PriMM™

LGC

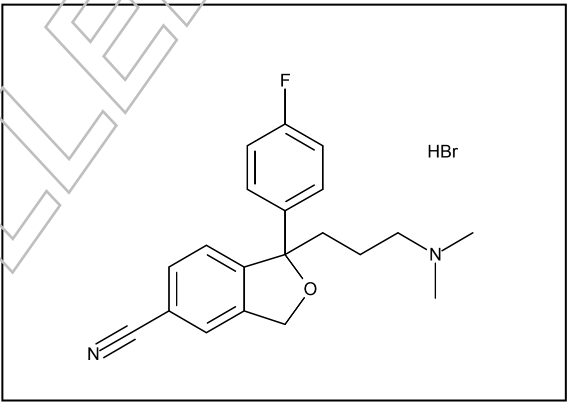
Certificate of analysis

Primary reference standard

Product name: Citalopram Hydrobromide

Catalogue number: P0242.00-B

Lot number: 110192



CAS number: 59729-32-7

Molecular formula: $C_{20}H_{21}FN_2O$ HBr

Molecular weight: 405.30

Appearance: white solid

Melting point (DSC): 186 °C

Assay[1] 'as is': **99.3 %**

Uncertainty[2] U: 0.4 %

Long-term storage: 2 to 8 °C, dark

Date of shipment: **2017-September-04**

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.

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[1] The value is based on the results of analytical techniques. Calibration and verification were carried out with standards traceable to SI-units. The value is expressed on an "as is" basis.
The identity is verified by data from international scientific literature.

[2] The uncertainty "U" is the expanded uncertainty estimated in accordance with the Guide to the Expression of Uncertainty in Measurement (GUM). It is corresponding to a level of confidence of about 95 %. Coverage factor *k* = 2.

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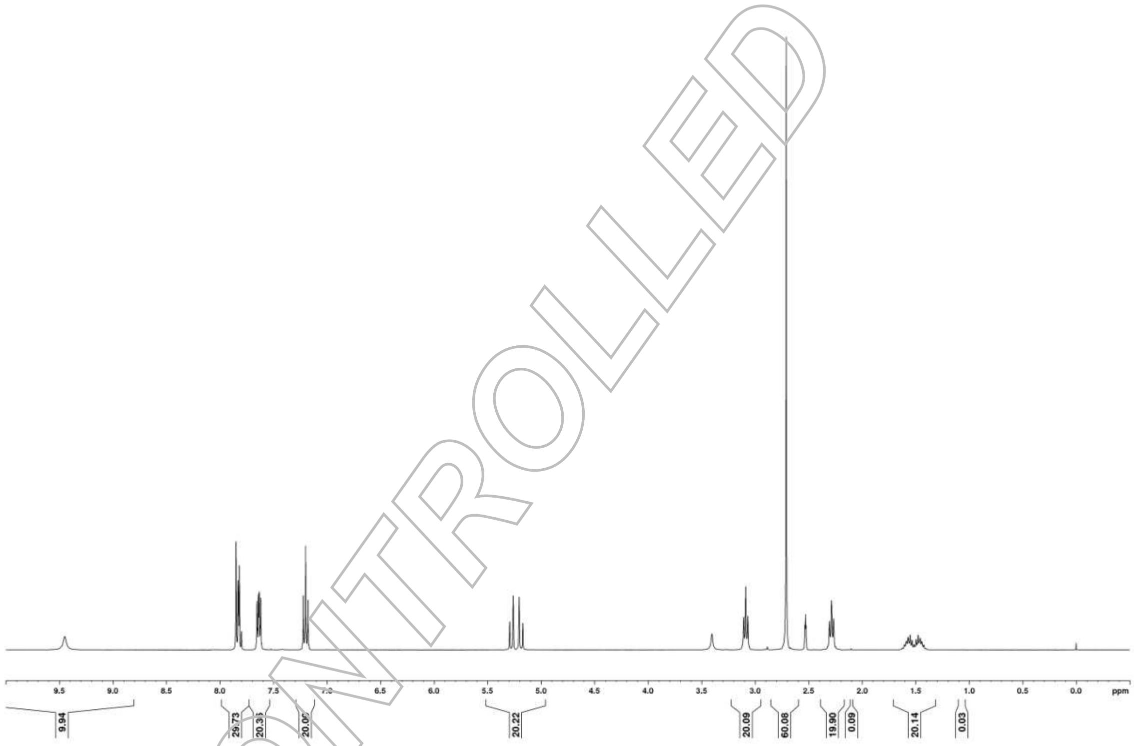
I. Identity

