B2MG

cobas®

Tina-quant β2-Microglobulin

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
11660551 216	Tina-quant β2-Microglobulin 2 x 70 tests	System-ID 07 6864 2	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
	β2-Microglobulin Calibrator included in **11660551** 216	Code 460	
11729683 216	β2-Microglobulin Control Set Serum Level I (2 x 1 mL) Level II (2 x 1 mL)	 Code 213 Code 214	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	
04593138 190	**cobas c** pack MULTI		
on request	Open/Close tool		

English

System information

For **cobas c** 311/501 analyzers:

B2MG: ACN 222

For **cobas c** 502 analyzer:

B2MG: ACN 8222

Intended use

Immunoturbidimetric assay for the quantitative in vitro determination of β2-microglobulin in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5]

β2-microglobulin (β2-M) was discovered in 1968 by Berggård et al. in the urine of patients with Wilson's disease and in patients with chronic cadmium poisoning. β2-M is a small globular peptide with a molecular weight of 11800 D. It is identical to the light chain of the major histocompatibility complex (MHC) antigen (HLA) 5. Its tertiary structure is homologous to the CH3-IgG immunoglobulin domain. Thus β2-M is expressed on the extraplasma surface of nearly all nucleated cells (exception: trophoblasts). β2-M consists of 100 amino acids with a disulfide-linked loop between amino acid 25 and 81. β2-M is non-covalently associated with the class 1 MHC antigen, and is identical to BDGF (bone-derived growth factor 2), CRG-8, and thymotaxin. β2-M is normally cleared exclusively by the kidneys. It passes freely through the glomerular membrane, and up to 99.9 % is reabsorbed by the proximal tubules.

It has been published that elevated serum levels of β2-M occur in renal diseases such as glomerulopathies, tubulopathies, renal failure, and amyloidosis. In addition, it has been reported that other increased serum levels are found in rheumatoid arthritis and autoimmune diseases.

Various assay methods are available for β2-microglobulin determination, such as radioimmunoassays (RIA), enzyme-linked immunosorbent assays (ELISA), nephelometric immunoassays, and turbidimetric methods. The Roche β2-microglobulin assay is based on the principle of immunological agglutination with latex reaction enhancement.

Test principle[1]

Immunoturbidimetric assay.

Latex-bound anti-β2-microglobulin antibodies react with antigen from the sample to form antigen/antibody complexes which are determined turbidimetrically after agglutination.

Reagents - working solutions

R1	TRIS/HCl buffer: 23 g/L, pH 8.7; NaCl: 19 g/L; EDTA: 2 g/L; preservative
R2	Latex particles coated with polyclonal anti-human β2-microglobulin antibody (rabbit): 0.5 g/L; preservative
Calibrator	β2-microglobulin (human); contains 1.6 % NaN_3

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: For prescription use only.

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

Warning

H302	Harmful if swallowed.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P264	Wash skin thoroughly after handling.
P270	Do not eat, drink or smoke when using this product.
P273	Avoid release to the environment.

Response:

P301 + P312 + P330	IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. Rinse mouth.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling primarily follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV.
The testing methods applied were FDA-approved or cleared in compliance with the European Directive 98/79/EC, Annex II, List A.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[6,7]

Reagent preparation and cobas c pack MULTI assembly

Reagent handling

R1	Ready for use.
R2	Ready for use.
Calibrator (bottle 3)	Open the bottle, being careful to avoid the loss of lyophilizate, and pipette in exactly 1.0 mL of distilled/deionized water. Then close the bottle carefully and dissolve the contents by gentle swirling, avoiding the formation of foam. Store calibrator tightly capped when not in use.

Labeling the **cobas c** *pack MULTI*

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Turn the barcode labeled side of a new **cobas c** pack MULTI toward you. Affix the supplied B2MG barcode label directly over the existing barcode label.

Filling the **cobas c** *pack MULTI*

1. Turn the **cobas c** pack MULTI toward you as shown above.
2. Position A of the **cobas c** pack is now in the center, position B on the left side, position C on the right side of the **cobas c** pack.
3. Unscrew the screw cap of the bottle in position B on the left side of the **cobas c** pack MULTI using the Open/Close tool.
4. Pour the content of bottle 1 (12 mL) into the opened bottle of the **cobas c** pack (position B).
5. Close the bottle tightly using the Open/Close tool.
6. Unscrew the screw cap of the bottle in position C on the right side of the **cobas c** pack MULTI using the Open/Close tool.
7. Pour the content of bottle 2 (12 mL) into the opened bottle of the **cobas c** pack (position C).
8. Close the bottle tightly using the Open/Close tool.
9. Leave position A empty.

The B2MG **cobas c** pack is now ready for use.

Mix **cobas c** pack well before placing on the analyzer.

