Primary standards

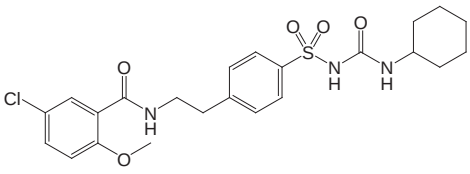
Crescent
Chemical Company

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

Glibenclamide



Catalogue Number:	LGCQUANT0008.00
Lot Number:	25894
Long-term Storage:	15 to 25 °C, dark
Appearance:	white solid
Melting Point:	172 °C
Assay[1] 'as is':	99.7 %
Uncertainty[2] U:	0.4 %

Molecular Formula:	$C_{23}H_{28}ClN_3O_5S$
Molecular Weight:	494.00
CAS Number:	[10238-21-8]

Date of shipment:

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.

LGC GmbH, Im Biotechnologiepark, TGZ II, D-14943 Luckenwalde, Germany
10 pages

LGC Standards
Excellence through measurement

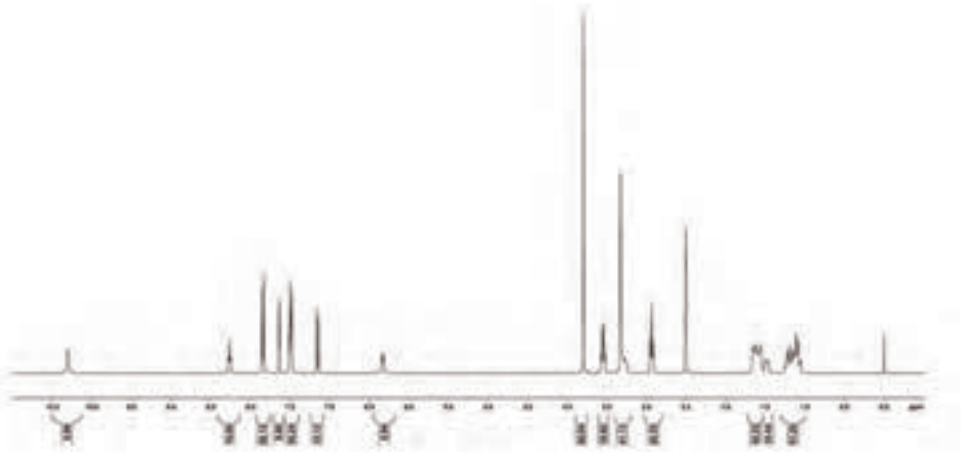
I. Identity

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

Ia. ^{1}H-NMR Spectrum

Conditions: 400 MHz, DMSO-d_6

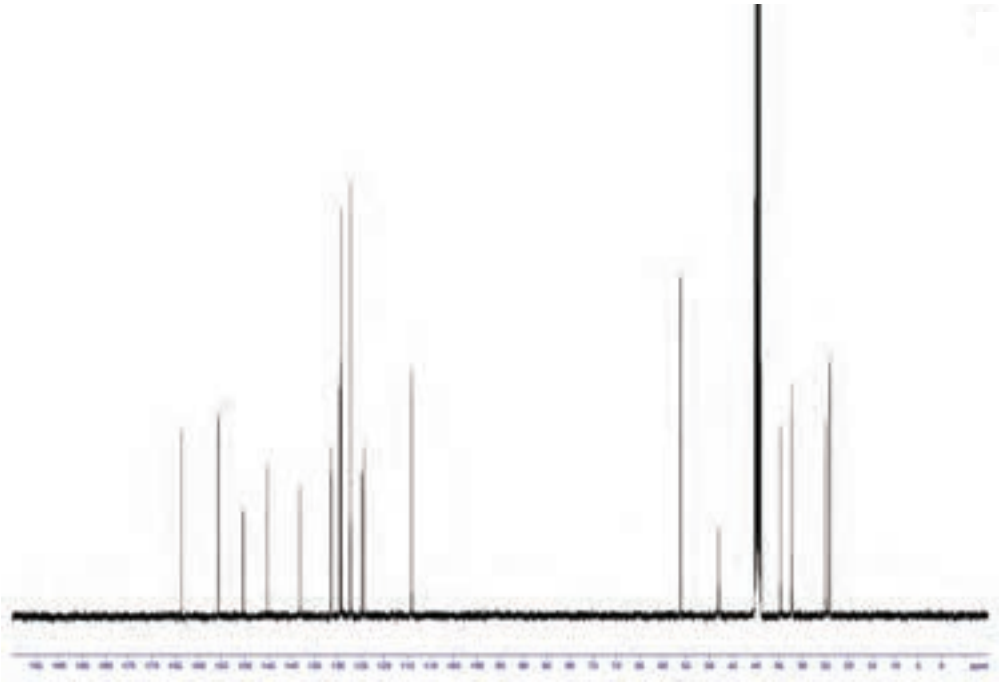
The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Glibenclamide CRS, G0325000, Batch 3.0, Id00DQP3.



