MG2

cobas®

Magnesium Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08058016190*	08058016500	Magnesium Gen.2 (690 tests)	System-ID 2089 001	**cobas c** 303, **cobas c** 503, **cobas c** 703
08058016214*	08058016500	Magnesium Gen.2 (690 tests)	System-ID 2089 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 20401	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

* Some kits shown may not be available in all countries.

English

System information

MG2: ACN 20890 (Serum/plasma)

MG2U: ACN 20891 (Urine)

Intended use

In vitro test for the quantitative determination of magnesium in human serum, plasma and urine on **cobas c** systems.

Summary

Magnesium measurements, performed with this assay, in human serum, plasma and urine are used as an aid in diagnosis and monitoring disorders of magnesium metabolism associated with hypomagnesemia (magnesium deficiency) and hypermagnesemia (magnesium excess).

Magnesium is mainly found in the intracellular space (40 %) and in bones and teeth (60 %). Approximately 0.3 % of the body's total magnesium is found in serum.[1] As important intracellular cation, Mg^{2+} is a cofactor in more than 300 enzyme-catalyzed reactions involved in phosphorylation, protein synthesis, and DNA metabolism processes. All ATP-dependent enzymatic reactions require Mg^{2+} as a cofactor. In addition, magnesium is a dynamic ion for transcellular transport, altering membrane potentials and ion transport. It is involved in neuromuscular conduction and excitability of skeletal and cardiac muscle.[2]

Approximately 99 % of magnesium ions are stored in bone, skeletal muscle and other soft tissues and less than 1 % is present in the extracellular fluid. The Mg^{2+} serum level is kept constant within very narrow limits (0.7-1.10 mmol/L). Approximately 20 % of this is protein bound (especially to albumin), 65 % is ionized and the rest is complexed with various anions such as phosphate and citrate.[3] Serum levels are mainly regulated via the kidneys, especially via the ascending loop of Henle.[4,5] Emerging evidence suggests that the serum magnesium/calcium quotient is an important indicator of magnesium status and/or turnover.[1]

Hypomagnesemia is common, with a prevalence of up to 15 % in the general population and up to 65 % in patients in the intensive care units.[5] Hypomagnesemia is usually due to loss or impaired absorption of magnesium from the gastrointestinal tract or increased excretion by the kidneys.[2,5] Symptomatic magnesium depletion is often correlated with multiple other biochemical abnormalities, such as hypokalaemia, hypocalcaemia and metabolic acidosis. Manifestations of severe hypomagnesaemia include neuromuscular symptoms (muscular weakness, apathy, tremors, paraesthesia, tetany, vertical nystagmus and positive Chvostek and Trousseau signs) and cardiovascular manifestations (e.g. atrial and ventricular arrhythmias).[4] Intravenous magnesium is usually prescribed in cases of symptomatic hypomagnesaemia, while oral replacement is indicated for asymptomatic patients.[4]

Hypermagnesemia is generally occurring in the setting of renal insufficiency (acute and chronic renal failure) and excessive magnesium intake resulting in neuromuscular and cardiovascular manifestations as well as non-specific manifestations like nausea, vomiting and cutaneous flushing.[4]

In addition to atomic absorption spectrometry (AAS), complexometric methods can also be used to determine magnesium.[2,6]

The method described here is based on the reaction of magnesium with xylidyl blue in alkaline solution containing EGTA to mask the calcium in the sample.[7]

Urine magnesium is also often measured as part of a magnesium loading test.[8]

Test principle[7]

Colorimetric endpoint method

- Sample and addition of R1
- Addition of R2 and start of reaction:

  In alkaline solution, magnesium forms a purple complex with xylidyl blue, diazonium salt. The magnesium concentration is measured photometrically via the decrease in the xylidyl blue absorbance.

Reagents - working solutions

R1 TRIS[a)]/6-aminocaproic acid buffer: 500 mmol/L, pH 11.25; EGTA: 129 µmol/L; preservative

R3 Xylidyl blue: 0.28 mmol/L; detergent; preservative

a) TRIS = Tris(hydroxymethyl)-aminomethane

R1 is in position B and R3 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H315 Causes skin irritation.

H319 Causes serious eye irritation.

Prevention:

P264 Wash skin thoroughly after handling.

P280 Wear protective gloves/ eye protection/ face protection.

Response:

P302 + P352 IF ON SKIN: Wash with plenty of water.

