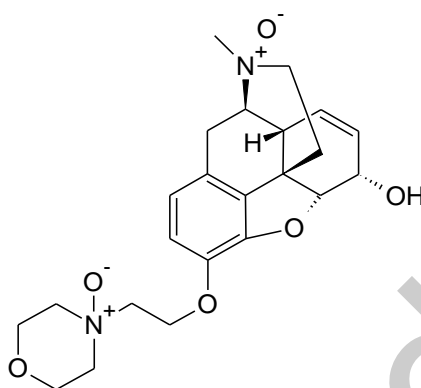


Reference Material Product Information Sheet

Epichem's Quality System conforms to ISO9001:2015 as certified by ECAAS Pty Ltd - Certification number 616061.



Name	pholcodine <i>N,N'</i> -dioxide
BP Name	Pholcodine Impurity F
Synonym(s)	(17 <i>RS</i>)-7,8-didehydro-4,5 α -epoxy-17-methyl-3-(2-(4-oxiomorpholin-4-yl)ethoxy)morphinan-6 α -ol 17-oxide
Epichem Item #	EPL-AA193 Batch 1
CAS #	433308-91-9
Molecular Formula	C ₂₃ H ₃₀ N ₂ O ₆
Molecular Weight	430.49 g/mol
Appearance	Brown powder
Combustion Analysis	Required (%): C:64.2 H:7.0; N:6.5. Found (%): C:55.3; H:7.6; N:5.6
Purity*	81.6%
Date of Manufacture	19 April 2016
Storage Requirements	Very hygroscopic. Protect from heat, light and moisture. Store sample in dry, inert atmosphere.
Special Precautions	This compound is for laboratory use only. Its toxicological properties may not have been fully established. It should be handled only by suitably qualified personnel.
Intended Use	This compound is suitable for the identification of impurities and degradants in pharmaceutical materials. The purity assay is considered as relative contribution.
Date of Shipment	TBA
	This certificate is valid for one year from the date of shipment provided the substance is unopened and stored under the recommended conditions.
Retest Date	TBA (Proper Storage and Handling Required)

* NATA accreditation does not cover the performance of this service

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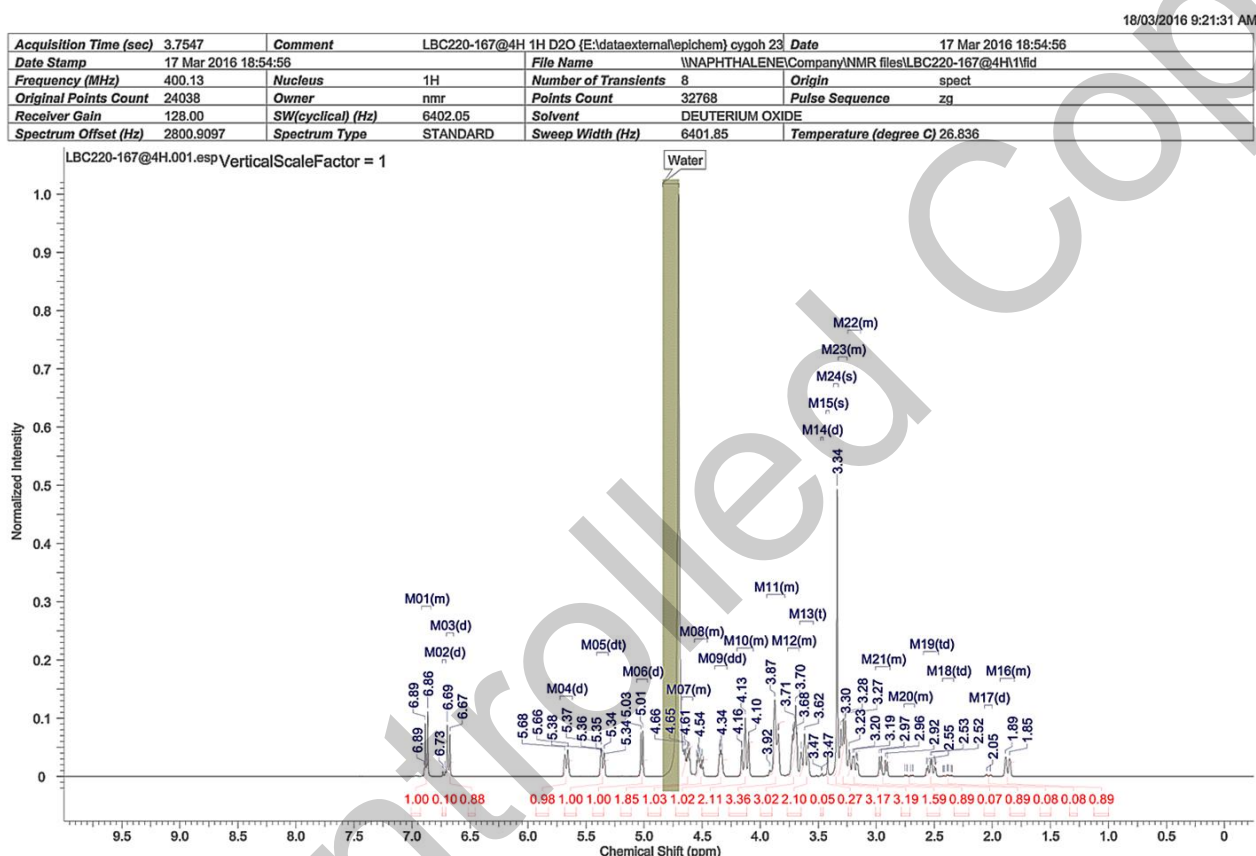
I. Identity