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

Ia. ^{1}H-NMR spectrum

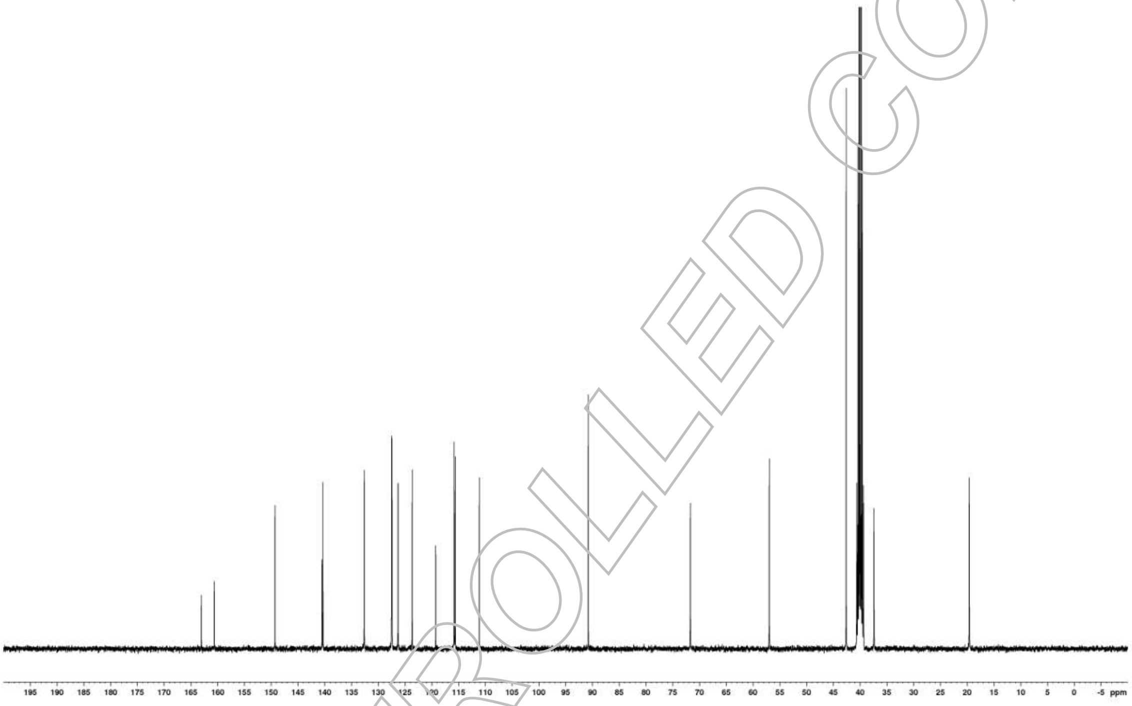
Conditions: 400 MHz, DMSO-d_6



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

Ib. ^{13}C-NMR spectrum

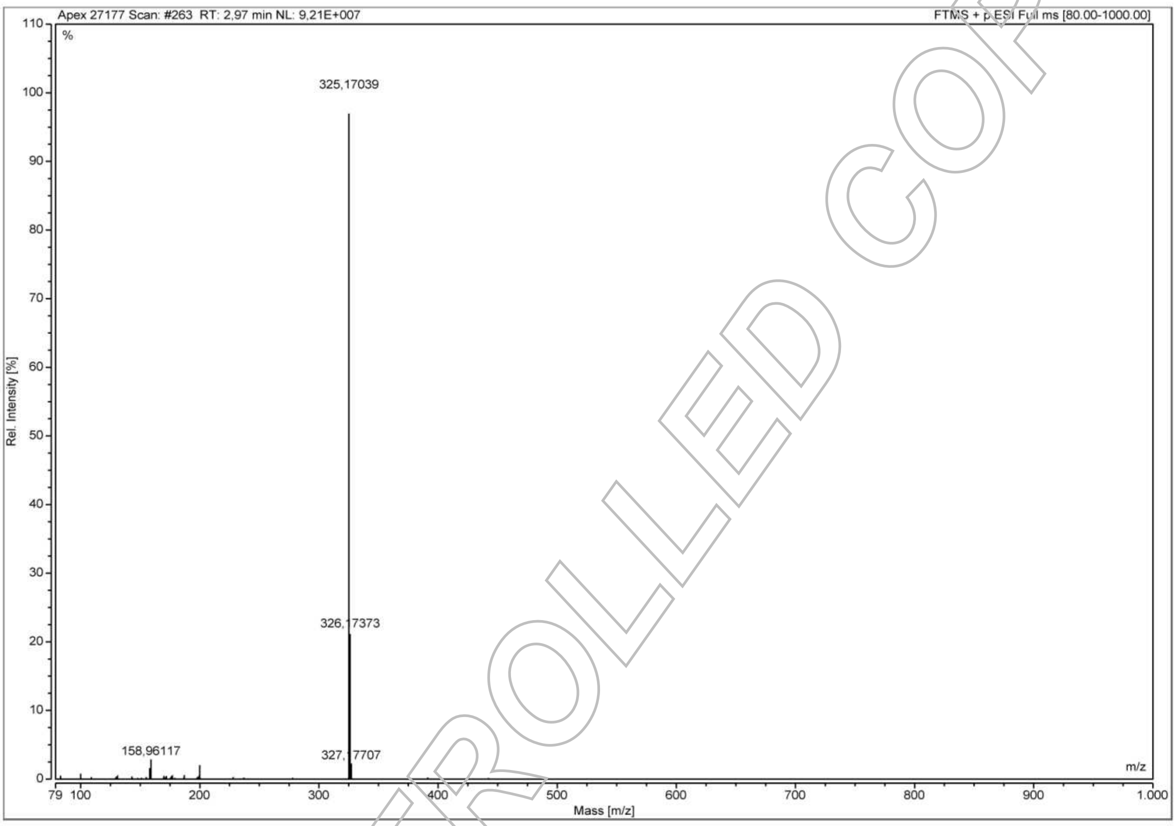
Conditions: 100 MHz, DMSO-d_6



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

Ic. Mass spectrum