Note
Use only the **cobas c** pack MULTI. Always use a new **cobas c** pack MULTI when preparing fresh reagent. Never reuse accessories designed for single use, as this may result in reagent contamination and could affect test results. If the **cobas c** pack MULTI bottles are not filled correctly, this may result in faulty reagent pipetting and could cause erroneous results.

Storage and stability

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Unopened kit components: Up to the expiration date at 2-8 °C.

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label
On-board in use and refrigerated on the analyzer:	12 weeks

Calibrator

Reconstituted shelf life at 2-8 °C:	90 days

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 and K_2-EDTA 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. 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.

Stability:[8]	3 days at 2-8 °C
	6 months at (-15)-(-25) °C

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

cobas c 311 **test definition**

Assay type	2 Point End	
Reaction time/Assay points	10/12-26	
Wavelength (sub/main)	-/700 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	124 µL	–
R2	124 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	10 µL	100 µL
Increased	2 µL	–	–

cobas c 501 **test definition**

Assay type	2 Point End	
Reaction time/Assay points	10/18-38	
Wavelength (sub/main)	-/700 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	124 µL	–
R2	124 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	10 µL	100 µL

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Increased	2 µL	–	–

cobas c 502 **test definition**

Assay type	2 Point End
Reaction time/Assay points	10/18-38
Wavelength (sub/main)	-/700 nm
Reaction direction	Increase
Units	mg/L (nmol/L)
Reagent pipetting	Diluent (H_2O)
R1	124 µL –
R2	124 µL –

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	10 µL	100 µL
Increased	4 µL	–	–

Calibration

Calibrators	S1: H_2O S2: β2-Microglobulin Calibrator
Calibration mode	Linear
Calibration frequency	2-point calibration - after reagent lot change - as required following quality control procedures

Traceability: This method has been standardized against the WHO standard.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

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

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factor: mg/L x 84.7 = nmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a β2-microglobulin concentration of 2.20 mg/L (186 nmol/L).

Icterus:[9] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[9] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[9] No significant interference up to an L index of 1000. 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.[10,11]

Rheumatoid factors < 200 IU/mL do not interfere.

High dose hook-effect: No false result occurs up to a β2-M concentration of 5082 nmol/L (60 mg/L).

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[12]

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 Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

0.1-8.0 mg/L (8.5-678 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:11 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 11.

Lower limits of measurement

Lower detection limit of the test

0.1 mg/L (8.5 nmol/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values[1]

0.8-2.2 mg/L (68-186 nmol/L)

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. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	mg/L (nmol/L)	*mg/L (nmol/L)*	*%*
Control set serum 1	2.40 (203)	0.02 (2)	0.8
Control set serum 2	5.34 (452)	0.06 (5)	1.2
Human serum 1	0.79 (66.8)	0.02 (1.7)	1.9
Human serum 2	6.07 (514)	0.08 (7)	1.4
Intermediate precision	*Mean*	*SD*	*CV*
	mg/L (nmol/L)	*mg/L (nmol/L)*	*%*
Control set serum 1	2.31 (196)	0.03 (3)	1.5
Control set serum 2	5.22 (442)	0.07 (6)	1.4
Human serum 3	1.76 (149)	0.02 (2)	1.2
Human serum 4	4.76 (403)	0.07 (6)	1.5

Method comparison

β2-Microglobulin values for human serum samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 73

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Passing/Bablok[13]	Linear regression
y = 0.978x - 0.051 mg/L	y = 0.980x - 0.049 mg/L
τ = 0.976	r = 1.000

The sample concentrations were between 0.350 and 7.75 mg/L (29.6 and 656 nmol/L).

References

1 Junge W, Schlottmann A, Thormeyer I, et al. Evaluation of a Homogeneous Immunoassay for the Determination of Beta-2-Microglobulin in Serum/Plasma. Poster No. 287, 48th Annual Meeting of the American Association for Clinical Chemistry, July 28-August 1 (Chicago, Illinois) 1996.

2 Berggard I, Bearn AG. Isolation and Properties of a Low Molecular Weight β2-Globulin Occurring in Human Biological Fluids. J Biol Chem 1968;243:4095.

3 Cunningham BA, Wang JL, Berggard I, et al. The complete amino acid sequence of β2-microglobulin. Biochem 1973;12:4811-4822.

4 Steinhoff J, Feddersen A, Wood WG, et al. β2-Microglobulinurie bei Cytomegalievirusinfektionen nach Nierentransplantation. Dtsch med Wschr 1991;116:1008-1012.

5 Niederau CM. β2-Microglobulin - a protein with multiple diagnostic relevance in the past and in the future. Institute of Clinical Chemistry and Laboratory Diagnostics, Heinrich-Heine University, Dusseldorf, Germany 1996.

6 Occupational Safety and Health Standards: bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

7 Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.

8 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia: WB Saunders, 1995:436-437.

9 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

10 Breuer J. Report on the Symposium “Drug effects in Clinical Chemistry Methods”. Eur J Clin Chem Clin Biochem 1996;34:385-386.

11 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

12 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

13 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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