

Certificate of Analysis

LGC Quality

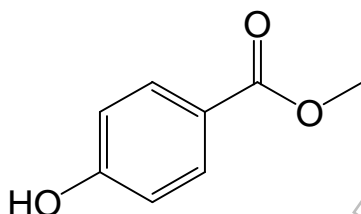
ISO Guide 34:2009
DAkKS D-RM-14176-01-00

ISO/IEC 17025:2005
DAkKS D-PL-14176-01-00

ISO 9001:2008
DQS 102448 QM08

Primary Reference Standard

Methyl Parahydroxybenzoate



Molecular Formula: C₈H₈O₃
Molecular Weight: 152.15
CAS Number: [99-76-3]

Catalogue Number: LGCQUANT0431.00

Lot Number: 11045

Long-term Storage: 15 to 25 °C, dark

Appearance: white solid

Melting Point: 127 °C

Assay¹ 'as is': 99.95 %

Uncertainty² U: 0.4 %

Date of shipment: **2014-May-26**

This certificate is valid for one year from the date of shipment provided the substance is stored under the recommended conditions.

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 $k = 2$.

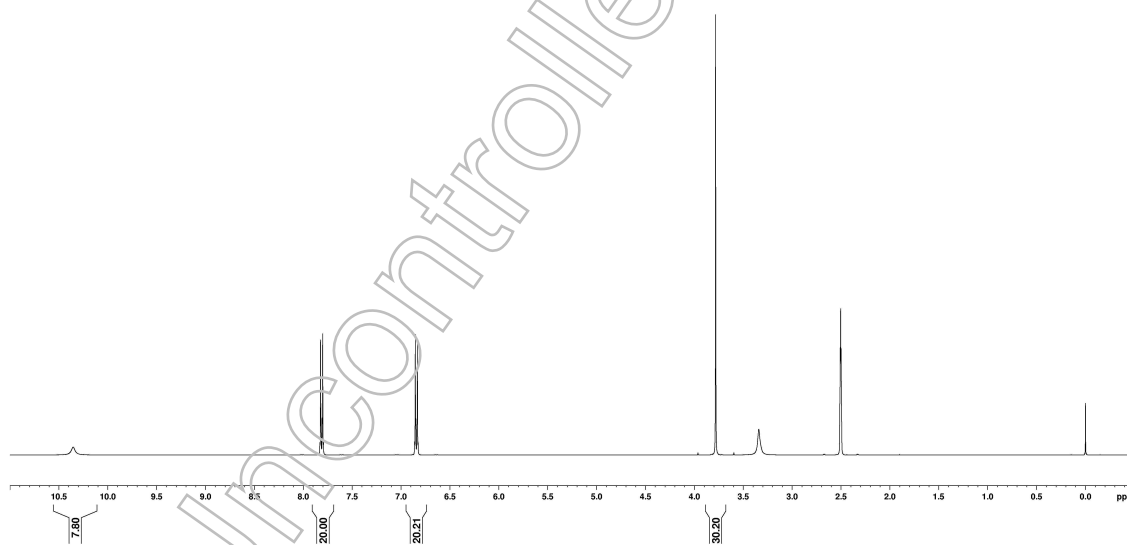
I. Identity

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

Ia. ¹H-NMR Spectrum

Conditions: 400 MHz, DMSO-d₆

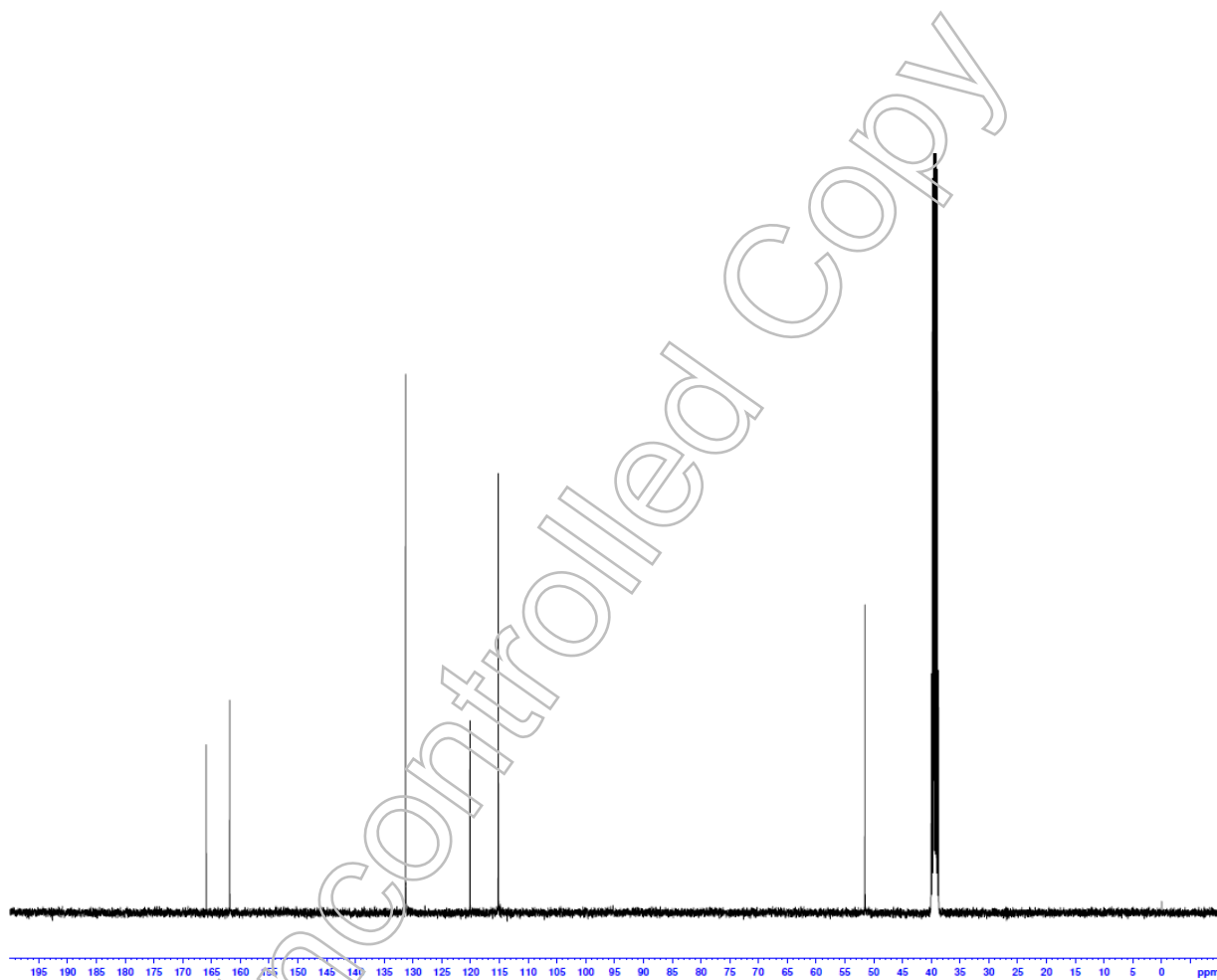
The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Methyl Parahydroxybenzoate CRS, M1650000, Batch 3.0, Id01GDT4.