The identity of this product was established using the following analyses:

Ia. ¹H NMR Spectrum

Conditions: 400 MHz, D₂O

¹H NMR spectrum consistent with chemical structure.



EPL-AA193 Batch 1

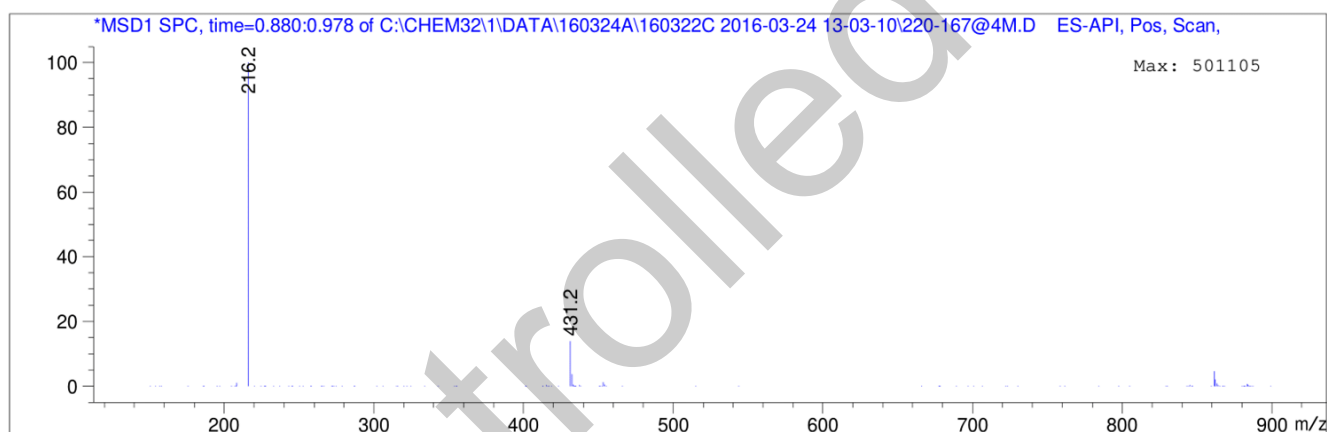
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Ib. Mass Spectrum

The mass spectrum of this material was analysed by Liquid Chromatography Mass Spectroscopy (LCMS) using in-house EM005.WI08.

Method: 5% to 100% ACN in water gradient (+0.1% formic acid)
Poroshell 120 EC-C18, 4.6 x 50 mm, 2.7 micron

Retention Time (MS)	MS Area	Mol. Weight or Ion
0.923	4866241	431.20 I 216.20 I
0.979	3362948	431.10 I 216.20 I
1.356	1774447	431.15 I 216.30 I
1.649	429189	431.20 I 216.20 I



Theoretical value: 431.2 [M+H]⁺.

