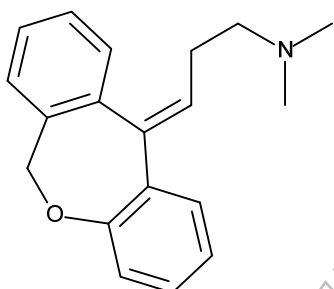




# Certificate of Analysis

## Reference Standard

Doxepin Hydrochloride



Molecular Formula: C<sub>19</sub>H<sub>21</sub>NO HCl  
Molecular Weight: 315.84  
CAS Number: 1229-29-4

Catalogue Number: MM0032.00  
Lot Number: 147967  
Long-term Storage: 2 to 8 °C, dark  
Appearance: white solid  
very hygroscopic  
Melting Point: 189 °C  
Assay 'as is': 99.9 %

Date of shipment: **2017-September-05**

This certificate is valid for two years from the date of shipment provided the substance is stored under the recommended conditions unopened in the original container.

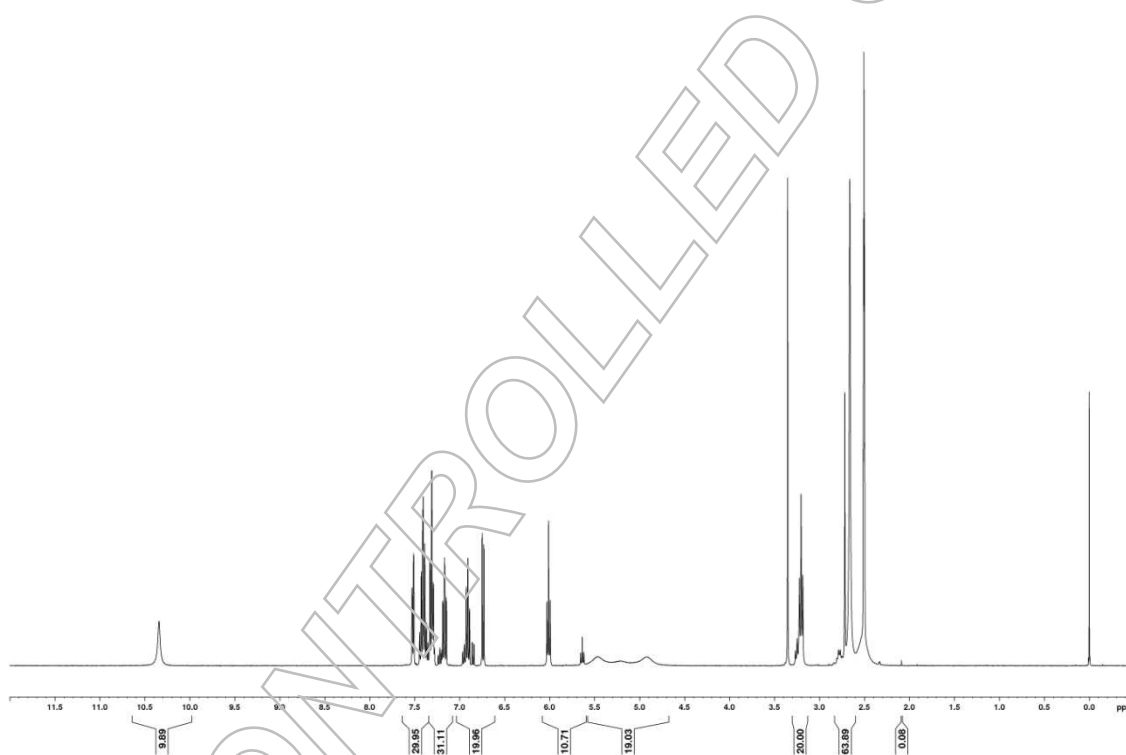


## I. Identity

The identity of the reference substance was established by following analyses.