Ib. ^{13}C-NMR Spectrum

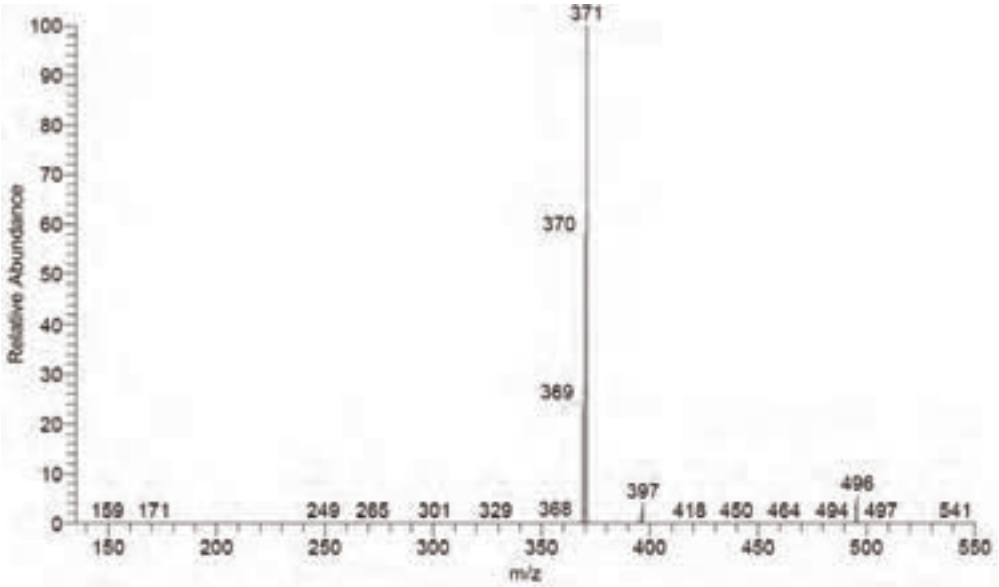
Conditions: 100 MHz, DMSO-d_6

The signals of the NMR spectrum and their interpretation are consistent with the spectrum of EP reference substance Glibenclamide CRS, G0325000, Batch 3.0, Id00DQP3.



Ic. Mass Spectrum

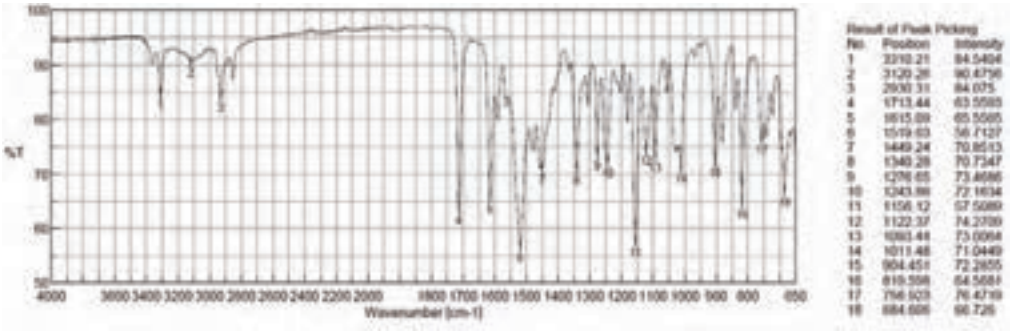
Method: 4.5 kV ESI; vaporization temperature: 200 °C, direct inlet



The signals of the MS spectrum and their interpretation are consistent with the spectrum of EP reference substance Glibenclamide CRS, G0325000, Batch 3.0, Id00DQP3.

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 Glibenclamide CRS, G0325000, Batch 3.0, Id00DQP3.

