TRIMERO Diagnostics, SL
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CE IVD

EN

INSTRUCTIONS FOR USE

Reagents for professional use,
for *In Vitro* use only in clinical laboratory (IVD)

3diag - C1q - TIA

C1q Complement for Turbidimetry

REF **TD-42551**

(Product included in REF TD-42555)

INTENDED USE

Quantitative determination of C1q Complement (C1q), in human serum, by turbidimetric method in automatic Clinical Chemistry Analyzers.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, bound to polystyrene particles, when combined with the antigens (Ag) of the patient sample, form insoluble compounds causing a change in the absorbance and dispersion of the light, proportional to the antigen concentration, which can be quantified by turbidimetric (TIA) or nephelometric (NIA) method, by comparison with calibrators of known concentration.

CONTENTS - COMPOSITION - PREPARATION

- Antiserum Reagent: REAG | Ab | C1q
  REF TD-42551-RA ▽ 100 test (*1) - 5 ml
  Anti-C1q antibodies, bound to polystyrene particles.
- Reaction Buffer: BUF | C1q
  REF TD-42551-BF ▽ 100 test (*1) - 20 ml
  TRIS Buffer, with PEG.

Note (*1): with the recommended assay general parameters.

As a preservative, the reagents contain <0.1% (1 g/l) Sodium Azide (NaN_3).

The reagents are ready for use and require no preparation.

Before each use it is convenient that the reagents are homogenized, shaking them gently avoiding the formation of foam or bubbles.

WARNINGS - PRECAUTIONS

- Sodium Azide is toxic. Even if sodium azide is not harmful at the concentration present in the reagents, take the necessary precautions to avoid accidental ingestion or contact with the eyes.
- Sodium Azide can react with lead or copper to give explosive compounds. For disposal it is recommended to rinse with plenty of running water to avoid accumulation in drains.
- Since the absence of infectious agents can not be proven with absolute certainty, components containing materials of human or animal origin must be handled with caution, as potentially infectious, following the recommended safety standards for biological risk.
- Do not mix components belonging to different lot kits.
- Clinical diagnosis should not be based on the results of a single test, but should always integrate all relevant clinical and laboratory data.

STORAGE - SHELF LIFE

- Store refrigerated at +2...+8ºC. Do not freeze, as the functionality of the reagents may be altered.
- Properly stored and unopened, the reagents are stable until the expiration date indicated on the label.
- Once opened, the shelf life of the reagents is at least 4 weeks, provided that after each use they are stored immediately in the original containers, tightly capped and refrigerated at +2...+8ºC. This information should be taken as a guideline given that, obviously, the shelf life depends on the particular environmental and use conditions, which may differ from those of the stability studies carried out.

MATERIALS NEEDED, NOT SUPPLIED

- Automatic Clinical Chemistry Analyzer, capable of running photometric assays at 540...600 nm, and accessories: reagent containers, cuvettes, etc..
- 3diag - C1q - CAL SET REF TD-42542
- 3diag - C1q - CAL REF TD-42552
- 3diag - C1q - CONTROL REF TD-42543

SAMPLES

Fresh Serum.

Samples with presence of fibrin should be centrifuged.

Do not use hemolyzed, lipemic or contaminated samples.

In bibliography(1) it is reported the following stability in serum:

- Refrigerated: 10 days
- Freezed: 29 days.

PROCEDURE

If necessary, carefully transfer the reagents to the containers used by the analyzer, preventing leakage and foaming or bubbles.

To program and calibrate assays, follow the instructions for use of the analyzer used, with the recommended general parameters that are detailed below.

Please, contact the Customer Support Service (support@3diag.com - ☎ +34 93 2448679) for further information about applications to specific analyzers.

Assay Parameters

- ①Dispense and mix:
  - Sample/Calibrator/Control: 10 µl (diluted 1:30)
  - BUF | C1q 200 µl
- ②Incubate a fixed time between 1 and 5 minutes
- ③Dispense and mix:
  - REAG | Ab | C1q 50 µl
- ④Read absorbance A1 (Blank) at 540...600 nm
- ⑤Incubate a fixed time of about 5 minutes
- ⑥Read absorbance A2 (End Point) at 540...600 nm
- ⑦Interpolate the absorbance increment (A2-A1) of the samples and controls in the curve obtained with the calibrators
- ⑧Samples with concentrations higher than the upper limit of the assay range should be analyzed again, diluted manually, or by programming a larger sample dilution in the analyzer, to recover a value close to the midpoint of the measurement range. It is recommended to use Saline as diluent.

As an alternative, reagents can be mixed as first step, and the sample dispensed as starter.

Calibration Parameters

- Use the 3diag - C1q - CAL SET or, if using the 3diag - C1q - CAL program in the analyzer or prepare the following dilutions: 1:1, 2:3, 1:2, 1:3, 1:6 and 1:12 (100, 66.7, 50, 33.3, 16.7 and 8.33 %).
- It is recommended to use Saline as diluent.
- If the analyzer allows it, it is recommended to program two replicates of each calibration point.