### 1a. <sup>1</sup>H-NMR Spectrum

Conditions: 400 MHz, DMSO-d<sub>6</sub>

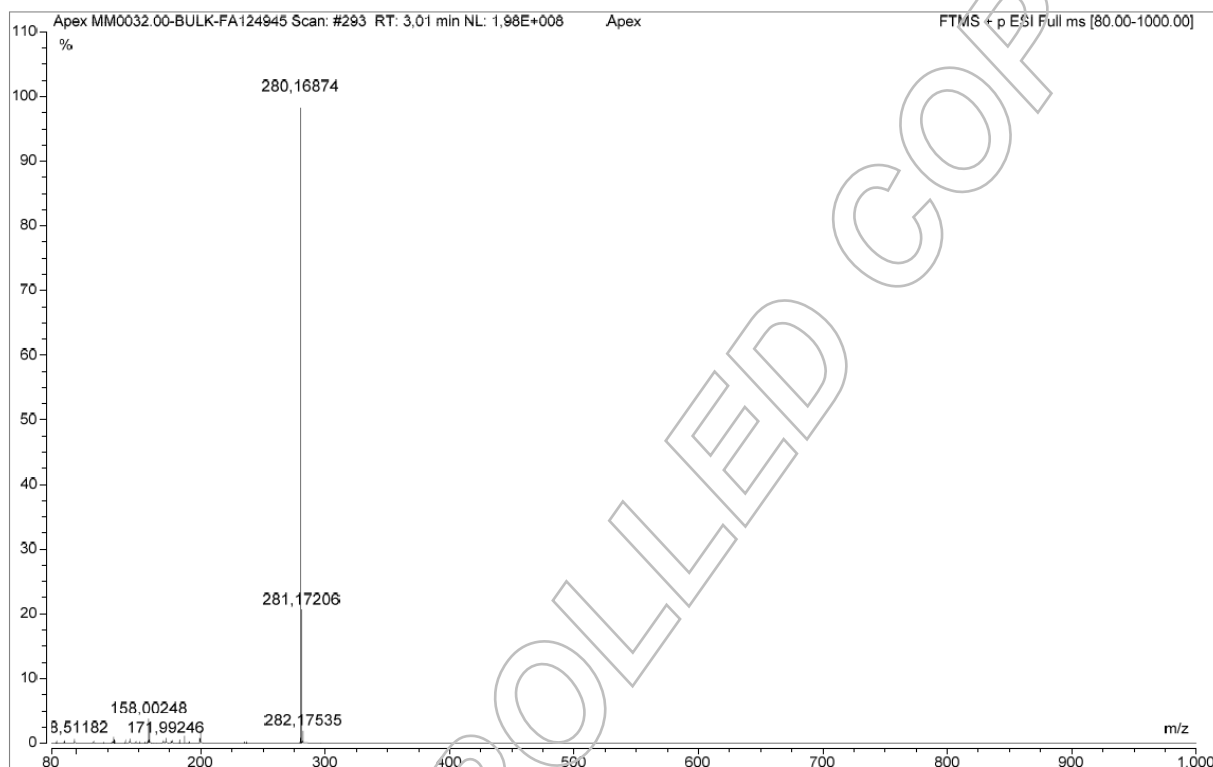


The structure is confirmed by the signals of the spectrum and their interpretation.



## Ib. Mass Spectrum

Method: 3.5 kV ESI+; capillary temperature: 269 °C



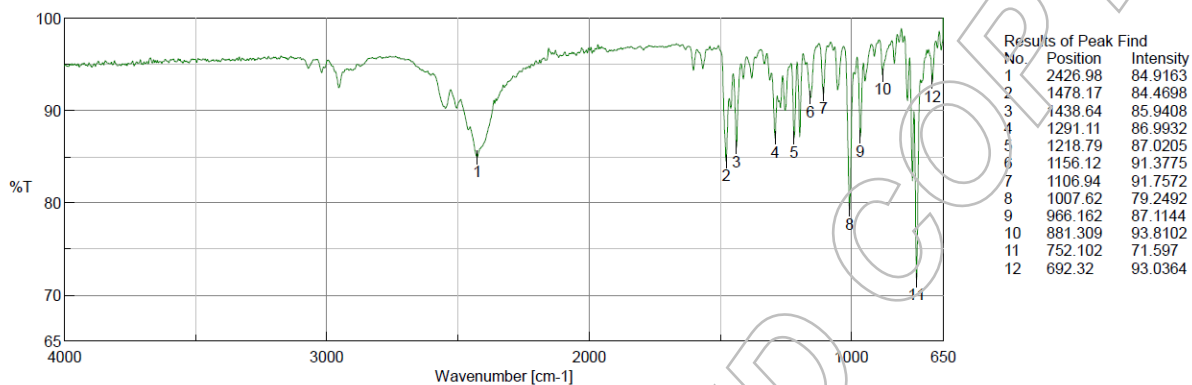
Theoretical value: 280.16959

The signal of the MS spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.



### Ic. IR Spectrum

Method: Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) Spectroscopy



The signals of the IR spectrum and their interpretation are consistent with the structural formula.

## II. Purity

### Ila. High Performance Liquid Chromatography (HPLC)

The purity of the reference substance was analysed by high performance liquid chromatography (HPLC).

