0008896534190c501V2.0

KFLC

DIAZYME

Kappa (κ) Free Light Chains

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08896534 190	Kappa (κ) Free Light Chains (100 tests)	System-ID 07 7625 6	**cobas c** 311, **cobas c** 501/502
	Calibrator Set included in **08896534** 190	Codes 450-455	
08896577 190	Kappa - Lambda FLC Control Set	Level I: Code 165 Level II: Code 166	

English

Roche does not hold the product registration for Partner Channels. The legal manufacturer indicated on the kit is solely responsible for all of the design, legal, and regulatory aspects of the product.

System information

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

KFLC: ACN 564

For **cobas c** 502 analyzer:

KFLC: ACN 8564

Intended use

The Diazyme Human Kappa (κ) Free Light Chain Assay is intended as a latex particle enhanced immunoturbidimetric assay for the quantitative determination of Kappa Free Light Chain (FLC) concentration in serum on validated analyzers. The measurement of Kappa FLC in conjunction with Lambda FLC aids in the diagnosis and monitoring of multiple myeloma in conjunction with other laboratory findings. For *in vitro* diagnostic use only.

Summary

Normal immunoglobulins are composed of smaller units called heavy chains and light chains. There are 5 types of heavy chains (alpha, delta, epsilon, gamma, and mu), and 2 types of light chains (kappa and lambda). The heavy and light chains are produced separately within plasma cells and are assembled to form a whole ("intact") immunoglobulin. When the light chains are attached to the heavy chains they are called bound, and when they are not attached they are called free. Kappa Free Light Chain (FLC) is a 22 kDa protein while Lambda FLC is usually a dimer of 44 kDa as present in the serum. Elevated levels of Kappa or Lambda FLC are associated with plasma cell disorders such as multiple myeloma, lymphocytic neoplasms, Waldenström's macroglobulinemia, AL amyloidosis, light chain deposition disease and connective tissue diseases such as systemic lupus erythematosus.[1,2,3,4,5]

Test principle

Kappa (κ) Free Light Chains is based on a latex enhanced immunoturbidimetric assay. Kappa FLC in the sample binds to specific anti-Kappa FLC antibody, which is coated on latex particles, and causes agglutination. The degree of the turbidity caused by agglutination can be measured optically and is proportional to the amount of Kappa FLC in the sample. The instrument calculates the Kappa FLC concentration by interpolation of obtained signals of a 6-point calibration curve prepared from calibrators of known concentrations.

Reagents - working solutions

R1 TRIS buffer solution

R3 Latex particles coated with polyclonal rabbit and goat anti-Kappa FLC antibodies

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

Calibrator

Reactive components:

Human serum and additives.

Non-reactive components:

Sodium azide (NaN_3) < 0.1 %.

The Kappa (κ) Free Light Chains Calibrator Set is a 5-level set that is supplied in liquid form (5 x 1.5 mL). The calibrator levels are manufactured from human serum. The concentrations of the calibrators are lot specific and Kappa FLC concentrations are stated in the value sheet in mg/L. Calibrator lots are reagent lot specific. The 5 levels of calibrator and DIH_2O are to be used for a 6-point calibration.

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.

Avoid ingestion and contact with skin and eyes. See the Safety Data Sheet (SDS).

Additional safety information concerning storage or handling of this product is provided within the SDS for this product.

Specimens containing human sourced material should be handled as if potentially infectious using safe laboratory procedures, such as those outlined in Biosafety in Microbiological and Biomedical Laboratories (HHS Publication Number [CDC] 93-8395).

The reagent contains < 0.1 % sodium azide (NaN_3) as preservative. Sodium azide may react with lead and copper to form highly explosive metal azide. On disposal, flush with a large volume of water to prevent azide buildup.

Caution: Federal law restricts this device to sale by or on the order of a physician or other practitioner licensed by laws of the State in which he/she practices, to use or order the use of the device.

Reagent handling

Ready for use

Deionized water is needed to dilute high Kappa FLC samples.

Storage and stability

The Kappa (κ) Free Light Chains reagent and calibrators must be stored at 2-8 °C. **Do not freeze.**

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board stability for the reagent in use and refrigerated on the analyzer is 4 weeks.

The opened calibrators are stable at least for 1 month when stored at 2-8 °C and capped tightly to minimize exposure to air and evaporation. Unopened calibrators are stable until expiration date printed on the vial.

Do not use the reagents and calibrators after the expiration date labeled on the outer box.

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.

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

Stability: 21 days at 2-8 °C

For longer storage, keep samples at -20 °C.

Repeated freeze/thaw cycles must be avoided to minimize potential protein degradation.

Severely turbid samples must not be used.