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

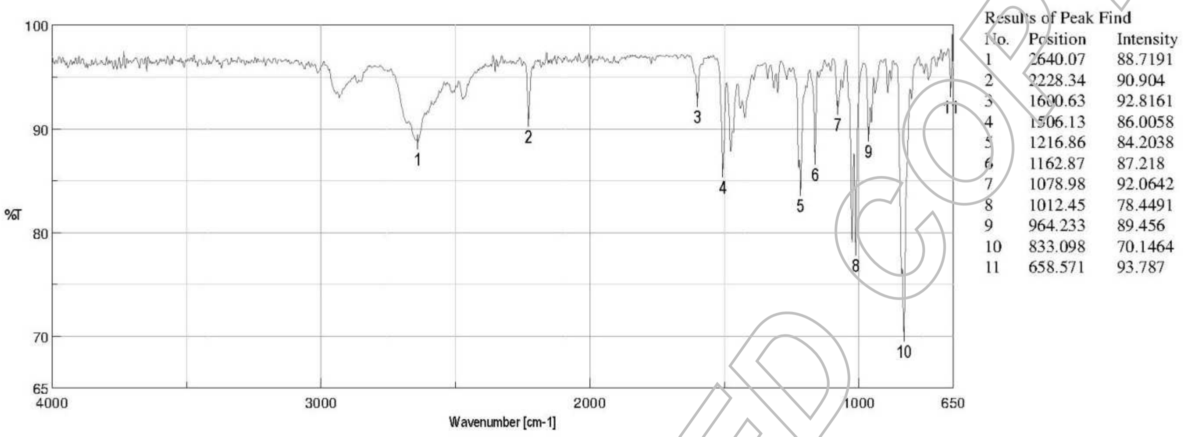


Theoretical value: 325.17107

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

Id. IR spectrum

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



Results of Peak Find

No.	Position	Intensity
1	2640.07	88.7191
2	2228.34	90.904
3	1600.63	92.8161
4	1506.13	86.0058
5	1216.86	84.2038
6	1162.87	87.218