P332 + P313 If skin irritation occurs: Get medical advice/attention.

P337 + P313 If eye irritation persists: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

Storage and stability

Shelf life at 15-25 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	26 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested.

Chelating anticoagulants such as EDTA, fluoride and oxalate must be avoided.

Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Stability in *serum/plasma*:[9]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at -20 °C (± 5 °C)

Freeze only once.

Urine:

Urine samples should be acidified to pH 1 with concentrated HCl to prevent precipitation of magnesium ammonium phosphate. Collect urine samples in metal-free container.[10] Urine samples are automatically prediluted with 0.9 % NaCl by the instrument. If stabilizers are added to the sample, the sample index feature must not be used.

Stability in *urine*:[9]	3 days at 15-25 °C
	3 days at 2-8 °C
	1 year at -20 °C (± 5 °C)

Freeze only once.

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

See “Order information” section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

Test definition

Reporting time	10 min	
Wavelength (sub/main)	505/600 nm	
Reagent pipetting		Diluent (H_2O)
R1	78 µL	–
R3	78 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.4 µL	–	–
Decreased	1.2 µL	–	–
Increased	2.4 µL	–	–

Application for urine

Test definition

Reporting time	10 min	
Wavelength (sub/main)	505/600 nm	
Reagent pipetting		Diluent (H_2O)
R1	78 µL	-
R3	78 µL	-

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.4 µL	20 µL	90 µL
Decreased	2.4 µL	10 µL	100 µL
Increased	2.4 µL	20 µL	90 µL

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Application for serum/plasma (ACN 20890)

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	Automatic full calibration - after reagent lot change
	Full calibration - every 4 weeks on-board - as required following quality control procedures

Application for urine (ACN 20891)
Transfer of calibration from serum/plasma application (ACN 20890)

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against atomic absorption spectrometry.

Quality control

For quality control, use control materials as listed in the “Order information” section. In addition, other suitable control material can be used.

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Magnesium Gen.2

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Serum/plasma:	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
Urine:	Quantitative urine controls are recommended for routine quality control.

The control intervals and limits should be adapted to each laboratory's individual requirements.

It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, mg/L, mval/L).

Conversion factors:	mmol/L x 2.43 = mg/dL
	mmol/L x 24.3 = mg/L
	mmol/L x 2.0 = mval/L
	mval/L = mEq/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a magnesium concentration of 0.7 mmol/L (1.7 mg/dL, 1.4 mval/L).

Serum/plasma

Icterus:[11] No significant interference up to an I index of 60 for conjugated bilirubin and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 60 mg/dL or 1026 µmol/L).

Hemolysis:[11] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 496 µmol/L (800 mg/dL)).

Hemolysis elevates results depending on the content of the analyte in the lysed erythrocytes.

Lipemia (Intralipid):[11] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[12,13]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[14]

Urine

Drugs: No interference was found at therapeutic concentrations using common drug panels.[13]

Criterion: Recovery within ± 10 % of initial value at a magnesium concentration of 1.7 mmol/L (4.1 mg/dL, 3.4 mval/L).

Hemolysis: No significant interference up to an H index of 1000 (approximate hemoglobin concentration of 621 µmol/L or 1000 mg/dL).

Urea: No significant interference from urea up to a concentration of 1500 mmol/L (9009 mg/dL).

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

Serum/plasma

0.10-2.0 mmol/L (0.243-4.86 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Urine

0.56-11.0 mmol/L (1.36-26.7 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Serum/plasma

Limit of Blank	= 0.05 mmol/L (0.122 mg/dL)
Limit of Detection	= 0.10 mmol/L (0.243 mg/dL)
Limit of Quantitation	= 0.10 mmol/L (0.243 mg/dL)

Urine

Limit of Blank	= 0.28 mmol/L (0.68 mg/dL)
Limit of Detection	= 0.56 mmol/L (1.36 mg/dL)
Limit of Quantitation	= 0.56 mmol/L (1.36 mg/dL)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration magnesium samples.

