LAMB2

cobas®

Tina-quant Lambda Gen.2

Specific proteins

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
06749992 190	Tina-quant Lambda Gen.2 (100 tests)	System-ID 07 6813 8	COBAS INTEGRA 400 plus

Materials required (but not provided):

11355279 216	C.f.a.s. Proteins (5 × 1 mL)	System-ID 07 6557 0	
10557897 122	Precinorm Protein (3 × 1 mL)	System-ID 07 9105 9	
11333127 122	Precipath Protein (3 x 1 mL)	System-ID 07 9106 7	
20756350 322	NaCl Diluent 9 % (6 × 22 mL)	System-ID 07 5635 0	

English

System information

Test LAMB2, test ID 0-303

Intended use

In vitro test for the immunoturbidimetric quantitative determination of bound and free immunoglobulins of the lambda light chain type in human serum and plasma on COBAS INTEGRA systems.

Summary

References[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

- Sample and addition of R1 (buffer)
- Addition of SR (anti-lambda antibody) and start of reaction

Anti-lambda antibodies react with 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

SR 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 SR 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.

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	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: Collect serum using standard sampling tubes.
Plasma: Li-, Na-, NH_4^+-heparin; 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 2-8 °C
	2 months at (-15)-(-25) °C

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

NaCl Diluent 9 %, Cat. No. 20756350322, system-ID 07 5635 0 for automatic sample dilution and standard serial dilutions. NaCl Diluent 9 % is placed in its predefined rack position and is stable for 4 weeks on-board the COBAS INTEGRA 400 plus analyzers.

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.

Application for serum/plasma

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint

LAMB2

Tina-quant Lambda Gen.2

cobas®

Specific proteins

Reaction mode	D-R1-S-SR
Reaction direction	Increase
Wavelength A/B	340/659 nm
Calc. first/last	33/63
Typical prozone effect	> 49 g/L
Antigen excess check	No
Predilution factor	21
Unit	g/L

Pipetting parameters

		Diluent (H_2O)
R1	125 µL	
Sample	4.5 µL	5 µL
SR	45 µL	
Total volume	179.5 µL	

Calibration

Calibrator	C.f.a.s. Proteins
Calibration dilution ratio	1:7, 1:12, 1:24, 1:35, 1:42, 1:57 performed automatically by the instrument
Calibration mode	Logit/log 4
Calibration replicate	Duplicate recommended
Calibration interval	Each lot and as required following quality control procedures

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

Enter the assigned lot-specific lambda value of the undiluted calibrator indicated in the package insert for the calibrator C.f.a.s. Proteins.

Traceability: This method has been standardized against the CRM 470 standard using the Lievens equation.[6]

Quality control

Reference range	Precinorm Protein
Pathological range	Precipath Protein
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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

The COBAS INTEGRA 400 plus analyzer automatically calculates the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

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).[a)]

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

Lipemia (Intralipid):[9] 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.[10, 11]

High dose hook-effect: No false result occurs up to a lambda concentration of 49 g/L.

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 250 IU/mL.

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.

a) Measured at analyte concentrations up to approximately 1.1 g/L

b) Measured at analyte concentrations up to approximately 1.19 g/L

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

Limits and ranges

Measuring range

0.9-7.5 g/L

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.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the rerun function reduces the sample predilution factor to 3.5. The results are automatically multiplied by the reduced predilution factor.

Lower limits of measurement

Lower detection limit of the test:

0.3 g/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 a zero sample (zero sample + 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 (1 aliquot per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
Precinorm Protein	1.23	0.01	1.1
Precipath Protein	2.20	0.02	0.7
Human serum	1.42	0.01	0.9

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
Precinorm Protein	1.35	0.04	2.6
Precipath Protein	2.30	0.03	1.3
Human serum	1.50	0.03	1.9

Method comparison

Lambda light chain values for human serum and plasma samples obtained on a COBAS INTEGRA 700 analyzer (y) were compared with those determined using the same reagent on a Roche/Hitachi 917 analyzer (x).

Roche/Hitachi 917 analyzer	Sample size (n) = 114
Passing/Bablok[15]	Linear regression
y = 0.994x - 0.030 g/L	y = 0.998x - 0.067 g/L
τ = 0.934	r = 0.990

The sample concentrations were between 0.31 and 12.5 g/L.

References

1 Skvaril F, Barandum S, Morell A, et al. Imbalances of kappa/lambda immunoglobulin light chain ratios in normal individuals and in immunodeficient patients. In: Proteides of biological fluids, Peeters H, ed 1975;23:415-420.

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.

4 Keren DF, Warren JS, Lowe JB. Strategy to diagnose monoclonal gammopathies in serum: high-resolution electrophoresis, immunofixation and kappa/lambda quantification. Clin Chem 1988;34:2196-2201.

5 Duc J, Morel B, Peitrequin R, et al. Identification of monoclonal gammopathies: a comparison of immunofixation, immunoelectrophoresis and measurements of kappa- and lambda-immunoglobulin levels. J Clin Lab Immunol 1988;26:141-146.

6 Lievens M. Medical and technical usefulness of measurement of kappa and lambda immunoglobulin light chains in serum with an M-component. J Clin Chem Clin Biochem 1989;27:519-523.

7 Whicher JT, Ritchie RF, Johnson AM, et al. New international reference preparation for proteins in human serum (RPPHS). Clin Chem 1994;40:934-938.

8 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th ed. St. Louis (MO): Saunders Elsevier 2006:674-675.

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 Hafner G, Endler T, Oppitz M, et al. Effects of standardization with the new international reference preparation for proteins in human serum on method comparability and reference values. Clin Lab 1995;41:743-748.

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

CE 0123

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