7	1078.98	92.0642
8	1012.45	78.4491
9	964.233	89.456
10	833.098	70.1464
11	658.571	93.787

The signals of the IR spectrum and their interpretation are consistent with scientific literature.

II. Purity

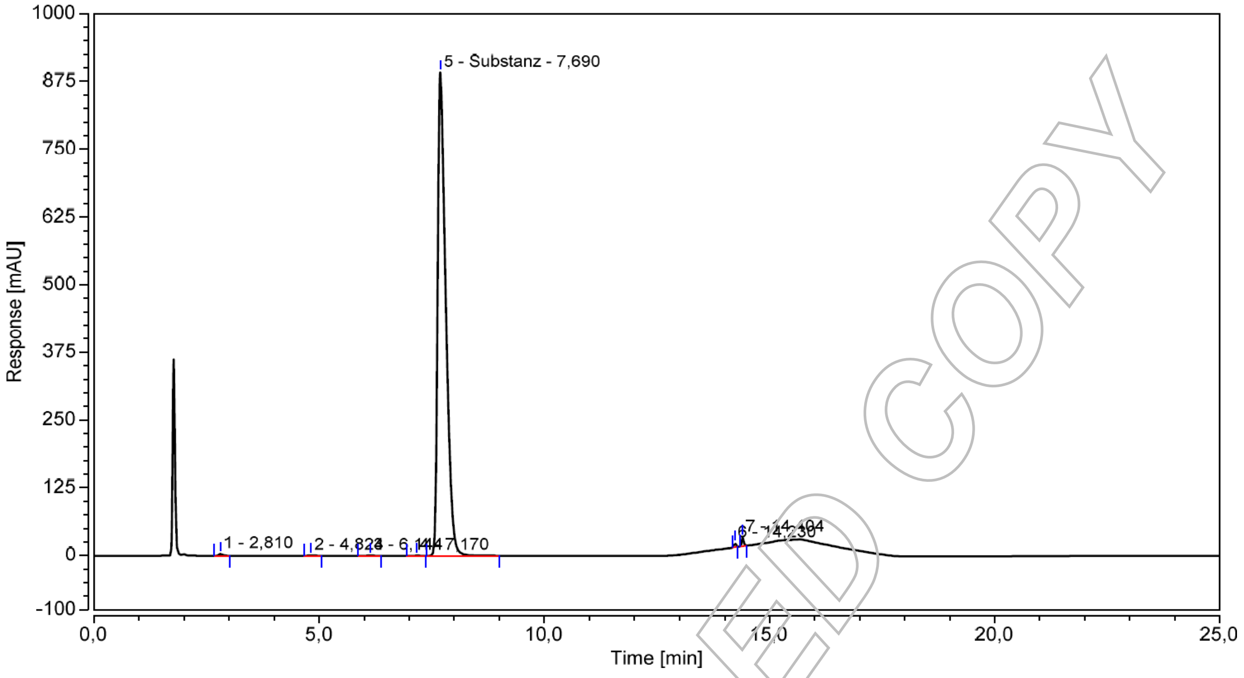
IIa. High performance liquid chromatography (HPLC)

The purity of the reference material was determined by high performance liquid chromatography (HPLC).

