

Complement C4 FS*

Order Information

Cat. No.

1 1812 99 10 921

Kit size



400 (4 x 100)

Intended Use

Diagnostic reagent for quantitative in vitro determination of complement C4 in human serum or heparin plasma on automated respons[®]910.

Summary

The complement system is a complex innate immune surveillance system, playing a key role in defense against microbial pathogens and prevention of immune complex depositions. It consists of more than 30 plasma proteins and several membrane proteins and serves as a "complement" to antibody-mediated immunity. The complement cascade can be activated by the classical pathway, alternative pathway or by the mannan binding lectin pathway. The classical pathway is activated by immune complexes or by antibodies bound to bacteria or virus. The complement cascade starts with the binding of the C1q part of C1 to the Fc-part of the antibodies and it activates C3 by proteolysis of C4. Microorganisms, polysaccharides, autolysis of C3 or aggregated immunoglobulins activate the alternative pathway. The activation results in decreased concentrations of C3 and/or C4 due to consumption of the intact proteins. Since C3 is common to both pathways, lowered concentrations indicate a general complement activation. In order to differentiate between the pathways C4 levels are measured, considering that C4 is not involved in the alternative pathway. Lowered C3 values are found in inflammatory and infectious diseases, especially in glomerulonephritis and systemic lupus erythematosus (SLE). Depending on the activated pathway, C4 values may be lowered or stay normal. Decreased C4 concentrations without simultaneously lowered C3 levels occur in hereditary or acquired angioneurotic edema. Moreover, hereditary deficiency states of both complement factors have been reported. As acute phase proteins, the protein synthesis of C3 and C4 increases during an acute inflammatory episode. Therefore, a moderately increased complement consumption, due to an activation of the complement system, might not be detected during an acute inflammatory process [1,2].

Method

Immunoturbidimetric test

Determination of C4 concentration by photometric measurement of antigen antibody reaction of antibodies to human C4 with C4 present in the sample.

Reagents

Components and Concentrations

R1:	TRIS	pH 7.5	100 mmol/L
	NaCl		320 mmol/L
R2:	TRIS	pH 8.0	100 mmol/L
	NaCl		300 mmol/L
	Anti-human C4 antibody (goat)		< 1%

Storage and Stability

Reagents are stable up to the date of expiry indicated on the kit, if stored at 2 – 8°C and contamination is avoided. Do not freeze and protect from light.

The open-vial stability of the reagent is 18 months until expiry date.

Warnings and Precautions

- Components contained in Complement C4 FS are classified according to EC regulation 1272/2008 (CLP) as follows:



⚠ Reagent 1: Warning. H319 Causes serious eye irritation. P280 Wear protective gloves/protective clothing/eye protection. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P337+P313 If eye irritation persists: Get medical advice/attention.

- The reagents contain sodium azide (0.95 g/L) as preservative. Do not swallow! Avoid contact with skin and mucous membranes.
- Reagent 2 contains material of biological origin. Handle the product as potentially infectious according to universal precautions and good clinical laboratory practice.
- In very rare cases, samples of patients with gammopathy might give falsified results [3].
- In case of product malfunction or altered appearance that could affect the performance, contact the manufacturer.
- Any serious incident related to the product must be reported to the manufacturer and the competent authority of the Member State where the user and/or patient is located.
- Please refer to the safety data sheets (SDS) and take the necessary precautions for the use of laboratory reagents. For diagnostic purposes, the results should always be assessed with the patient's medical history, clinical examinations and other findings.
- For professional use only.

Waste Management

Refer to local legal requirements for chemical disposal regulations as stated in the relevant SDS to determine the safe disposal.

Warning: Handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Reagent Preparation

The reagents are ready to use. The bottles are placed directly into the reagent rotor.

Materials Required

General laboratory equipment

Specimen

Human serum or heparin plasma

Only use suitable tubes or collection containers for specimen collection and preparation.

When using primary tubes, follow the manufacturer's instructions.

Stability [4]:

2 days	at	20 – 25°C
8 days	at	4 – 8°C
3 months	at	-20°C

Only freeze once. Discard contaminated specimens.