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

See “Order information” section

General laboratory equipment

Deionized water

KFLC

Kappa (κ) Free Light Chains

DIAZYME

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

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 28-57		
Wavelength (sub/main)	-/570 nm		
Reaction direction	Increase		
Units	mg/L		
Reagent pipetting		Diluent (H_2O)	
R1	84 µL	–	
R3	28 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent* (H_2O)
Normal	6.5 µL	–	–
Decreased	6.5 µL	8 µL	152 µL
Increased	6.5 µL	–	–

cobas c 501/502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 38-70		
Wavelength (sub/main)	-/570 nm		
Reaction direction	Increase		
Units	mg/L		
Reagent pipetting		Diluent (H_2O)	
R1	84 µL	–	
R3	28 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent* (H_2O)
Normal	6.5 µL	–	–
Decreased	6.5 µL	8 µL	152 µL
Increased	6.5 µL	–	–

Calibration

Calibrators	S1: DIH_2O S2: Kappa FLC Calibrator 1 S3: Kappa FLC Calibrator 2 S4: Kappa FLC Calibrator 3 S5: Kappa FLC Calibrator 4 S6: Kappa FLC Calibrator 5
Calibration mode	Spline
Calibration frequency	Full calibration - after **cobas c** pack change - as required following quality control procedures

Traceability: The Kappa (κ) Free Light Chains assay is traceable to an internally assigned master standard.

Quality control

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

In addition, other validated control material can be used.

The range of acceptable control limits should be established by individual laboratories. Follow federal, state and local guidelines for testing QC materials.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample.

Limitations - interference

There are no known international standards for Kappa FLC, however, this assay is predicated to a legally marketed device.

The Diazyme Human Kappa (k) Free Light Chain Assay should be used only with validated instruments using Diazyme provided applications.

To determine the level of interferences from the substances normally present in serum, the Kappa (κ) Free Light Chains assay is tested with normal Kappa FLC and abnormal Kappa FLC (high) serum samples spiked with various concentrations of substances following CLSI EP7-A2 "Interference Testing in Clinical Chemistry" Approved guideline-Second Edition.

The following substances normally present in serum produced less than 10 % deviation when tested at levels equal to the concentrations listed below.

Triglycerides: No significant interference from triglycerides up to a concentration of 1000 mg/dL.

Bilirubin: No significant interference from conjugated and unconjugated bilirubin up to a concentration of 40 mg/dL.

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 10 mM.

Hemoglobin: No significant interference from hemoglobin up to a concentration of 1000 mg/dL.

Rheumatoid factor: No significant interference from rheumatoid factor up to a concentration of 100 IU/mL.

Due to the inherent nature of Kappa and Lambda FLC monoclonal proteins, some samples may be non-linear at different dilutions. If the results do not match patient's medical history, clinical examination and other laboratory findings, the sample should be re-assayed with dilution.

High-dose hook effect: High dose hook effect tolerance was measured up to a Kappa FLC concentration of 100000 mg/L.

All immunoassays have the potential for antigen excess and a small percentage of samples may exhibit prozone behavior due to antigen excess or presence of unknown intrinsic interferents. Undetected antigen excess or unknown intrinsic interferences are low frequency events during FLC immunoassay testing but cannot be excluded. If the result do not match patient's medical history, clinical examination, other laboratory findings and if the sample is from a patient that has previously demonstrated antigen excess, the sample schould be re-assayed with dilution.

Altrough verification and validation studies have examined the effect of likely interferents in this assay, there is a potential for interference from unknown substances. For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other laboratory 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. 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.

Limits and ranges

Measuring range

2.3-150 mg/L (standard mode)

46-3000 mg/L (extended mode)

Determine samples having higher concentrations than the standard mode via the rerun function. Dilution of samples via the rerun function is a 1:20 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 20.

Resolving Kinetics flags >Kin and <Test:

If the first result is flagged >Kin and the rerun result is flagged <Test, the sample should be manually diluted 1:10 with DIH2O and rerun in standard mode. If after manual 1:10 dilution the sample is still flagged <Test, perform a manual 1:5 dilution with DIH2O on the original sample. After dilution, multiply the result by the dilution factor.

The linearity of the Kappa (κ) Free Light Chains assay was evaluated according to CLSI EP6-A guideline.

Reference range

The reference interval of Kappa (κ) Free Light Chains was evaluated according to CLSI C28-A3 protocol with serum samples from 120 apparently healthy individuals. The central 95 % reference interval of 2.37-20.73 mg/L was established.

The ratio of the Kappa (κ) FLC to Lambda (λ) FLC was evaluated. Serum samples from 315 apparently healthy individuals were tested with the Kappa (κ) Free Light Chains assay and Lambda (λ) Free Light Chains assay. The ratio was calculated as Kappa FLC / Lambda FLC. The total range of the ratio was from 0.22 to 1.74, mean ratio was 0.84, and median ratio was 0.81.