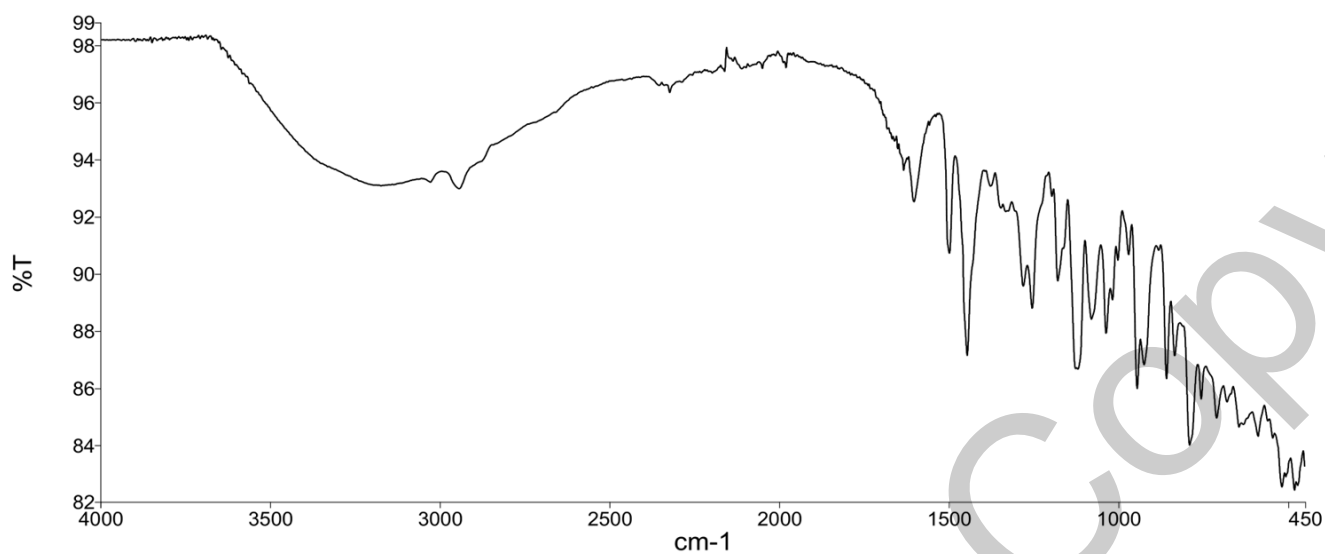
The signal of the Mass Spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.

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Ic. IR Spectrum

The infra-red spectrum of this material was analysed by Fourier-Transform Infra-red Spectroscopy (FTIR) using in-house EM005.WI09.



The interpretation of the signals of the Fourier Transform Infra-red Spectrum is consistent with the structural formula.

EPL-AA193 Batch 1

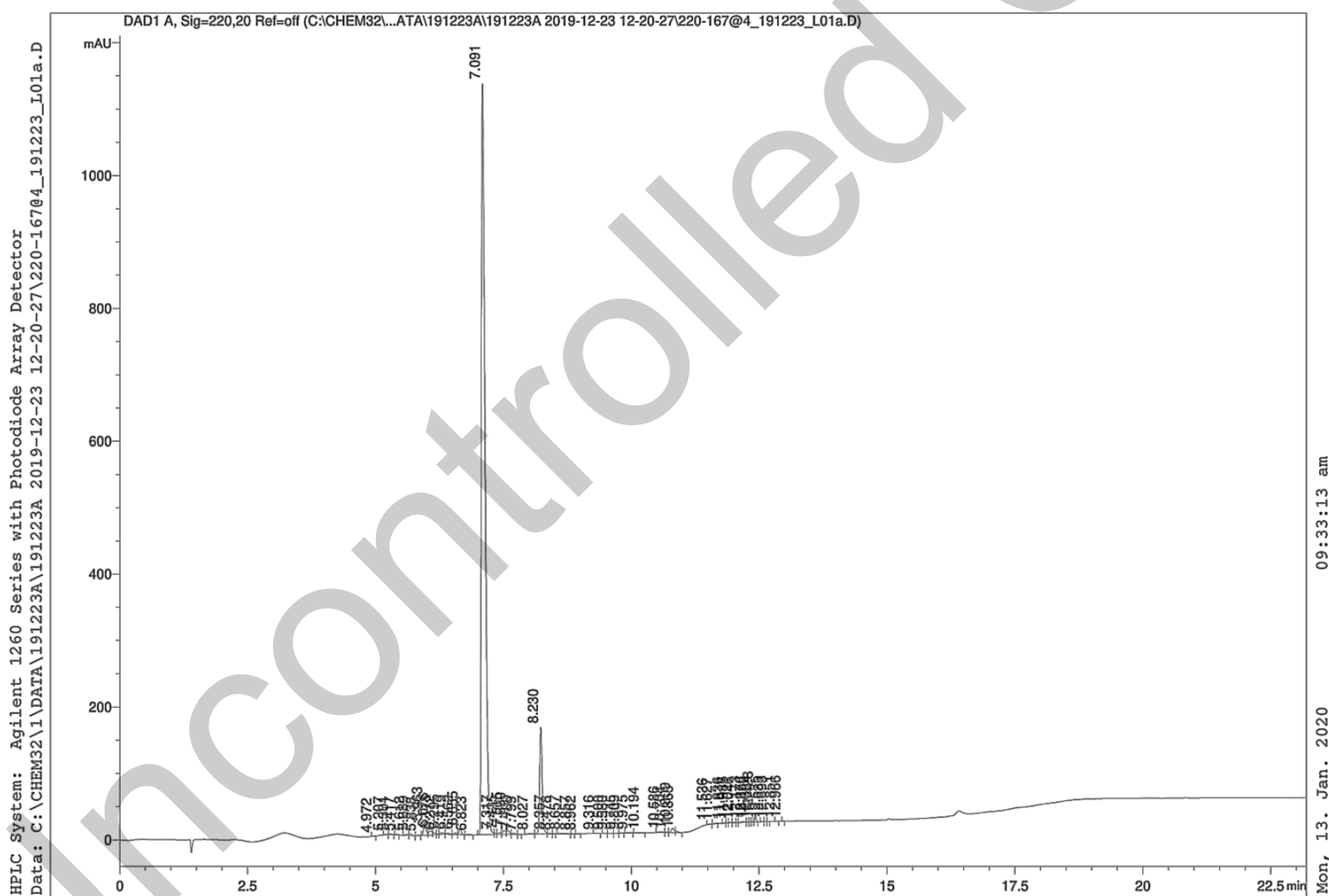
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II. Purity