#### HPLC Conditions:

##### Column:

LiChrospher  
60 RP-select B  
5 µm, 125 x 4 mm

##### Conditions:

1.0 ml/min, 40 °C  
mob. phase A: 30 g/l NaH<sub>2</sub>PO<sub>4</sub>, pH 2.5  
mob phase B: Methanol

##### Detector:

DAD

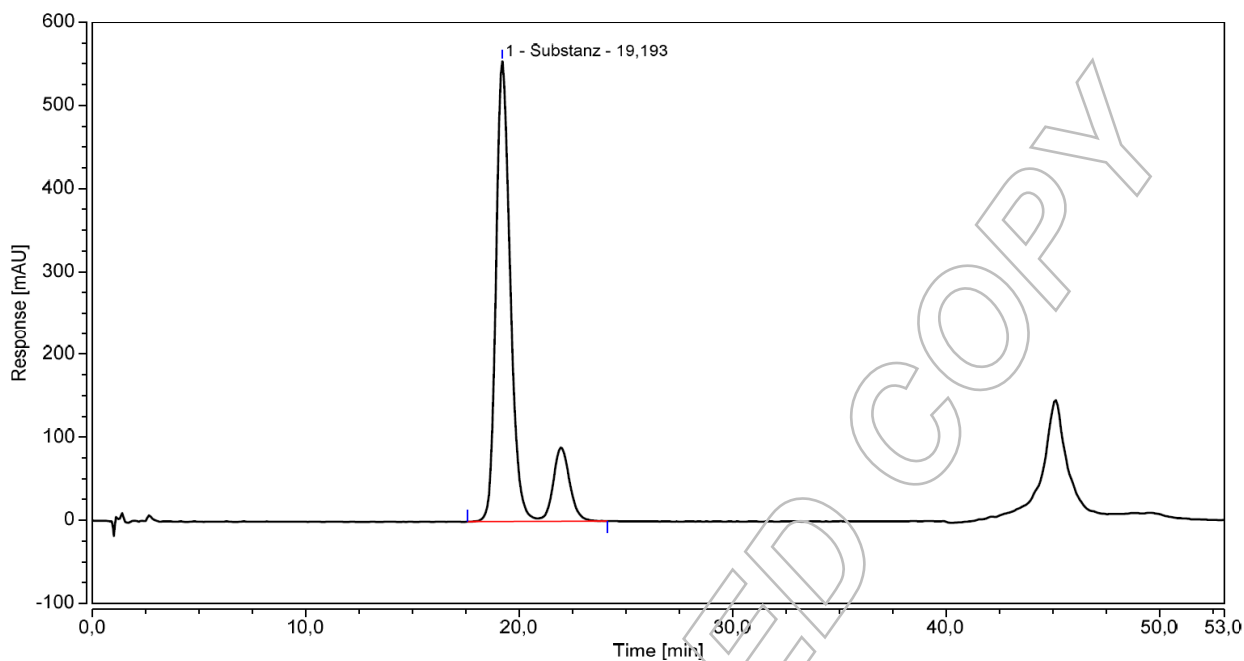
##### Injector:

Auto

215 nm

12 µl; 0.0762 mg/ml in  
Water/Acetonitrile 50/50 (v/v)

0-38 min	A/B		70/30
38-43 min	A/B	to	40/60
43-48 min	A/B	to	70/30
48-53 min	A/B		70/30 (v/v)



#### Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	19.193	506.946	100.00
Totals		506.946	100.00

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

#### Results:

Average 100 %  
Number of results n=3  
Standard deviation < 0.01 %

#### IIb. Water Content

Method: Karl Fischer titration

#### Results:

Average 0.06 %  
Number of results n=3  
Standard deviation 0.01 %



## IIc. Residual Solvents

Method: <sup>1</sup>H-NMR

No significant amounts of residual solvents were detected (< 0.05 %).

## III. Assay by Elementary Analysis (Carbon Titration)

Method: percentage carbon found in relation to percentage carbon as calculated for molecular formula

### Results:

Arithmetic mean (n=3) 100.14 % (mass fraction)

## IV. Final Result

Chromatographic purity (HPLC)	100 %
Water content	0.06 %
Residual solvents	No significant amounts of residual solvents were detected (< 0.05 %).
Assay (100 % method) <sup>1</sup>	99.94 %

The assay is assessed to be 99.9 % 'as is'

The assay 'as is' is equivalent to the assay based on the not anhydrous and not dried substance respectively.

Release Date:

Luckenwalde, 2017-07-14

Dr. Sabine Schröder  
Product Release

<sup>1</sup> The calculation of the 100 % method follows the formula:

$$\text{Assay (\%)} = (100 \% - \text{volatile contents}) * \frac{\text{Purity (\%)}}{100 \%}$$

Volatile contents are considered as absolute contributions, purity is considered as relative contribution.