Each laboratory, however, is recommended to establish a range of normal values for the population in their region.

Lower limits of measurement

Limit of Blank	= 0.9 mg/L
Limit of Detection	= 1.4 mg/L
Limit of Quantitation	= 2.3 mg/L

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined according to CLSI EP17-A2.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

The Kappa (κ) Free Light Chains assay performance was established on a Roche/Hitachi 917 analyzer with a 6-point calibration using deionized water and separately provided calibrator levels 1-5. Results obtained from individual laboratories may vary.

The precision of the Kappa (κ) Free Light Chains assay was determined in accordance with the CLSI EP5-A requirements. In the study, 8 levels of serum specimens containing Kappa FLC spanning Analytical Measuring Range (AMR) and 2 levels of serum based Kappa FLC controls were tested with 2 runs per day with duplicates over 20 working days using multiple lots of reagents on multiple analyzers. The precision data was analyzed according to 3-way nested ANOVA and the results of mean (mg/L) and CV (%) are summarized below:

1 lot of reagent on 3 analyzers (n = 240)

ID	*Mean*	*Within-run CV*	*Between-run CV*	*Between-day CV*	*Between - instrument CV*	*Total*
S1	9.38	7.6	4.9	3.5	5.1	11.0
S2	35.30	2.1	1.5	1.3	2.0	3.5
S3	122.37	2.4	0.9	1.8	0.8	3.2
S4	5.95	7.5	3.0	8.5	N/A	11.7
S5	15.76	2.9	1.6	2.1	0.2	3.9
S6	25.92	1.7	1.3	0.5	0.4	2.2
S7	139.23	1.5	1.5	0.7	1.1	2.5
S8	2588.59	1.4	0.6	2.6	1.5	3.3
Control 1	16.70	3.2	2.6	2.4	0.9	4.9
Control 2	29.10	2.1	1.2	2.1	5.9	6.7

3 lots of reagents on 1 analyzer (n = 240)

ID	*Mean*	*Within-run CV*	*Between-run CV*	*Between-day CV*	*Between lot CV*	*Total*
S1	9.49	7.9	5.7	5.7	2.6	11.6
S2	35.14	2.9	0.8	1.5	0.8	3.5
S3	121.53	2.6	1.5	2.3	N/A	3.8
S4	5.81	6.3	2.6	2.7	0.7	7.4
S5	15.40	2.4	0.9	0.6	2.2	3.5
S6	25.66	1.1	0.3	0.6	1.0	1.7
S7	138.28	1.1	N/A	1.0	1.0	1.8
S8	2588.45	1.3	1.0	2.5	1.5	3.3
Control 1	16.64	4.2	1.4	3.0	1.6	5.6
Control 2	27.82	3.2	N/A	2.7	1.8	4.6

Method comparison

The method comparison studies of the Kappa (κ) Free Light Chains assay was evaluated following CLSI EP9-A2 protocol. A total of 126 serum samples were tested in comparison with a predicate assay. Among the 126 samples, 39 were Multiple Myeloma (MM), 12 were Monoclonal Gammopathy of Undetermined Significance (MGUS), 34 were Abnormal (due to other disease states) and 41 were Normal (no disease). The concordance between the subject and predicate Kappa FLC is 98 %.

Method	Linear regression	Deming regression
Slope	0.958	0.969
95 % CI	0.932-0.985	0.943-0.996
Intercept	-2.536	-4.813
95 % CI	-14.703-9.632	-17.014-7.388
Correlation coefficient	0.977	0.977

The sample concentrations were between 4.63 and 2975.80 mg/L.

References

1 International Myeloma Foundation. Understanding Serum Free Light Chain Assay 2011.

2 Drayson M, Tang LX, Drew R, Mead GP, Carr-Smith H, Bradwell AR. Serum free light-chain measurements for identifying and monitoring patients with nonsecretory multiple myeloma. Blood 2001;97(9):2900-2.

3 Nelson M, Brown RD, Gibson J, Joshua DE. Measurement of free kappa and lambda chains in serum and the significance of their ratio in patients with multiple myeloma. British Journal of Haematology 1992;81(2):223-30.

4 Nakano T, Miyazaki S, Takahashi H, Matsumori A, Maruyama T, Komoda T, Nagata A. Immunochemical quantification of free immunoglobulin light chains from an analytical perspective. Clinical Chemistry Laboratory Medicine 2006;44(5):522-32.

5 Bradwell AR, Carr-Cmith HD, Mead GP, Harvey TC, Drayson MT. Serum test for assessment of patients with Bence Jones myeloma. Lancet 2003;361(9356):489-91.

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 (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

KFLC

Kappa (κ) Free Light Chains

DIAZYME

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

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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