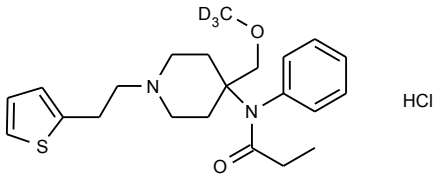
BDG SYNTHESIS

Certificate of Analysis

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

Barry Dent

Barry R. Dent, PhD, Director
19 December 2011

Name:	**Sufentanil-d_3 HCl**
CAS Number:	56030-54-7 (unlabelled free base)
Structure:	
Molecular Weight:	$C_{22}H_{27}D_3N_2O_2S \cdot HCl = 426.03$
Lot Number:	BDG 6597.3
Appearance:	White, crystalline solid
Corrected Purity:	99.5 % (HPLC) - 0.4 % (water) = 99.1 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	19 December 2016

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.

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. The complexity of the spectrum indicates two rotamers of the product are present in solution.
Isotopic Labelling: signals at the site of deuteration are absent, compared with what would be expected for unlabelled material, indicating clean deuteration. .
Residual Solvents: a trace (under 0.1 % *w/w*) of diethyl ether 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. Most signals are duplicated indicating that two rotamers of the product are present in solution.
Isotopic Labelling: signals at the site of deuteration have collapsed to small multiplets compared with what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 390.2295. $C_{22}H_{28}D_3N_2O_2S$ $[M+H]^+$ requires *m/z* 390.2289. The deviation of 1.5 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 (99.5 %). The small signals before the main peak are also present in the solvent blank. 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 61.55, H 6.55, D 1.41, N 6.56 %
$C_{22}H_{27}D_3N_2O_2S{\cdot}HCl{\cdot}0.1H_2O$	Requires:	C 61.76, H 6.64, D 1.41, N 6.55 %, H_2O 0.42 %
$C_{22}H_{27}D_3N_2O_2S{\cdot}HCl$	Requires:	C 62.02, H 6.62, D 1.42, N 6.58 %

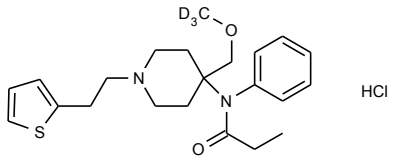
The elemental analyses fall slightly outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend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

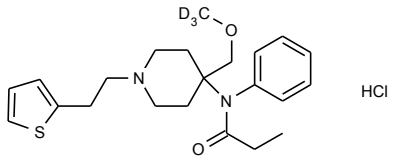
Proton NMR Spectrum of Sufentanil-d_3 HCl in DMSO-d_6



Lot Number: BDG 6597.3

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Sufentanil-d_3 HCl in DMSO-d_6



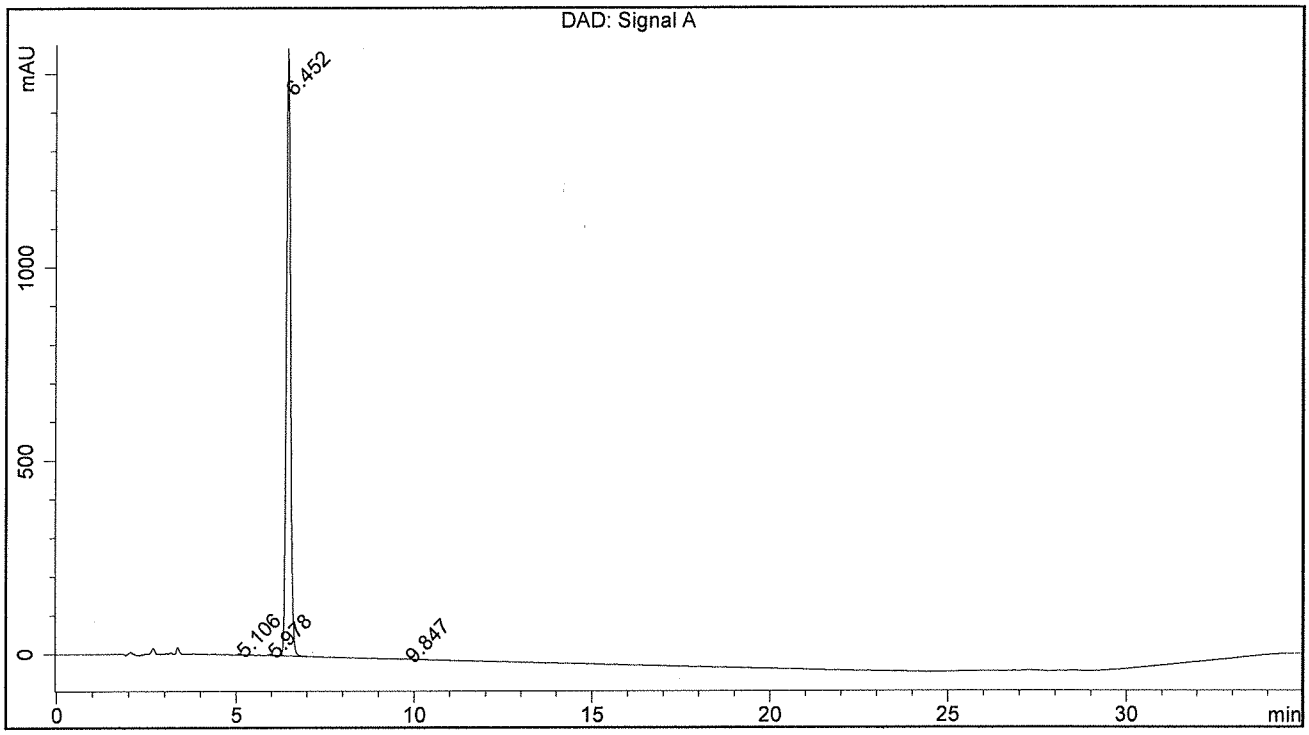
HCl

Lot Number: BDG 6597.3

BDG - Analysis of Sufentanil-d3 HCl

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 Water : Tetrahydrofuran containing 5 g/L Ammonium Carbonate
Mobile Phase B : Acetonitrile
Gradient : T0=20:80, T20=10:90, T25=10:90, T30=20:80, T35=20:80
Flow Rate : 1 mL/min
Sample Solvent : Initial Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 220 nm

Sample Name	BDG 6597.3	Instrument	AnalyticalLC01
Acquisition	19/12/2011, 14:13:59	Method (rev.)	LC10095a (9)
Sequence	BDG_19Dec2011a	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.11 min	2.7888	18.0528	0.1015 min	0.137 %
2	5.98 min	3.4348	29.7162	0.1329 min	0.225 %
3	6.45 min	1568.8338	13148.9870	0.1298 min	99.543 %
4	9.85 min	1.0624	12.5503	0.1898 min	0.095 %