

**Tina-quant  $\beta$ 2-Microglobulin (urine application)****Order information**

REF	CONTENT	Analyzer(s) on which <b>cobas c</b> pack(s) can be used
08047499190	Tina-quant $\beta$ 2-Microglobulin (140 tests)	System-ID 01 6864 2 <b>cobas c</b> 701/702
Materials required (but not provided):		
08047545190	Calibrator $\beta$ 2-Microglobulin	Code 474
08362785190	Control Set $\beta$ 2-Microglobulin	Level I: Code 144 Level II: Code 145
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3

**English**

For use in the USA only

**System information**For **cobas c** 701/702 analyzers:**B2MGU**: ACN 8231**Intended use**Immunoturbidimetric assay for the quantitative in vitro determination of  $\beta$ 2-microglobulin (B2MG) in human urine on **cobas c** systems.**Summary**

B2MG is a low-molecular-weight protein with approximately 12 kDa. It is identical to the light chain of the major histocompatibility complex (MHC) antigens (HLA, A, B, C). Thus B2MG is expressed on the cell membrane of nearly all nucleated cells (exception: trophoblasts).<sup>1,2</sup> Lymphocytes are the major location of synthesis. B2MG is constantly released into the blood in small quantities. Due to its low molecular weight, it is rapidly filtered through the renal glomeruli. Thereafter, up to 99.9 % is reabsorbed by the proximal tubules.<sup>3</sup>

Drug nephrotoxicity causing severe, acute changes in tubular reabsorption and progressive renal diseases causing irreversible structural tubular defects impair tubular reabsorption of numerous smaller proteins including B2MG.<sup>4</sup> Thus, urinary B2MG is discussed as a marker for the diagnosis and monitoring of tubulointerstitial renal damage.<sup>2</sup> Excretion of B2MG is increased in Fanconi syndrome, a generalized dysfunction of the proximal tubules. Causes for acquired Fanconi syndrome include exposure to toxins and drugs.<sup>5</sup>

Elevated B2MG values may identify patients at higher risk of glomerular filtration rate (GFR) decline in other kidney diseases such as membranous nephropathy.<sup>6</sup> Furthermore, there is evidence that B2MG excretion is associated with acute allograft rejection in renal transplant recipients.<sup>7</sup>

Various assay methods are available for B2MG determination, such as radioimmunoassays (RIA), enzyme-linked immunosorbent assays (ELISA), nephelometric immunoassays, and turbidimetric methods.<sup>2</sup> The Roche B2MG assay is based on the principle of immunological agglutination with latex reaction enhancement.

**Test principle**

Immunoturbidimetric assay.

Latex-bound anti- $\beta$ 2-microglobulin antibodies react with antigen from the sample to form antigen/antibody complexes which are determined turbidimetrically after agglutination.<sup>8</sup>

**Reagents - working solutions**

<b>R1</b>	TRIS/HCl buffer: 23 g/L, pH 8.2; NaCl: 19 g/L; EDTA: 1.3 g/L; preservative
<b>R3</b>	Latex particles coated with polyclonal anti-human $\beta$ 2-microglobulin antibody (rabbit): 1.9 g/L; preservative

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**

- H317 May cause an allergic skin reaction.  
H412 Harmful to aquatic life with long lasting effects.

**Prevention:**

- P261 Avoid breathing mist or vapours.  
P273 Avoid release to the environment.  
P280 Wear protective gloves.

**Response:**

- P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.  
P362 + P364 Take off contaminated clothing and wash it before reuse.

**Disposal:**

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

Product safety labeling follows EU GHS guidance.

Contact phone: 1-800-428-2336

**Reagent handling**

Ready for use

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

**Storage and stability**

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

On-board on the Reagent Manager: 24 hours

**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. Urine.

Each urine sample must be centrifuged (10 minutes at approximately 3000 x g) prior to testing.<sup>9</sup>

B2MG is unstable in acidic conditions and degradation occurs at pH < 6 within 2 hours.<sup>2,10</sup> Thus, pre-analytical conditions are highly important. Since the degradation also takes place in the bladder, collection of a spot urine sample should not be performed in the morning due to a lower urine pH.<sup>2</sup>

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A strict control of the urine pH after collection is required: urine samples must be adjusted to pH 7-9 by the addition of 1 N NaOH as soon as possible after receipt.<sup>10</sup>

Centrifuge samples containing precipitates before performing the assay.