Ib. ¹³C-NMR Spectrum

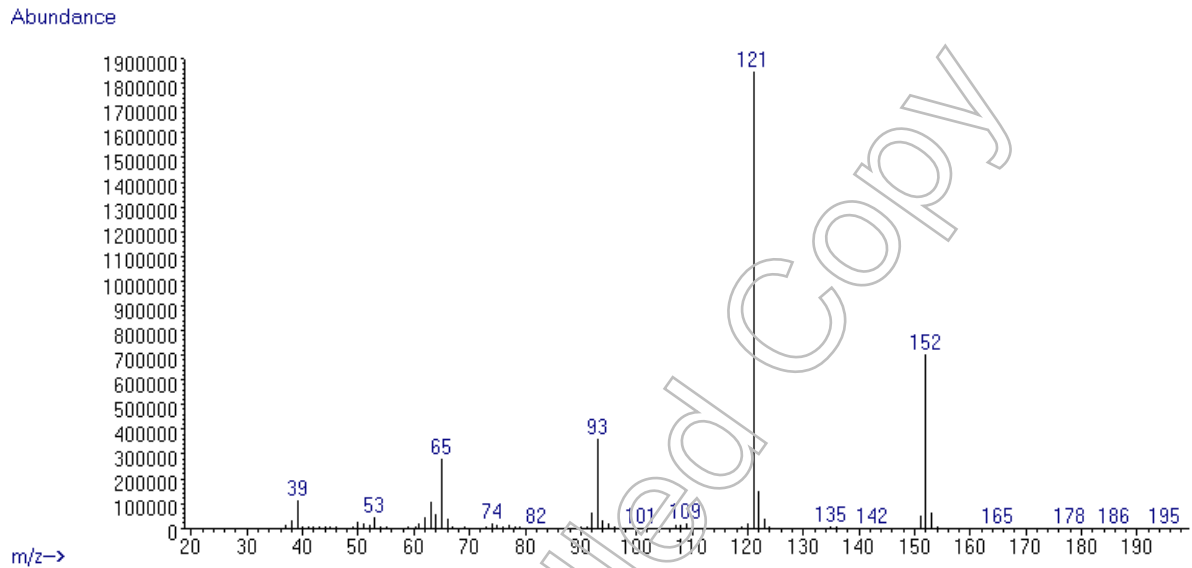
Conditions: 100 MHz, DMSO-d₆

The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Methyl Parahydroxybenzoate CRS, M1650000, Batch 3.0, Id01GDT4.



Ic. Mass Spectrum

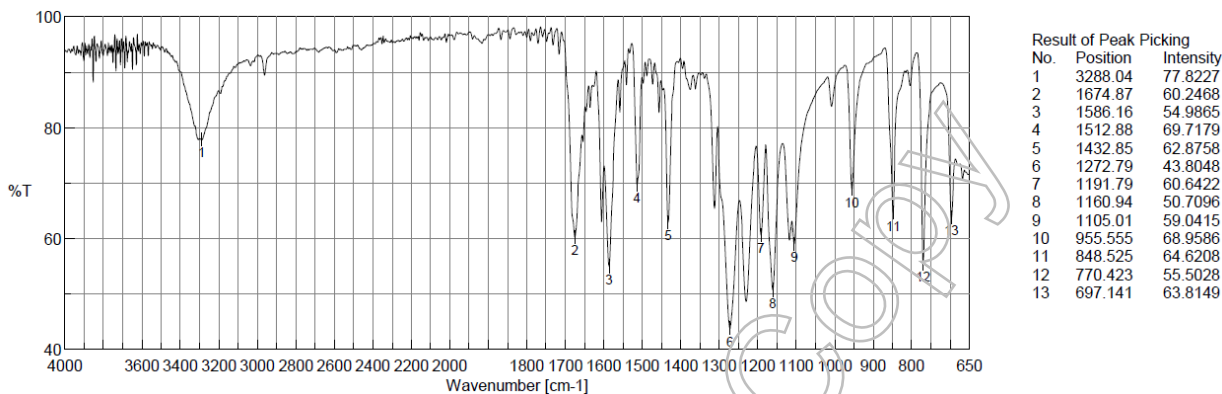
Method: EI, 70eV, detector temperature: 280 °C



The signals of the MS spectrum and their interpretation are consistent with the spectrum of EP reference substance Methyl Parahydroxybenzoate CRS, M1650000, Batch 3.0, Id01GDT4.

Id. 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 spectrum of EP reference substance Methyl Parahydroxybenzoate CRS, M1650000, Batch 3.0, Id01GDT4.