HPLC conditions*:

Column:	**Conditions:**	**Detector:**	**Injector:**
Hypersil Gold C18 5 µm, 150 x 4.6 mm	1.0 ml/min, 40 °C 0-10 min Water/Acetonitrile 72/28 10-13 min Water/Acetonitrile to 30/70 13-15 min Water/Acetonitrile to 72/28 15-25 min Water/Acetonitrile 72/28 (v/v); 0.1 % H_3PO_4	DAD 210 nm	Auto 4 µl; 0.1314 mg/ml in Water/Acetonitrile 50/50 (v/v)

*not accredited testing method



Area Percent Report - Sorted by Signal

Pk #	Retention time	Area	Area %
1	2.810	0.316	0.17
2	4.824	0.051	0.03
3	6.144	0.062	0.03
4	7.170	0.044	0.02
5	7.690	184.52	99.02
6	14.230	0.414	0.22
7	14.404	0.941	0.50
Totals		186.342	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 impurities, added up to 100 %.

Results:

Average	99.02 %
Number of results	n=6
Standard deviation	0.02 %

IIb. Water content

Method: Karl Fischer titration

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

IIc. Residual solvents

Method: ^{1}H-NMR (not accredited testing method)

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

IId. Inorganic residues

Method: Sulphated ash, EP 8.7 (2.4.14) (not accredited testing method)

According to the available data, the presence of inorganic impurities in the reference substance others than those detectable by sulphated ash is highly unlikely. The test for sulphated ash (Method: EP 8.7, chapter 2.4.14) resulted in values below the set specification of 0.1 %. Therefore, no assay correction was performed for inorganic impurities.

III. Assay by elementary analysis (carbon titration)

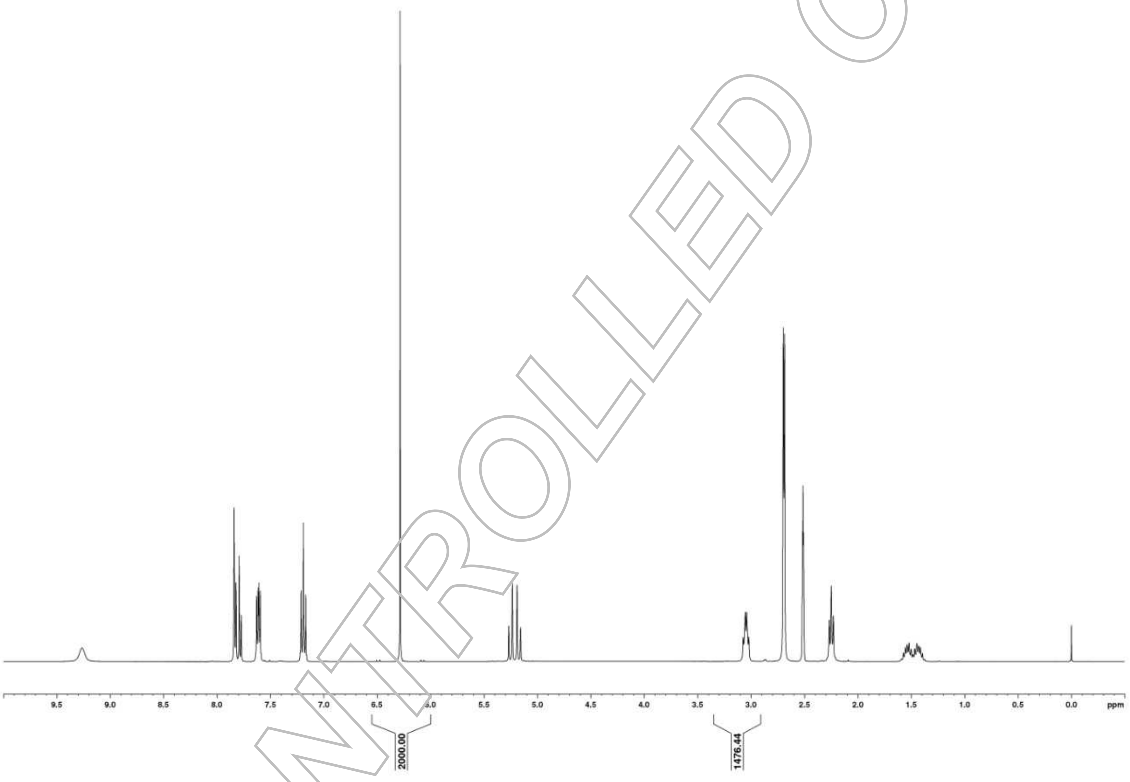
Method: percentage carbon found in relation to percentage carbon as calculated for molecular formula