The purity of this material was analysed by high performance liquid chromatography (HPLC) using in-house EM005.WI07.

HPLC Conditions:

Column	Conditions				Detector	Injector
Fortis H2o	25°C				DAD 220nm	Auto 2.0 µL 1.8 mg/mL in 100% water (NO MODIFIERS)
4.6 x 100mm	Time (min)	% Line A (Water + 0.1% (v/v) TFA)	% Line B (Acetonitrile + 0.1% (v/v) TFA)	Flow rate (mL/min)		
3 micron	0.00	98	2	1.0		
	9.00	80	20	1.0		
	16.50	5	95	1.0		
	21.50	5	95	1.0		
	22.50	98	2	1.0		
	28.50	98	2	1.0		



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Area Percent Report – Sorted by Signal

Peak Number	Retention Time (rounded)	Area	Area % (rounded)
1	4.97	0.33	0.01
2	5.21	0.63	0.01
3	5.30	1.52	0.02
4	5.42	0.48	0.01
5	5.61	6.43	0.10
6	5.69	9.21	0.14
7	5.84	3.72	0.06
8	5.96	55.06	0.85
9	6.08	27.65	0.43
10	6.12	11.40	0.18
11	6.21	3.75	0.06
12	6.29	12.53	0.19
13	6.42	8.81	0.14
14	6.56	10.46	0.16
15	6.66	28.27	0.44
16	6.82	4.20	0.07
17	7.09	5556.01	85.96
18	7.32	6.00	0.09
19	7.42	9.35	0.14
20	7.52	21.22	0.33
21	7.59	21.13	0.33
22	7.70	7.27	0.11
23	7.80	0.64	0.01
24	8.03	7.53	0.12
25	8.23	555.09	8.59
26	8.36	4.02	0.06
27	8.48	0.64	0.01
28	8.66	4.93	0.08
29	8.86	0.32	0.01
30	8.96	0.55	0.01
31	9.32	1.30	0.02
32	9.50	0.91	0.01
33	9.58	0.64	0.01
34	9.74	0.36	0.01
35	9.81	0.48	0.01

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36	9.97	1.13	0.02
37	10.19	2.33	0.04
38	10.59	6.05	0.09
39	10.70	2.41	0.04
40	10.81	26.42	0.41
41	10.86	6.19	0.10
42	11.54	1.74	0.03
43	11.63	0.58	0.01
44	11.84	0.90	0.01
45	11.88	0.87	0.01
46	11.93	3.55	0.05
47	12.02	1.94	0.03
48	12.05	0.84	0.01
49	12.17	5.53	0.09
50	12.28	0.80	0.01
51	12.31	0.48	0.01
52	12.35	0.88	0.01
53	12.38	1.83	0.03
54	12.43	14.46	0.22
55	12.58	0.59	0.01
56	12.63	0.40	0.01
57	12.69	0.20	0.00
58	12.85	0.25	0.00
59	12.97	0.26	0.00
Totals			100 (rounded)

For the calculation the system peaks were ignored. The content of the analyte was determined as a ratio of the peak area of the analyte and the cumulative areas of the purities, added up to 100%.

Results:

Average 94.6% (average of 10 duplicate analyses)

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III. Water Content

Method: Karl-Fischer titration using in-house EM005.WI04.

Results:

Average 13.7%

IV. Ash Content

Method: BP2016 Ash (Appendix XI J)

Result:

Contains <0.1% ash.

V. Residual Solvents

Method: ¹HNMR

Result:

No significant impurities detected by ¹H NMR analysis.

VI. Final Result

Chromatographic purity (HPLC)	94.6%
Water content	13.7%
Ash content	<0.1%
Residual solvents	<0.1%
Purity*	81.6%

This purity is assessed to be 81.6%.

Product Reviewed By:

Product Released By:

John Moursounidis, PhD
Head Reference Standards

Boon Tan
Quality Manager

Release Date: 17 January 2020

*NATA accreditation does not cover the performance of this service.

The calculation of the purity follows the formula:

$$\text{Purity(\%)} = \frac{((\text{Chromatographic purity[HPLC]}) \times (100 - (\text{water content} + \text{ash content} + \text{volatile contents})))}{100}$$

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