Expected values[15]

mmol/L

Serum/plasma:

Newborn:	0.62-0.91 mmol/L
5 months-6 years:	0.70-0.95 mmol/L
6-12 years:	0.70-0.86 mmol/L
12-20 years:	0.70-0.91 mmol/L
Adults:	0.66-1.07 mmol/L
60-90 years:	0.66-0.99 mmol/L
> 90 years:	0.70-0.95 mmol/L
Urine (24 h):	3.0-5.0 mmol/d

mg/dL

Serum/plasma:

Newborn:	1.5-2.2 mg/dL
5 months-6 years:	1.7-2.3 mg/dL
6-12 years:	1.7-2.1 mg/dL
12-20 years:	1.7-2.2 mg/dL
Adults:	1.6-2.6 mg/dL
60-90 years:	1.6-2.4 mg/dL
> 90 years:	1.7-2.3 mg/dL
Urine (24 h):	72.9-121.5 mg/d

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days).
Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Serum/plasma

Repeatability	*Mean mmol/L*	*SD mmol/L*	*CV %*
PCCC1[b)]	0.812	0.00352	0.4
PCCC2[c)]	1.30	0.00546	0.4
Human serum 1	0.258	0.00386	1.5
Human serum 2	0.624	0.00384	0.6
Human serum 3	0.986	0.00346	0.4
Human serum 4	1.36	0.00567	0.4
Human serum 5	1.74	0.00577	0.3

Intermediate precision	*Mean mmol/L*	*SD mmol/L*	*CV %*
PCCC1[b)]	0.812	0.00940	1.2
PCCC2[c)]	1.30	0.0127	1.0
Human serum 1	0.258	0.00648	2.5
Human serum 2	0.624	0.00699	1.1
Human serum 3	0.986	0.00651	0.7
Human serum 4	1.37	0.00812	0.6
Human serum 5	1.74	0.00896	0.5

b) PreciControl ClinChem Multi 1
c) PreciControl ClinChem Multi 2

Urine

Repeatability	*Mean mmol/L*	*SD mmol/L*	*CV %*
Control 1[d)]	1.73	0.0231	1.3
Control 2[d)]	3.67	0.0252	0.7
Human urine 1	1.50	0.0243	1.6
Human urine 2	2.90	0.0238	0.8
Human urine 3	4.08	0.0262	0.6
Human urine 4	5.30	0.0334	0.6
Human urine 5	9.02	0.0425	0.5

Intermediate precision	*Mean mmol/L*	*SD mmol/L*	*CV %*
Control 1[d)]	1.72	0.0302	1.8
Control 2[d)]	3.67	0.0313	0.9
Human urine 1	1.50	0.0288	1.9
Human urine 2	2.89	0.0336	1.2
Human urine 3	4.08	0.0298	0.7
Human urine 4	5.27	0.0424	0.8
Human urine 5	9.02	0.0609	0.7

d) commercially available control material

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Serum/plasma

Sample size (n) = 97

Passing/Bablok[16]	Linear regression
y = 1.013x - 0.00748 mmol/L	y = 1.011x - 0.00537 mmol/L
τ = 0.984	r = 1.000

The sample concentrations were between 0.100 and 1.96 mmol/L.

Urine

Sample size (n) = 62

Passing/Bablok[16]	Linear regression
y = 0.963x - 0.0757 mmol/L	y = 0.973x - 0.114 mmol/L
τ = 0.974	r = 0.999

The sample concentrations were between 0.670 and 11.0 mmol/L.

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Serum/plasma

Sample size (n) = 72

Passing/Bablok[16]	Linear regression
y = 1.011x + 0.000944 mmol/L	y = 1.012x + 0.000238 mmol/L
τ = 0.979	r = 1.000

The sample concentrations were between 0.140 and 1.94 mmol/L.

Urine

Sample size (n) = 67

Passing/Bablok[16]	Linear regression
y = 1.007x + 0.00729 mmol/L	y = 1.008x + 0.00459 mmol/L
τ = 0.984	r = 1.000

The sample concentrations were between 0.610 and 10.7 mmol/L.

Magnesium values for human serum, plasma and urine samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Serum/plasma

Sample size (n) = 68

Passing/Bablok[16]	Linear regression
y = 0.995x - 0.00153 mmol/L	y = 0.994x + 0.000658 mmol/L
τ = 0.995	r = 1.000

The sample concentrations were between 0.115 and 1.90 mmol/L.

Urine

Sample size (n) = 62

Passing/Bablok[16]	Linear regression
y = 0.994x + 0.0290 mmol/L	y = 0.992x + 0.0298 mmol/L
τ = 0.9996	r = 1.000

The sample concentrations were between 0.674 and 10.8 mmol/L.

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References

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606

Roche