Results:

Average	99.89 %
Number of results	n=3
Uncertainty U (expanded)	0.30 %

IV. Assay by quantitative NMR spectroscopy

The assay of the reference substance was established by quantitative NMR spectroscopy using DMSO-d_6 as the solvent and with Maleic acid (certified reference material, signal 6.00 – 6.55 ppm, 2 H) as internal standard.



Results:

Average	99.26 %
Number of results	n=6
Uncertainty U (expanded)	0.43 %

V. Final result

100 % method (HPLC)*	99.02 %
Quantitative NMR spectroscopy	99.26 %

*see formula in chapter “Further Information”

Assay:

Quantitative NMR spectroscopy	99.26 %

The assay is assessed to be 99.3 % ‘as is’

The assay 'as is' is equivalent to the assay based on the not anhydrous and not dried substance respectively. It is determined by quantitative NMR spectroscopy and its expanded uncertainty (*k* = 2) is 0.4 %.
The assay is verified by the 100 % method (HPLC): 99.0 % which is inside our acceptance criteria (less than 1.0 % difference to assay assigning technique).

VI. Stability and homogeneity

Accelerated stability studies indicate no significant instability. The given validity period is based on this data. Additionally further stability testing and historical data over the range of several years are considered.
Homogeneity assured by qualified process of preparation, verified by homogeneity testing.

Due to the homogeneity studies the minimum amount of sample to be used is 10 mg.

VII. Further information

General

For laboratory use only. Not suitable for human or animal consumption.

This material conforms to the characteristics of a primary standard as described within ISO Guide 30 (Terms and definitions used in connection with reference materials).
The values quoted in this certificate are LGC’s best estimate of the true values within the stated uncertainties and based on the techniques described in this certificate of analysis.

The production of this reference material was realized taking into account the principles of ISO Guide 34.

Intended use

Use for identification and quantification.

Handling of the RM

Before usage of the RM, it should be allowed to warm to room temperature. No drying required, as the assigned value is already corrected for the content of water and other volatile materials.

Assay and uncertainty

The identity and the assay are assessed by an ISO/IEC 17025 accredited testing method.

Uncertainty of the assay is expressed as an expanded uncertainty in accordance with ISO/IEC 17025 at the about 95 % level of confidence.

For quantitative applications use the assay as a calculation value on the as is basis. The uncertainty of the assay can be used for estimation/calculation of your own measurement uncertainty.

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.

Quality control assessment

The product quality is controlled by regularly performed quality control tests (retests).

Release date:
Luckenwalde, 2016-10-14

Dr. Sabine Schröder
Product Release

Revision	Date	Reason for Revision
00	2016-10-14	Release of the Certificate of Analysis – initial version
01	2017-08-03	Validity period extended