Ie. Melting Point

Method: Capillary Method

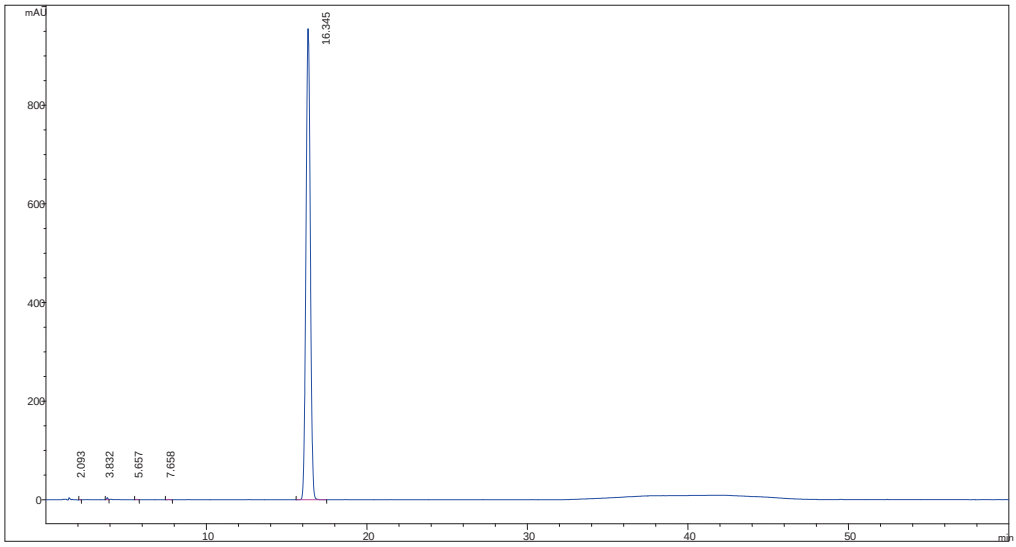
Arithmetic mean (n=3): 172 °C

II. Purity

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

HPLC Conditions:

Column:	**Conditions:**	**Detector:**	**Injector:**
Pro C 18 RS	1.0 ml/min, 40 °C	DAD	Auto
5 µm, 150 x 4.6 mm	0 – 30 min Water/Acetonitrile 55/45 30 – 35 min Water/Acetonitrile to 30/70 35 – 40 min Water/Acetonitrile 30/70 40 – 45 min Water/Acetonitrile to 55/45 45 – 60 min Water/Acetonitrile 55/45 (v/v); 0.1 % H_3PO_4	230 nm	5 µl; 0.19764 mg/ml in Methanol



Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	2.09	0.51	0.00
2	3.83	23.83	0.13
3	5.66	5.40	0.03
4	7.66	5.90	0.03
5	16.34	18008.72	99.80
Totals		18044.35	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	99.80 %
Number of results	n=6
Standard deviation	0.01 %

III. Loss on Drying

Conditions: 105 °C for 4 h, EP 7.6 (2.2.32)