- The calibrations are Non-linear. For the calculation it is recommended to use a 3rd Order Polynomial, a Logit or a Polygonal adjustment.
- The assay must be recalibrated, at least when a new batch of reagents is used or when its parameterization is changed.

PERFORMANCES OF THE METHOD

Detailed information on the characteristics and performances of the assay is given in the Technical Report, available on the website (www.3diag.com) or upon request to the Customer Support Service (support@3diag.com - ☎ +34 93 2448679).

QUALITY CONTROL

To monitor performances, it is recommended that internal controls be inserted into each analytical series. It is recommended to use the controls of the **3diag - C1q - CONTROL**.

For some analyzers, in order to process the controls it may be necessary to deactivate the clot detection system.

Each laboratory should establish its own quality scheme and corrective actions if controls do not meet the assigned tolerances.

The reagents have been subjected to quality control checks and should react as described in these instructions. Therefore, as a general recommendation, in case the controls do not give the expected reaction, as a precaution all reagents should be considered unreliable until their operation has been checked.

TRACEABILITY

Values in IU/ml are referred to the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: W1032) of the *WHO* (*World Health Organization*).

For the values in mg/dl, given that certified reference materials in these units are not available, the values are referred to internal standards of highly purified proteins. Traceability is ensured by measuring the C1q in the *WHO* standard.

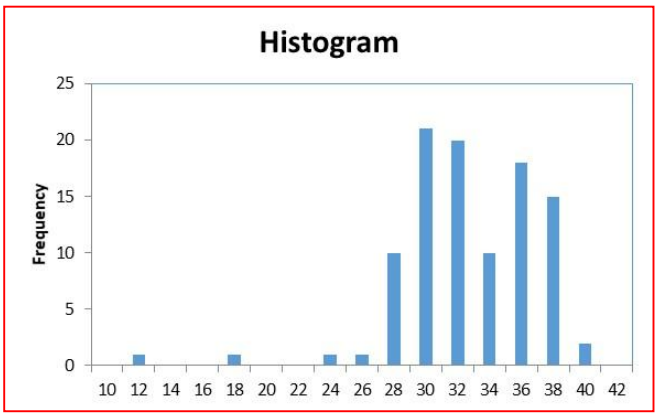
REFERENCE INTERVALS

It is always advisable for each laboratory to establish its own reference values.

The bibliography reports very variable reference values between publications, depending on the method used and the population analyzed: between 5.0 to 8.6 mg/dl[(1)], 10 to 25 mg/dl[(2)], 5.8 to 7.2 mg/dl[(3)], 12 to 22 mg/dl[(4)], and 17.5 to 48.5 mg/dl[(5)].

Analyzing, by turbidimetric method, serum samples from 100 presumably healthy adult patients from the Barcelona area, the following results have been obtained (see table and histogram):

units	mean	SD	range	95 percentile
IU/ml	127	16.7	47.4 - 154	**100 - 147**
mg/dl	32.7	4.30	12.2 - 39.5	**25.7 - 37.9**



In view of the results, a concentration lower than about 100 IU/ml, equivalent to about 25 mg/dl, can be taken as a significant value, since high values of C1q have no established clinical significance[(1)(3)(4)].

CLINICAL SIGNIFICANCE

C1q component of the complement system is a glycoprotein with an approximate molecular weight of 400 kDa, composed of 18 peptide chains divided in 3 sub-units of 6. Together with the components C1r and C1s, it constitutes the C1 complex.

C1q recognizes and binds to Fc fragments of IgG and IgM immunoglobulins bound to antigen, thus activating the classical complement pathway cascade. The conformational changes produced by immunoglobulin binding enzymatically activate C1r and C1s which then continue the complement cascade.

In addition to activation of the complement classical pathway, another function of C1q is the elimination of immune complexes and apoptotic cells from the body.

C1q congenital deficiency is extremely rare (a few dozen cases in which the majority of patients suffered from Systemic Lupus (SLE)). Sometimes acquired deficiency is due to the presence of anti-C1q auto-antibodies.

Its deficiency has a significant effect on the host defense mechanisms and in the elimination of immune complexes. It is normally associated with a high incidence of autoimmune and infectious diseases.

Reduced levels of C1q are often found in acquired angioedema, due to the hiperactivation of the classical pathway of complement.

SYMBOLS

In addition to the harmonized symbols provided on the European Standard EN 980:2008, in the labels and instructions of use has been used the complementary symbology proposed[(6)] by the *EDMA* (*European Diagnostic Manufacturers Association*), whose meaning is detailed below.

REAG	Reagent
Ab	Antibody / Antiserum
BUF	Buffer
C1q	C1q Complement

BIBLIOGRAPHY

(1) *Quest Diagnostics™* website (www.questdiagnostics.com), date of consultation: 14th June 2017.
(2) Putnam F.W. - "*The Plasma Protein - II Edition*".
(3) *"AEFA/AEBM Nomenclator de Laboratorio Clínico"* (*ISBN*: 84-486-0117-3).
(4) *Mayo Medical Laboratories* website (www.mayomedicallaboratories.com), date of consultation: 28th March 2018.
(5) M.C. Sánchez Pozo et al.: "*Estudio de Valores de Referencia del Complemento*" - Poster, XXII Congreso Nacional del Laboratorio Clínico, Bilbao, Oct-2018.
(6) EDMA Labelling Task Force: "*EDMA Symbols for IVD Reagents and Components - Revision, October 2009*".