Calibrators and Controls

DiaSys TruCal Protein is recommended for calibration. Calibrator values have been made traceable to the reference material ERM[®]-DA470k/IFCC. Lot specific uncertainties can be obtained on request. Use DiaSys TruLab Protein Level 1 and Level 2 for internal quality control. All target values of the controls are traceable to DiaSys reagent/calibrator system. Quality control must be performed after calibration. Control intervals and limits have to be adapted to the individual requirements of each laboratory. Results must be within the defined ranges. Follow the relevant legal requirements and guidelines. Each laboratory should establish corrective action in case of deviations in control recovery.

	Cat. No.	Kit size
TruCal Protein	5 9200 99 10 039	5 x 1 mL
TruLab Protein Level 1	5 9500 99 10 046	3 x 1 mL
TruLab Protein Level 2	5 9510 99 10 046	3 x 1 mL

Performance Characteristics

Measuring range from 4.20 mg/dL up to 90 mg/dL, depending on the concentration of the highest calibrator. Linearity is given within $\pm 10\%$.
In case of higher concentrations re-measure samples after manual dilution with NaCl solution (9 g/L) or use rerun function.

Limit of detection**	2.09 mg/dL
Limit of quantitation**	4.20 mg/dL
No prozone effect up to 190 mg/dL.	
Onboard stability	2 weeks
Calibration stability	7 days

Interference by	Interferences $\leq 10\%$ up to	Analyte concentration [mg/dL]
Bilirubin (conjugated)	60 mg/dL	13.6
	60 mg/dL	55.7
Bilirubin (unconjugated)	60 mg/dL	12.3
	60 mg/dL	55.4
Hemolysis	1200 mg/dL	12.7
	1200 mg/dL	34.1
IgA	6400 mg/dL	23.8
IgG	6400 mg/dL	16.5
IgM	4100 mg/dL	11.9
Lipemia (triglycerides)	1500 mg/dL	9.70
	2000 mg/dL	46.1
Rheumatoid factor	1200 IU/mL	20.3

For further information on interfering substances, refer to the literature [5-7].

Precision			
Repeatability (n=20)	Sample 1	Sample 2	Sample 3
Mean [mg/dL]	11.5	34.6	51.6
CV [%]	2.78	2.59	4.12
Between day (n=20)	Sample 1	Sample 2	Sample 3
Mean [mg/dL]	12.6	36.7	40.1
CV [%]	3.38	5.44	4.16

Method comparison (n=128)	
Test x	DiaSys Complement C4 FS (Hitachi 917)
Test y	DiaSys Complement C4 FS (respons [®] 910)
Slope	0.955
Intercept	0.734 mg/dL
Coefficient of correlation	0.993

** according to CLSI document EP17-A, Vol. 24, No. 34

Reference Range [8]

10 – 40 mg/dL 0.1 – 0.4 g/L

Each laboratory should check if the reference ranges are transferable to its own patient population and determine own reference ranges if necessary.

Literature

1. Thomas L. Clinical Laboratory Diagnostics [Internet]. Prof. Lothar Thomas; 2020 [cited 2021 Dec 30]. Available from: <https://www.clinical-laboratory-diagnostics.com>
2. Johnson AM, Rohlfis EM, Silverman LM. Proteins. In: Burtis CA, Ashwood ER. editors. Tietz textbook of clinical chemistry. 3rd ed. Philadelphia: W. B. Saunders Company; 1999. p. 502-7.
3. Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med. 2007;45:1240-1243.
4. Guder WG, da Fonseca-Wollheim F, Heil W, Schmitt Y, Töpfer G, Wisser H, Zawta B. Quality of Diagnostic Samples. 3rd edition; 2010. p. 40-1
5. Young DS. Effects of Drugs on Clinical Laboratory Tests. 5th ed. Volume 1 and 2. Washington DC: The American Association for Clinical Chemistry Press; 2000.
6. Young DS. Effects on Clinical Laboratory Tests - Drugs Disease, Herbs & Natural Products [Internet]. AACC Press and John Wiley and Sons, Inc; 2021 [cited 2022 April]. Available from: <https://clinfx.wiley.com/aaccweb/aacc/>
7. 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;38:376-85.
8. Dati F, Schumann G, Thomas L, Aguzzi F, Baudner S, Biennvenu J et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against the IFCC/BCR/CAP reference material (CRM 470). Eur J Clin Chem Clin Biochem 1996;34:517-20.