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

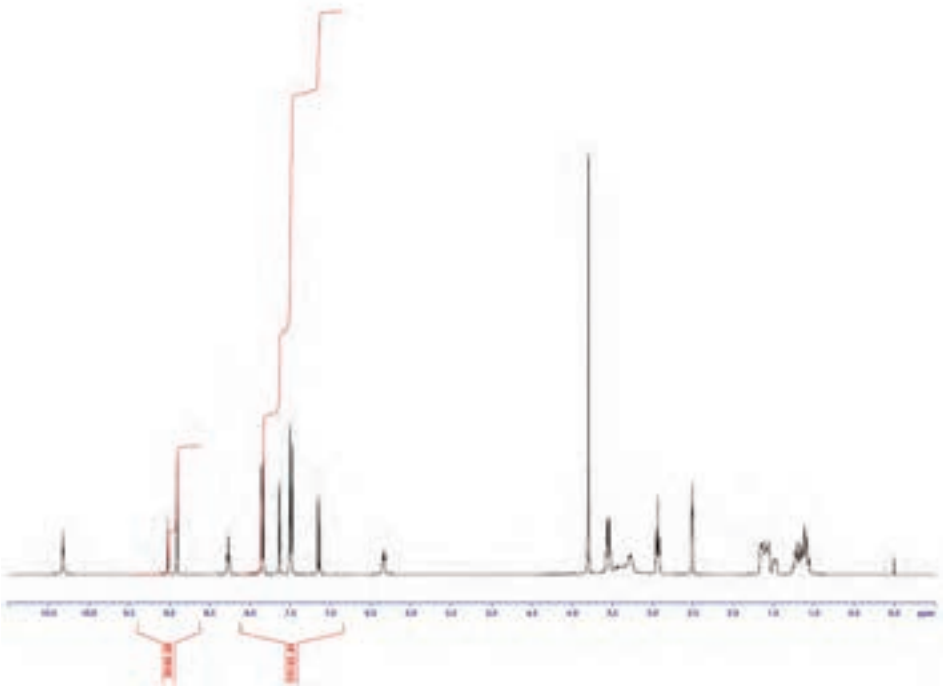
IV. Sulphated Ash

Method: EP 7.6 (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 7.6, chapter 2.4.14) resulted in values below the set specification of 0.1 %. Therefore, no assay correction was performed for inorganic impurities.

V. 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 3,5-Dinitrobenzoic acid (certified reference material, signal 8.62 – 9.40 ppm, 3 H) as internal standard.



Results:

Average	99.67 %
Number of results	n=6
Uncertainty U (expanded)	0.40 %

VI. Final Result

Chromatographic purity (HPLC)	99.80 %
Loss on drying	n. d. (not detected)
Sulphated ash	n. d. (not detected)

Assay:

Quantitative NMR spectroscopy	99.67 %

The assay is assessed to be 99.7 % ‘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): 99.8 % which is inside the expanded uncertainty of the assay by quantitative NMR spectroscopy.

VII. 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.

VIII. 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:

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

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.

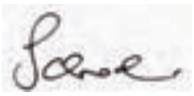
For quantitative applications use the assay as a calculation value on the as is basis. The uncertainty of the assay can be used for estimation/calculation of your own measurement uncertainty.

Quality Control Assessment

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

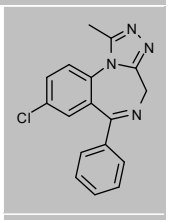
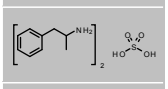
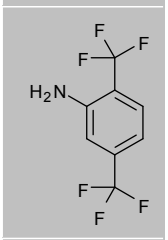
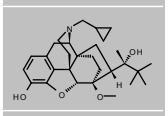
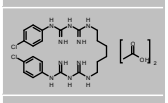
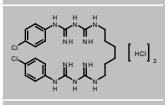
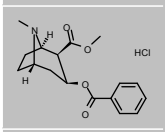
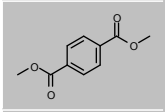
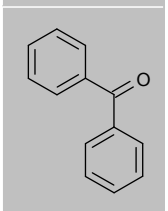
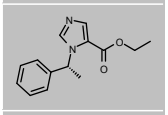
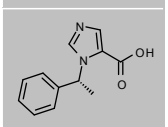
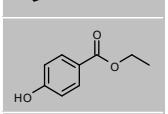
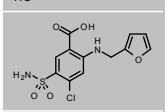
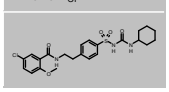
Release Date: 2013-04-26

LGC GmbH

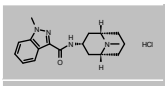
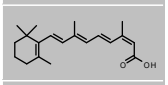
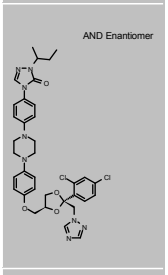
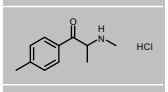
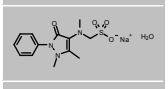
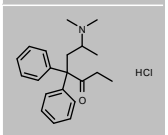
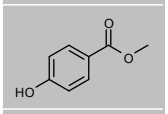
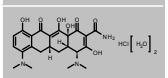
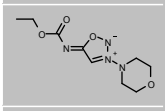
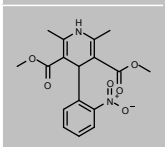
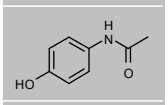
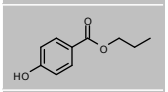
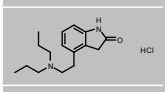
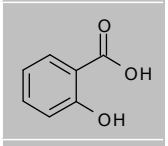
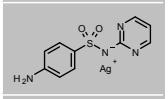
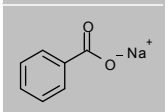
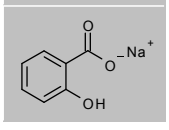


