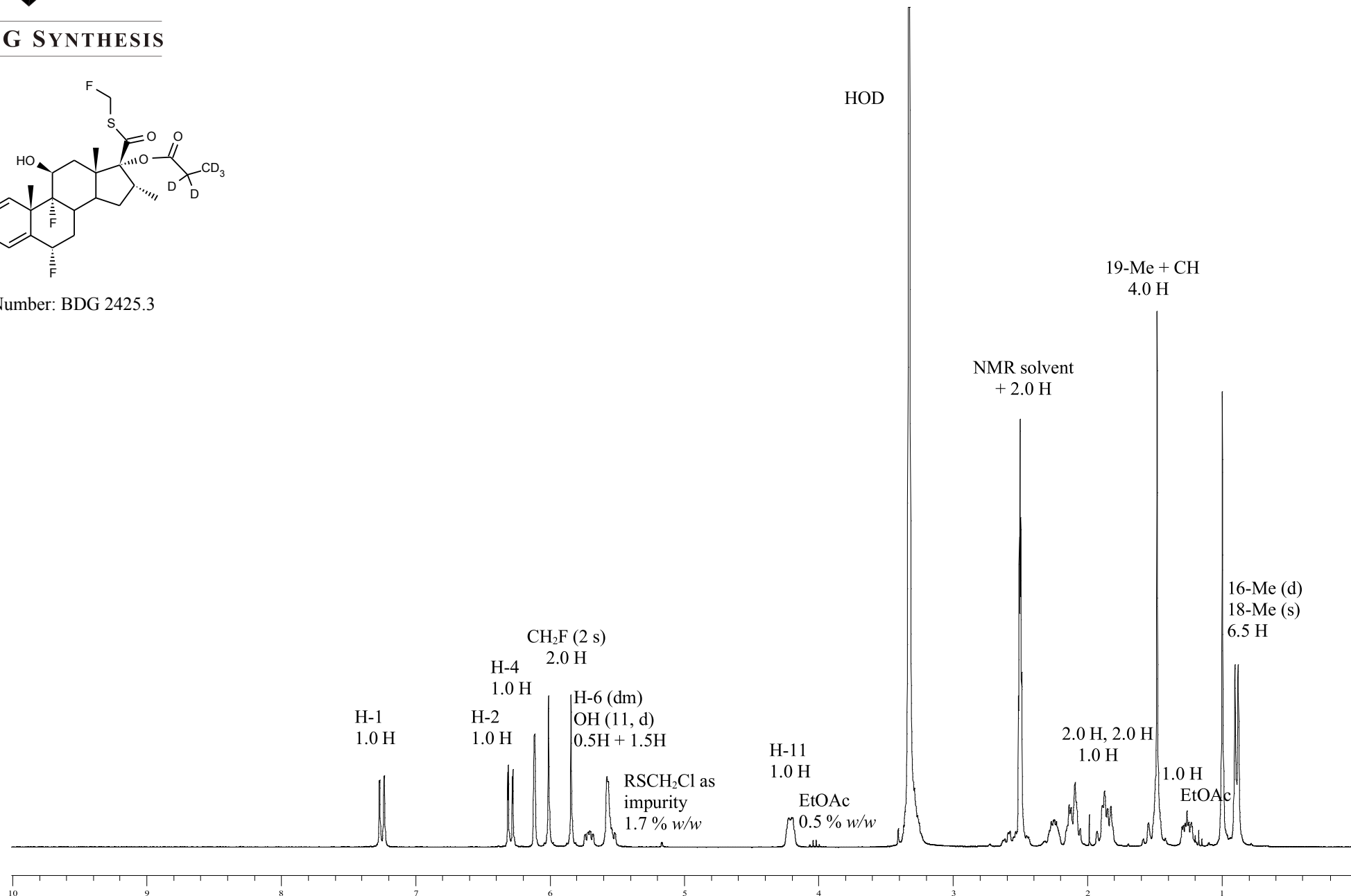


Proton NMR Spectrum of Fluticasone Propionate-d₅ in DMSO-d₆

BDG SYNTHESIS



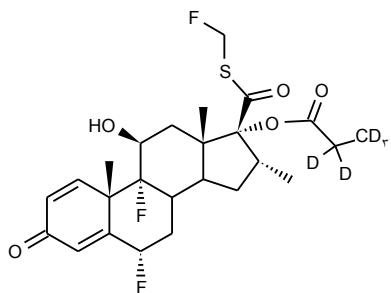
Lot Number: BDG 2425.3



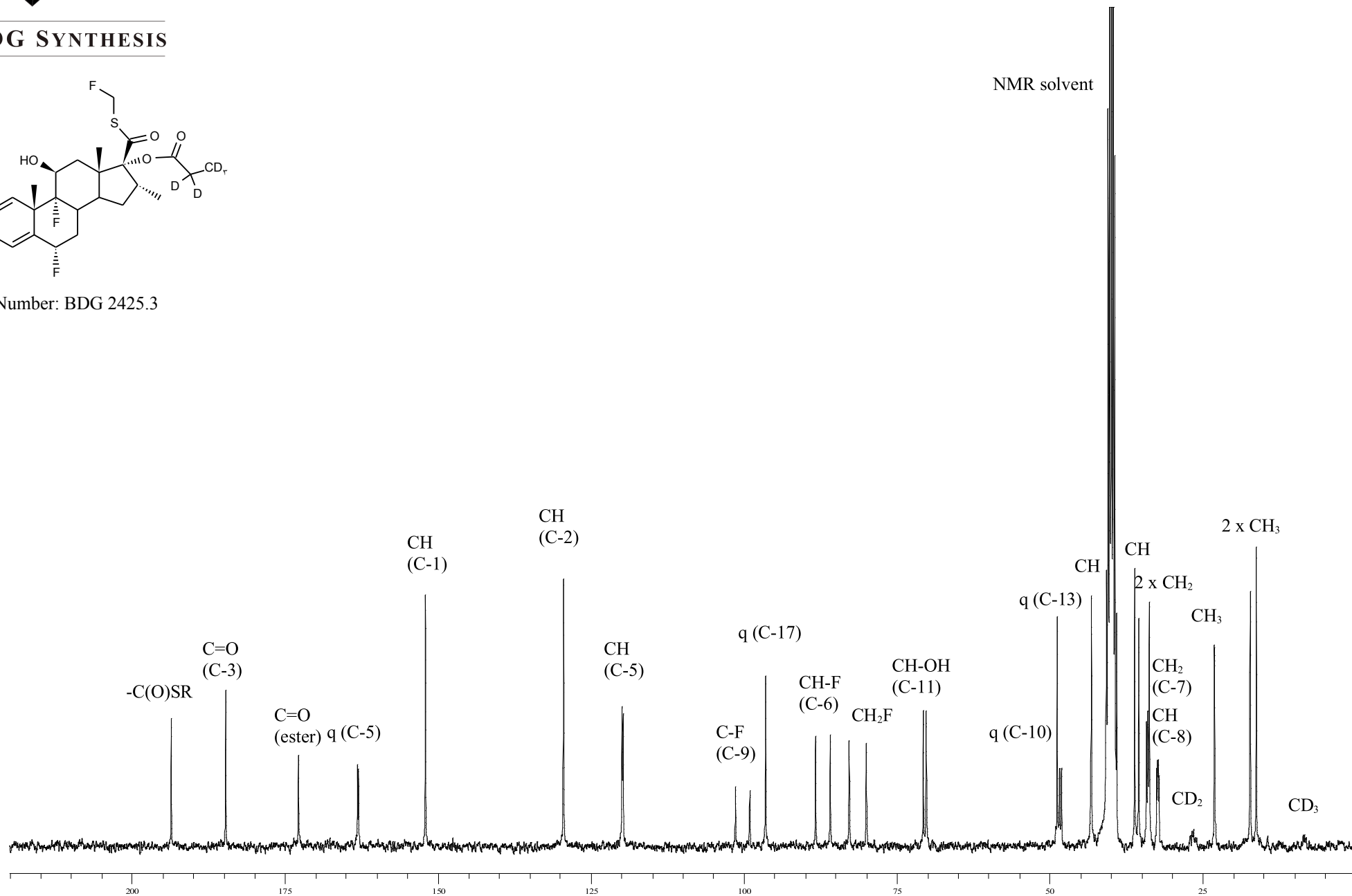


Carbon-13 NMR Spectrum of Fluticasone Propionate-d₅ in DMSO-d₆

BDG SYNTHESIS



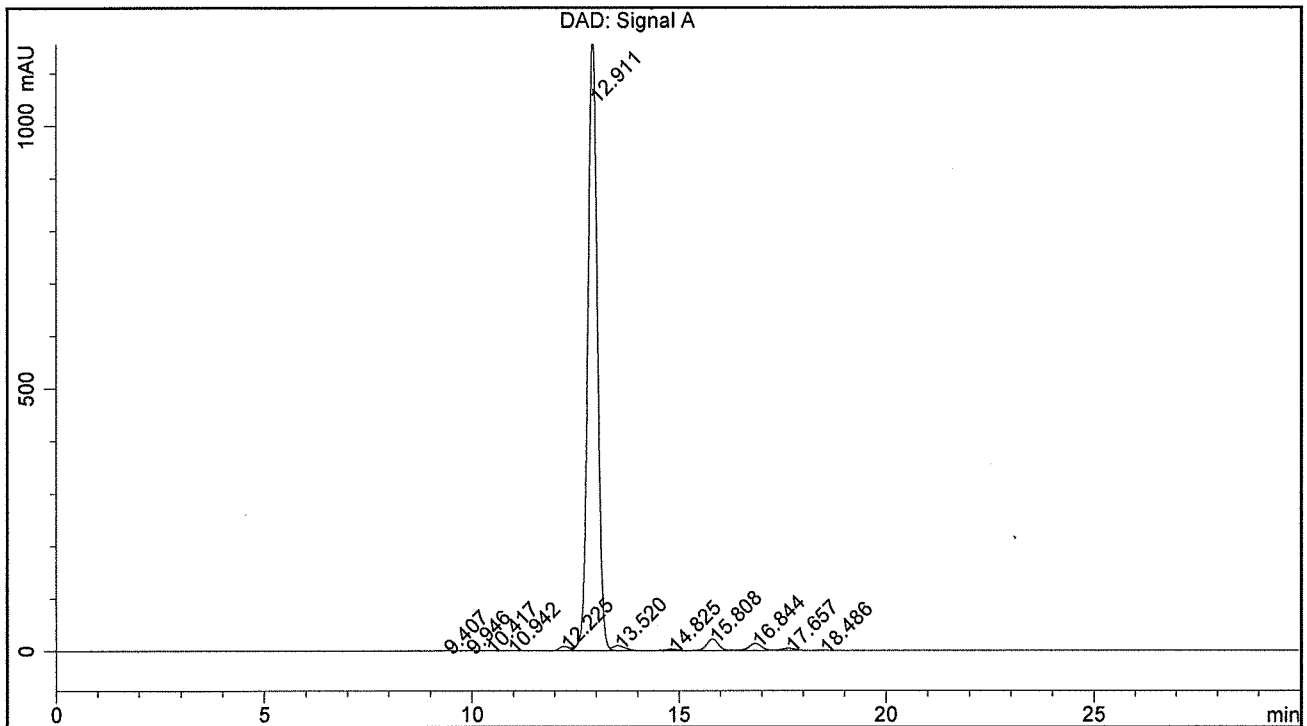
Lot Number: BDG 2425.3



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 : 60:40 Acetonitrile : Water
 Flow Rate : 1.0 mL/min
 Sample Solvent : 60:40 Acetonitrile : Water
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 239 nm

Sample Name	BDG 2425.3	Instrument	AnalyticalLC01
Acquisition	04/04/2008, 10:25:24	Method (rev.)	LC10240b (5)
Sequence	BDG_04Apr2008b - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	9.41 min	0.4501	6.2967	0.2132 min	0.031 %
2	9.95 min	0.5009	10.6281	0.2875 min	0.053 %
3	10.42 min	0.9189	11.5360	0.1945 min	0.058 %
4	10.94 min	0.7018	9.8824	0.2163 min	0.049 %
5	12.23 min	7.9885	148.3571	0.2707 min	0.740 %
6	12.91 min	1170.8080	18794.6312	0.2493 min	93.764 %
7	13.52 min	9.3308	194.5268	0.3032 min	0.970 %
8	14.82 min	2.7828	50.2702	0.2828 min	0.251 %
9	15.81 min	21.6892	423.1476	0.3036 min	2.111 %
10	16.84 min	13.3963	289.8973	0.3325 min	1.446 %
11	17.66 min	4.0507	92.1492	0.3494 min	0.460 %
12	18.49 min	0.4307	13.2499	0.4309 min	0.066 %