Additions and/or changes in the document are highlighted in grey. Deletions are communicated via customer info by stating the edition no. of the package insert/instruction for use.



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* Fluid Stable

Complement C4 FS

Application for serum and plasma samples

This application was set up and evaluated by DiaSys. It is based on the standard equipment at that time and does not apply to any equipment modifications undertaken by unqualified personnel.

Identification	
This method is usable for analysis:	Yes
Twin reaction:	No
Name:	C4
Shortcut:	
Reagent barcode reference:	705
Host reference:	705

Technic	
Type:	End point
First reagent:[μ L]	180
Blank reagent	Yes
Sensitive to light	
Second reagent:[μ L]	36
Blank reagent	No
Sensitive to light	
Main wavelength:[nm]	340
Secondary wavelength:[nm]	
Polychromatic factor:	
1 st reading time [min:sec]	(04:24)
Last reading time [min:sec]	10:00
Reaction way:	Increasing
Linear Kinetics	
Substrate depletion: Absorbance limit	
Linearity: Maximum deviation [%]	
Fixed Time Kinetics	
Substrate depletion: Absorbance limit	
Endpoint	
Stability: Largest remaining slope	
Prozone Limit [%]	

Reagents	
Decimals	
Units	

Sample	
Diluent	DIL A (NaCl)
Hemolysis:	
Agent [μ L]	0 (no hemolysis)
Cleaner	
Sample [μ L]	0
Technical limits	
Concentration technical limits-Lower	4.20
Concentration technical limits-Upper	90
SERUM	
Normal volume [μ L]	5
Normal dilution (factor)	1
Below normal volume [μ L]	10
Below normal dilution (factor)	1
Above normal volume [μ L]	3
Above normal dilution (factor)	1
URINE	
Normal volume [μ L]	5
Normal dilution (factor)	1
Below normal volume [μ L]	10
Below normal dilution (factor)	1
Above normal volume [μ L]	3
Above normal dilution (factor)	1
PLASMA	
Normal volume [μ L]	5
Normal dilution (factor)	1
Below normal volume [μ L]	10
Below normal dilution (factor)	1
Above normal volume [μ L]	3
Above normal dilution (factor)	1
CSF	
Normal volume [μ L]	5
Normal dilution (factor)	1
Below normal volume [μ L]	10
Below normal dilution (factor)	1
Above normal volume [μ L]	3
Above normal dilution (factor)	1
Whole blood	
Normal volume [μ L]	5
Normal dilution (factor)	1
Below normal volume [μ L]	10
Below normal dilution (factor)	1
Above normal volume [μ L]	3
Above normal dilution (factor)	1

Results	
Decimals	2
Units	mg/dL
Correlation factor-Offset	0.000
Correlation factor-Slope	1.000

Range	
Gender	All
Age	
SERUM	#
URINE	
PLASMA	#
CSF	
Whole blood	
Gender	
Age	
SERUM	
URINE	
PLASMA	
CSF	
Whole blood	

Contaminants	
Please refer to r910 Carryover Pair Table	

Calibrators details	
Calibrator list	Concentration
Cal. 1/Blank	0
Cal. 2	*
Cal. 3	*
Cal. 4	*
Cal. 5	*
Cal. 6	
	Max delta abs.
Cal. 1	0.1000
Cal. 2	0.0100
Cal. 3	0.0100
Cal. 4	0.0100
Cal. 5	0.0100
Cal. 6	0.0200
Drift limit [%]	5.0

Calculations	
Model	Akima Spline
Degree	Auto

* Enter calibrator value

Editable by user