Dr. Sabine Schröder
Product Release

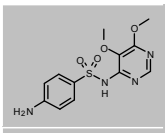
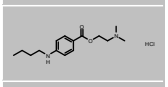
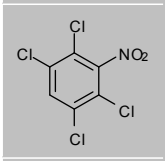
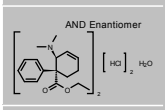
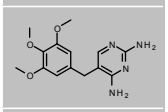
Revision	Date	Reason for Revision
00	2013-04-26	Release of the Lot – initial version
01	2013-10-29	Accreditation Number added

Code	Product	CAS No.	CS	Unit	
Primary Standards					
LGCQUANT0136.00-100	Alprazolam	28981-97-7	**CS**	100mg	
LGCQUANT0741.00-250	Amfetamine Sulfate	60-13-9	**CS**	250mg	
LGCQUANT1424.01	2,5-Bis-(trifluoromethyl)aniline	328-93-8		250mg	
LGCQUANT0120.00	Buprenorphine	52485-79-7	**CS**	250mg	
LGCQUANT0162.00-250	Chlorhexidine Diacetate	56-95-1		250mg	
LGCQUANT0946.00-250	Chlorhexidine Dihydrochloride	3697-42-5		250mg	
LGCQUANT1345.00-250	Cocaine Hydrochloride	53-21-4	**CS**	250mg	
LGCQUANT2520.00-250	Dimethyl Terephthalate	120-61-6		250mg	
LGCQUANT0630.01-250	Diphenylmethanone (Benzophenone)	119-61-9		250mg	
LGCQUANT1264.00	Etomidate	33125-97-2		1g	
LGCQUANT1264.04	Etomidate Acid (1-[(1R)-1-Phenylethyl]-1H-imidazole-5-carboxylic Acid)	56649-48-0		100mg	
LGCQUANT0498.00	Ethyl Parahydroxybenzoate	120-47-8		250mg	
LGCQUANT0014.00	Furosemide	54-31-9		250mg	
LGCQUANT0008.00	Glibenclamide	10238-21-8		250mg	

Primary standards

Code	Product	CAS No.	CS	Unit	
LGCQUANT0398.00	Granisetron Hydrochloride	107007-99-8		250mg	
LGCQUANT0143.00	Isotretinoin	4759-48-2		250mg	
LGCQUANT0258.00	Itraconazole	84604-65-9		1g	
LGCQUANT1387.01-50	Mephedrone Hydrochloride	1189726-22-4	**CS**	50mg	
LGCQUANT0052.00	Metamizole Sodium Monohydrate	5907-38-0		250mg	
LGCQUANT0531.00-250	Methadone Hydrochloride	1095-90-5	**CS**	250mg	
LGCQUANT0431.00	Methyl Parahydroxybenzoate	99-76-3		250mg	
LGCQUANT1410.00	Minocycline Hydrochloride Dihydrate	128420-71-3		250mg	
LGCQUANT0267.00	Molsidomine	25717-80-0		250mg	
LGCQUANT0003.00	Nifedipine	21829-25-4		250mg	
LGCQUANT0042.00	Paracetamol	103-90-2		1g	
LGCQUANT0432.00	Propyl Parahydroxybenzoate	94-13-3		250mg	
LGCQUANT0331.00	Ropinirole Hydrochloride	91374-20-8		250mg	
LGCQUANT0045.00	Salicylic Acid	69-72-7		250mg	
LGCQUANT1420.00	Silver Sulfadiazine	22199-08-2		250mg	
LGCQUANT0730.00	Sodium Benzoate	532-32-1		250mg	
LGCQUANT1370.00-250	Sodium Salicylate	54-21-7		250mg	

Primary standards

Code	Product	CAS No.	CS	Unit	
LGCQUANT0533.00	Sulfadoxine	2447-57-6		250mg	
LGCQUANT0504.00	Tetracaine Hydrochloride	136-47-0		250mg	
LGCQUANT2521.00	2,3,5,6-Tetrachloronitrobenzene	117-18-0		250mg	
LGCQUANT0134.00	Tilidine Hydrochloride Hemihydrate	255733-17-6	**CS**	500mg	
LGCQUANT0093.00	Trimethoprim	738-70-5		250mg	
LGCQUANT0634.00	L-Tyrosine	60-18-4		250mg