le. Melting Point

Method: Capillary Method

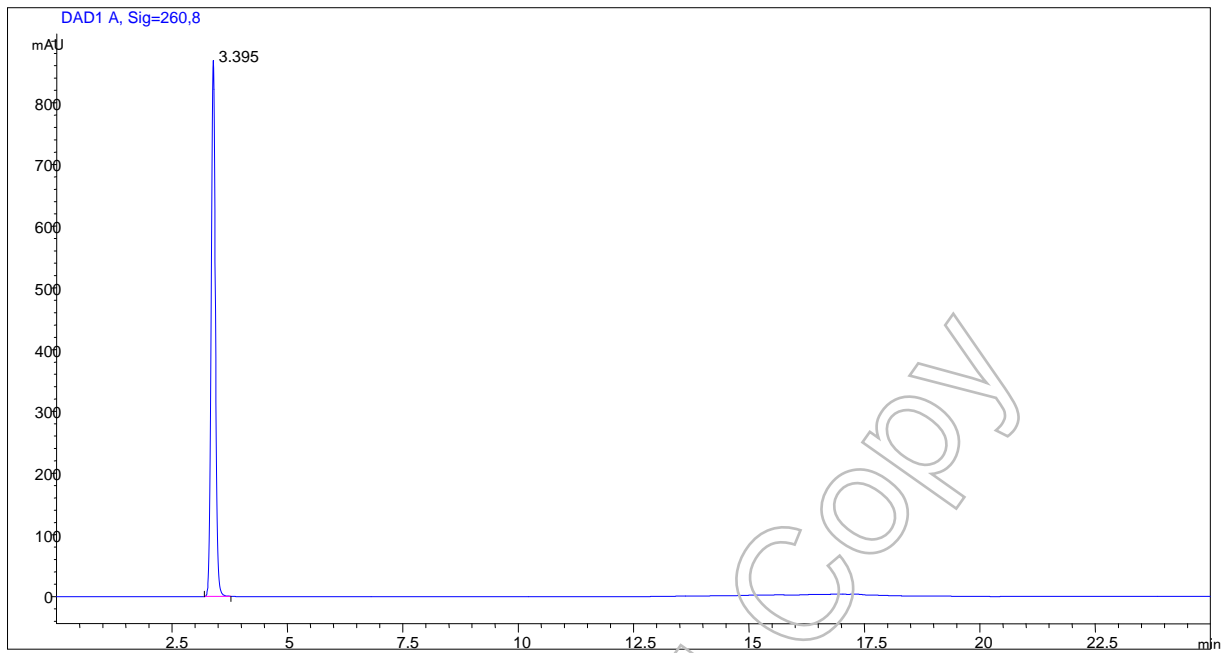
Arithmetic mean (n=3): 127 °C

II. Purity

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

HPLC Conditions:

Column:	Conditions:	Detector:	Injector:
RP 60 Select B	1.0 ml/min, 40 °C	DAD	Auto
5 µm, 125 x 4 mm	0 – 10 min Water/Acetonitrile 70/30	260 nm	3 µl; 0.05734 mg/ml in
	10 – 15 min Water/Acetonitrile to 30/70		Water/Acetonitrile 75/25 (v/v)
	15 – 20 min Water/Acetonitrile to 70/30		
	20 – 25 min Water/Acetonitrile 70/30 (v/v);		
	0.1 % H ₃ PO ₄		



Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	3.39	5509.75	100.00
Totals		5509.75	100.00

For the calculation the system peaks were ignored. The content of the analyte was determined as the 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=6
Standard deviation < 0.01 %



III. Water Content

Method: Karl Fischer titration

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

IV. Residual Solvents

Method: ¹H-NMR (not yet accredited testing method)

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

V. Sulphated Ash

Method: EP 6.8 (2.4.14)

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 6.8, chapter 2.4.14) resulted in values below the set specification of 0.1 %. Therefore, no assay correction was performed for inorganic impurities.

VI. Assay by comparison with EP Reference standard (HPLC)

Declared content of the EP-Standard (Batch 3.0, Id01GDT4): 100 %

HPLC Conditions:

Column:	Conditions:	Detector:	Injector:
RP 60 Select B	1.0 ml/min, 40 °C	DAD	Auto
5 µm, 125 x 4 mm	0 – 10 min Water/Acetonitrile 70/30 10 – 15 min Water/Acetonitrile to 30/70 15 – 20 min Water/Acetonitrile to 70/30 20 – 25 min Water/Acetonitrile 70/30 (v/v); 0.1 % H ₃ PO ₄	260 nm	3 µl; 0.05734 mg/ml in Water/Acetonitrile 75/25 (v/v)

Results from the analysis:

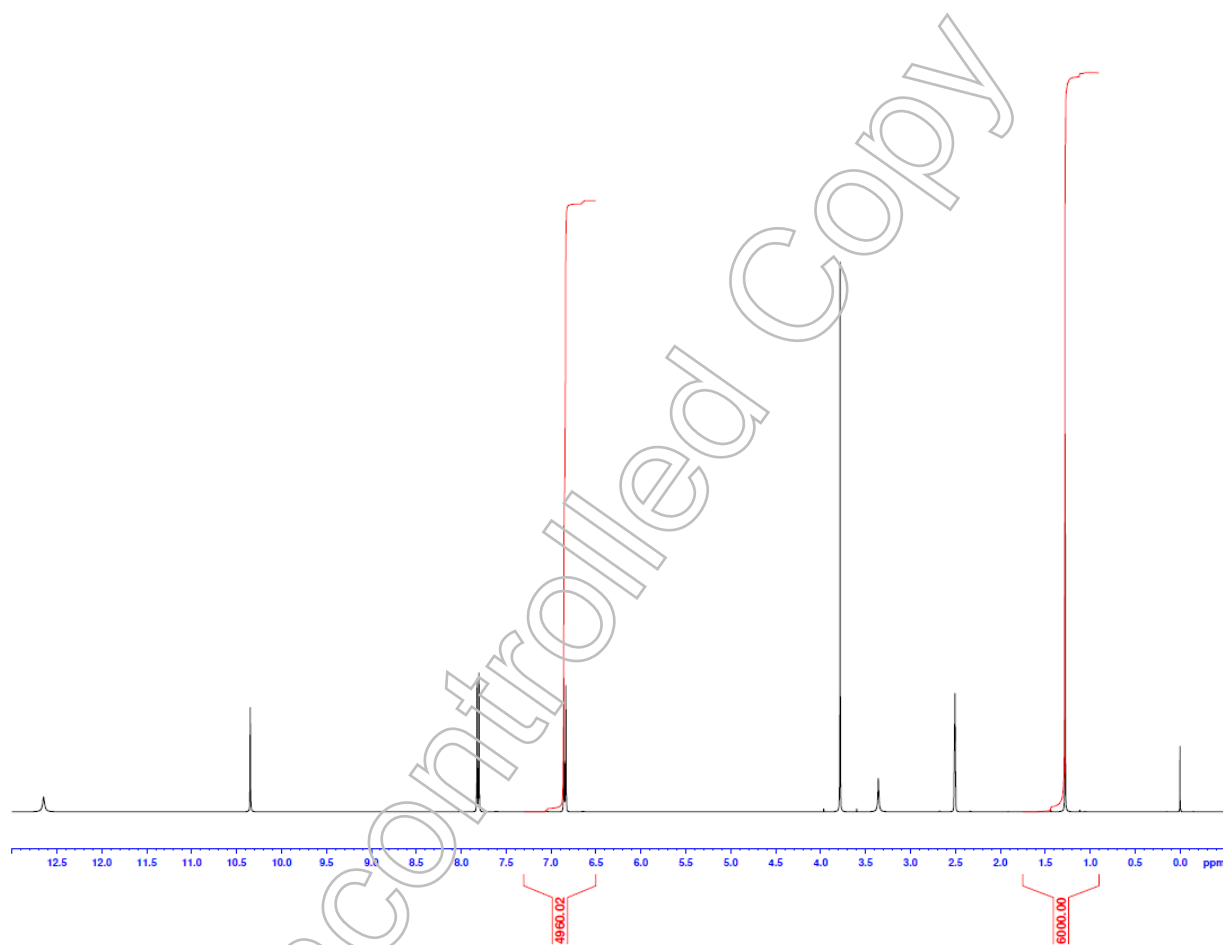
CRS	Area/conc	Sample	Area/conc
1	95989.64	1	95966.55
2	95956.23	2	96579.94
3	96218.89	3	96070.57
4	96180.39	4	96182.85
5	96117.70	5	95949.15
6	96239.68	6	96316.55
mean	96117.09	mean	96177.60
rsd	0.12	rsd	0.25

Multiple analysis runs based on multiple weighings were performed and the declared content of the EP reference substance was taken into consideration to assign an assay value to the secondary standard.

Result: 100.06 %

VII. Assay by quantitative NMR spectroscopy

The assay of the reference substance was established by quantitative NMR spectroscopy using DMSO-d₆ as the solvent and with Dimethylmalonic acid (certified reference material, signal 0.90 – 1.75 ppm, 6 H) as internal standard.



Results:

Average	99.95 %
Number of results	n=9
Uncertainty U (expanded)	0.42 %

VIII. Final Result

Chromatographic purity (HPLC)	100 %
Water content	n. d. (not detected)
Residual solvents	n. d. (not detected)
Sulphated ash	n. d. (not detected)

Assay:

Comparison with EP reference standard	100.06 %
Quantitative NMR spectroscopy	99.95 %

The assay is assessed to be 99.95 % '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): 100 % which is inside the expanded uncertainty of the assay by quantitative NMR spectroscopy.

IX. Stability and Homogeneity

Accelerated stability studies indicate no significant instability. The given validity period is based on this data. This is backed up by additional stability testing and historical data over the range of several years. 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.

X. 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.



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 reference material, it should be allowed to warm to room temperature.

Assay and uncertainty

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

The calculation of the 100 % method (HPLC) follows the formula:

$$\text{Assay (\%)} = (100 \% - \text{KF} - \text{RES}) \quad * \quad \frac{\text{Purity HPLC (\%)}}{100 \%}$$

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

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.

Quality Control Assessment

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

Release Date: 2013-06-12

LGC GmbH



Dr. Sabine Schröder

Product Release



Excellence through measurement

Revision	Date	Reason for Revision
00	2013-06-12	Release of the Lot – initial version
01	2013-10-29	Accreditation Number added

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