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

Stability in urine:	5 days at 15-25 °C
	14 days at 2-8 °C
	12 weeks at -20 °C ( $\pm$ 5 °C)
	Freezing and thawing up to 2 times is allowed.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

**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 urine****cobas c 701/702 test definition**

Assay type	2 Point End	
Reaction time / Assay points	10 / 24-34	
Wavelength (sub/main)	-700 nm	
Reaction direction	Increase	
Units	mg/L (nmol/L)	
Reagent pipetting	Diluent (H <sub>2</sub> O)	
R1	124 $\mu$ L	–
R3	124 $\mu$ L	–

Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2 $\mu$ L	–	–
Decreased	2 $\mu$ L	10 $\mu$ L	100 $\mu$ L
Increased	2 $\mu$ L	–	–

**Calibration**

Calibrators	S1: H <sub>2</sub> O S2: Calibrator $\beta$ 2-Microglobulin
Calibration mode	Linear
Calibration frequency	2-point calibration - after reagent lot change - as required following quality control procedures

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

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**

**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  $\pm$  0.1 mg/L (8.47 nmol/L) of initial values at a  $\beta$ 2-microglobulin concentration of  $\leq$  1.0 mg/L (84.7 nmol/L) and within  $\pm$  10 % for samples > 1.0 mg/L.

Hemolysis: No significant interference up to a hemoglobin concentration of 1100 mg/dL.<sup>11</sup>

High dose hook-effect: No false result occurs up to a B2MG concentration of 240 mg/L (20328 nmol/L).

Drugs: No interference was found at therapeutic concentrations using common drug panels.<sup>12</sup>

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.<sup>13</sup>

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, manual input is required in certain cases. The latest version of the carry-over evasion list can be found with the NaOH/SMS/SmpCln1+2/SCCS Method Sheet and for further instructions refer to the operator's manual.

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

**Limits and ranges****Measuring range**

0.2-5.8 mg/L (16.9-491 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**

*Limit of Blank, Limit of Detection and Limit of Quantitation*

Limit of Blank = 0.1 mg/L (8.5 nmol/L)

Limit of Detection = 0.15 mg/L (12.7 nmol/L)

Limit of Quantitation = 0.2 mg/L (16.9 nmol/L)

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 95<sup>th</sup> percentile value from  $n \geq 60$  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.

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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 human β2-microglobulin samples.

**Expected values**

B2MG (urine), male: ≤ 0.300 mg/L (25.4 nmol/L)<sup>14</sup>

B2MG (urine), female: ≤ 0.183 mg/L (15.5 nmol/L)<sup>14</sup>

B2MG/creatinine (urine): ≤ 0.029 mg/mmol<sup>14</sup>

24 h urine: 33-363 μg<sup>10</sup>

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**

Repeatability and intermediate precision were determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5 requirements (4 aliquots per run, 1 run per day, 21 days). The following results were obtained on the **cobas c 701** analyzer:

Repeatability	Mean	SD	CV
	mg/L (nmol/L)	mg/L (nmol/L)	%
Control 1	2.51 (213)	0.0282 (2.39)	1.1
Control 2	5.45 (462)	0.121 (10.2)	2.2
Human urine 1	0.269 (22.8)	0.0135 (1.14)	5.0
Human urine 2	0.346 (29.3)	0.0140 (1.19)	4.0
Human urine 3	0.825 (69.9)	0.0194 (1.64)	2.4
Human urine 4	2.86 (242)	0.104 (8.81)	3.6
Human urine 5	4.71 (399)	0.0470 (3.98)	1.0
Intermediate precision	Mean	SD	CV
	mg/L (nmol/L)	mg/L (nmol/L)	%
Control 1	2.51 (213)	0.0835 (7.07)	3.3
Control 2	5.45 (462)	0.301 (25.5)	5.5
Human urine 1	0.269 (22.8)	0.0193 (1.63)	7.2
Human urine 2	0.346 (29.3)	0.0271 (2.30)	7.8
Human urine 3	0.825 (69.9)	0.0557 (4.72)	6.8
Human urine 4	2.86 (242)	0.149 (12.6)	5.2
Human urine 5	4.71 (399)	0.187 (15.8)	4.0

**Method comparison**

β2-Microglobulin values for human urine samples obtained on a **cobas c 701** analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c 501** analyzer (x).

Sample size (n) = 118

Passing/Bablok <sup>15</sup>	Linear regression
$y = 0.967x - 0.001 \text{ mg/L}$	$y = 0.959x + 0.015 \text{ mg/L}$
$\tau = 0.978$	$r = 0.999$

The sample concentrations were between 0.210 and 5.76 mg/L (17.8 and 488 nmol/L).

**References**

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- 3 Stadius van Eps LW, Schardijn GH. Value of determination of beta2-microglobulin in toxic nephropathy and interstitial nephritis. *Wien Klin Wochenschr* 1984 Sep;96(18):673-678.
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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](http://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.

# B2MG

Tina-quant  $\beta$ 2-Microglobulin (urine application)



## FOR US CUSTOMERS ONLY: LIMITED WARRANTY

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