0106749992190c501V5.0

LAMB2

Tina-quant Lambda Gen.2

cobas®

REF	CONTENT		Analyzer(s) on which kit(s) can be used
06749992 190	Tina-quant Lambda Gen.2 (100 tests)	System ID 07 6813 8	Roche/Hitachi **cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

11355279 216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
10557897 122	Precinorm Protein (3 x 1 mL)	Code 302	
11333127 122	Precipath Protein (3 x 1 mL)	Code 303	
04489357 190	Diluent NaCl 9 % (50 mL)	System ID 07 6869 3	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	

English

System information

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

LAMB2: ACN 284

For **cobas c** 502 analyzer:

LAMB2: ACN 8284

Intended use

Immunoturbidimetric in vitro assay for the quantitative determination of bound and free immunoglobulins of the lambda light chain type in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6,7]

Measurement of the various amounts of the different types of light chains aids in the diagnosis of multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinemia, and connective tissue diseases such as rheumatoid arthritis or systemic lupus erythematosus.

Every plasma cell clone normally produces a uniform immunoglobulin molecule of the kappa or lambda light chain type. The kappa:lambda ratio in serum is normally around 2:1.

Pathological increases of a cell clone lead to elevated formation of monoclonal immunoglobulins or immunoglobulin fragments (free light chains), which bring about a change in the kappa:lambda ratio. A kappa:lambda ratio outside the normal range is indicative of monoclonal gammopathy.

This test encompasses both bound and free immunoglobulins of the light chain type.

It is known that the so-called paraproteins secreted in monoclonal gammopathies (monoclonal immunoglobulinemia) may differ from the respective immunoglobulins of polyclonal origin in amino acid composition and size. This may impair the binding to antibody and consequently cause antigen excess below the limits determined with immunoglobulins of polyclonal origin. Antigen excess may be detected after appropriate dilution of such samples.

Furthermore, the occurrence of two monoclonal gammopathies producing differing light chain types could theoretically lead to kappa:lambda ratios in the normal range.

Accordingly, quantitative determination of the kappa and lambda light chains cannot completely replace high-resolution electrophoresis, immunoelectrophoresis or immunofixation electrophoresis in the diagnosis of monoclonal gammopathy.

Test principle

Immunoturbidimetric assay

Anti-lambda antibodies react with the antigen in the sample to form antigen/antibody complexes that, following agglutination, are measured turbidimetrically.

Reagents - working solutions

R1 TRIS/HCl buffer: 50 mmol/L, pH 8.0; PEG 7 %; stabilizers and preservative

R2 Polyclonal anti-human lambda antibody (goat): dependent on titer; TRIS/HCl buffer: 20 mmol/L, pH 7.5; stabilizers and preservative

R1 is in position B and R2 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.

Storage and stability

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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

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 or 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.

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

Stability:[8]	7 days at 15-25 °C
	4 weeks at 4-8 °C
	2 months at (-15)-(-25) °C

Materials provided

See “Reagents – working solutions” section for reagents.

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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 / 6-57		
Wavelength (sub/main)	800/340 nm		
Reaction direction	Increase		
Units	g/L (mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	125 µL	–	
R2	45 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	4.5 µL	9 µL	180 µL
Decreased	4.5 µL	3 µL	150 µL
Increased	4.5 µL	9 µL	180 µL

cobas c 501/502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-70		
Wavelength (sub/main)	800/340 nm		
Reaction direction	Increase		
Units	g/L (mg/dL)		
Reagent pipetting		Diluent (H_2O)	
R1	125 µL	–	
R2	45 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	4.5 µL	9 µL	180 µL
Decreased	4.5 µL	3 µL	150 µL
Increased	4.5 µL	9 µL	180 µL

Calibration

Calibrators	S1-S6: C.f.a.s. Proteins
	Multiply the lot-specific C.f.a.s. Proteins calibrator value by the factors below to determine the standard concentrations for the 6-point calibration curve:
	S1: 0.103 S4: 0.541
	S2: 0.181 S5: 2.03
	S3: 0.271 S6: 3.62
Calibration mode	RCM2
Calibration frequency	Full 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 CRM 470 standard using the Lievens equation.[6]

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 factors:	mg/dL x 0.01 = g/L
	g/L x 100 = mg/dL

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a lambda concentration of 0.9 g/L (90 mg/dL).

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: No significant interference from rheumatoid factors up to a concentration of 450 IU/mL.

High dose hook-effect: No false result occurs up to a lambda concentration of 30 g/L.

Samples from patients with unclear clinical diagnosis should be subject to protein electrophoresis to identify a possible antigen excess or monoclonal gammopathy. Antigen excess may be detected by appropriate predilution of the specimen with 0.9 % sodium chloride solution.

In sera with monoclonal lambda components, differing results may be obtained with commercial assays employing antibodies from different sources (rabbit, sheep, goat).

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 required in certain cases.

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

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Limits and ranges

Measuring range

0.5-7.5 g/L (50-750 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.4 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.4.

Lower limits of measurement

Lower detection limit of the test

0.2 g/L (20 mg/dL)

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

	lambda[6,13]	kappa/lambda ratio[14]
Serum	0.83-2.24 g/L	1.29-2.61

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*
	g/L (mg/dL)	*g/L (mg/dL)*	*%*
Precinorm Protein	1.08 (108)	0.02 (2)	1.7
Precipath Protein	2.26 (226)	0.02 (2)	1.1
Human serum 1	0.88 (88)	0.01 (1)	1.3
Human serum 2	2.39 (239)	0.03 (3)	1.1
Intermediate precision	*Mean*	*SD*	*CV*
	g/L (mg/dL)	*g/L (mg/dL)*	*%*
Precinorm Protein	1.06 (106)	0.02 (2)	1.9
Precipath Protein	2.30 (230)	0.03 (3)	1.4
Human serum 1	0.88 (88)	0.02 (2)	2.5
Human serum 2	2.41 (241)	0.03 (3)	1.2

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

Lambda light chain 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) = 268

Passing/Bablok[15]	Linear regression
y = 0.959x + 0.023 g/L	y = 0.939x + 0.077 g/L
τ = 0.943	r = 0.996

The sample concentrations were between 0.558 and 6.37 g/L (55.8 and 637 mg/dL).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

References

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2 Sun T, de Szalay H, Lien YY, et al. Quantitation of kappa and lambda light chains for the detection of monoclonal gammopathy. J Clin Lab Anal 1988;2:84-90.

3 Whicher JT, Wallage M, Fifield R. Use of immunoglobulin heavy- and light-chain measurements compared with existing techniques as a means of typing monoclonal immunoglobulins. Clin Chem 1987;33:1771-1773.

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

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

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14 Jones RG, Aguzzi F, Bienvenu J, et al. Use of Immunoglobulin Heavy-chain and Light-chain measurement in a multicenter trial to investigate Monoclonal components: I. Detection. Clin Chem 1991;37:1917-1921.

15 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.

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 dialog.roche.com for definition of symbols used):

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

Additions, deletions or changes are indicated by a change bar in the margin.

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Tina-quant Lambda Gen.2

CE 0123

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