TEXT REVISION DATE

13th January 2023.

Modifications highlighted in blue.

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INSTRUCTIONS FOR USE

Reagents for professional use,
for *In Vitro* use only in clinical laboratory (IVD)

3diag - C1q - CAL

C1q Complement
Calibrator
REF **TD-42552**

INTENDED USE

Elaboration of the calibration curve for the quantitative determination of C1q Complement (C1q), in human serum, by immunochemical methods.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, bound to polystyrene particles, when combined with the antigens (Ag) of the patient sample, form insoluble compounds causing a change in the absorbance and dispersion of the light, proportional to the antigen concentration, which can be quantified by turbidimetric (TIA) or nephelometric (NIA) method, by comparison with calibrators of known concentration.

CONTENTS - COMPOSITION - PREPARATION

- Calibrator : CAL | C1q
  REF TD-42552 CONT 1 ml

The calibrators are human serum solutions, delipidated, filtered by 0.2 µm.
As preservatives, the calibrators contain <0.1% (1 g/l) Sodium Azide (NaN_3), <0.02% (0.2 g/l) Methylisothiazolone and <0.02% (0.2 g/l) Bromonitrodioxane.
The calibrators are ready for use and require no preparation.
Before each use it is convenient that the calibrators are homogenized, shaking them gently avoiding the formation of foam or bubbles.
The values of the calibrators are lot dependent and are indicated in the table of values of their Instructions for Use.

WARNINGS - PRECAUTIONS

- Sodium Azide is toxic. Even if at the concentrations present neither Sodium Azide nor the other preservatives are harmful, take the necessary precautions to avoid accidental ingestion or contact with the eyes.
- Sodium Azide can react with lead or copper to give explosive compounds. For disposal it is recommended to rinse with plenty of running water to avoid accumulation in drains.
- Materials of human origin have been tested and found negative for the presence of HBsAg, HCV, and anti-HIV 1 and 2 antibodies.
- Since the absence of infectious agents can not be proven with absolute certainty, components containing materials of human or animal origin must be handled with caution, as potentially infectious, following the recommended safety standards for biological risk.
- Do not mix components belonging to different lot kits.
- Clinical diagnosis should not be based on the results of a single test, but should always integrate all relevant clinical and laboratory data.

STORAGE - SHELF LIFE

- Store refrigerated at +2...+8ºC. Do not freeze, as the functionality of the calibrators may be altered.
- Properly stored and unopened, the calibrators are stable until the expiration date indicated on the label.
- Once opened, the shelf life of the calibrators is at least 4 weeks, provided that after each use they are stored immediately in the original containers, tightly capped and refrigerated at +2...+8ºC. This information should be taken as a guideline given that, obviously, the shelf life depends on the particular environmental and use conditions, which may differ from those of the stability studies carried out.

MATERIALS NEEDED, NOT SUPPLIED

The calibrators are intended to be used in conjunction with the Reagents and Controls:

- 3diag - C1q - TIA — REF TD-42551
- 3diag - C1q - CONTROL — REF TD-42543

PROCEDURE

Follow the Instructions for Use of the analyzer used to program and calibrate an assay, with the general parameters recommended in the Instructions for Use of Reagents.
In some analyzers, in order to process the calibrators it may be necessary to deactivate the clot detection system.

TRACEABILITY

Values in IU/ml are referred to the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: W1032) of the *WHO* (*World Health Organization*).
For the values in mg/dl, given that certified reference materials in these units are not available, the values are referred to internal standards of highly purified proteins. Traceability is ensured by measuring the C1q in the *WHO* standard.

SYMBOLS

In addition to the harmonized symbols provided on the European Standard EN 980:2008, in the labels and instructions of use has been used the complementary symbology proposed(1) by the *EDMA* (*European Diagnostic Manufacturers Association*), whose meaning is detailed below.

(1) EDMA Labelling Task Force: "*EDMA Symbols for IVD Reagents and Components - Revision, October 2009*".

CAL	Calibrator
C1q	C1q Complement
CONT	Contents

TEXT REVISION DATE

5th March 2020.

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INSTRUCTIONS FOR USE

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3diag - C1q - CONTROL

C1q Complement
Controls (2 lev.)
REF **TD-42543**
(Product included in REF TD-42540)

INTENDED USE

Internal controls, with assigned values, for the quantitative determination of C1q Complement (C1q), in human serum, by immunochemical methods.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, bound to polystyrene particles, when combined with the antigens (Ag) of the patient sample, form insoluble compounds causing a change in the absorbance and dispersion of the light, proportional to the antigen concentration, which can be quantified by turbidimetric (TIA) or nephelometric (NIA) method, by comparison with calibrators of known concentration.

CONTENTS - COMPOSITION - PREPARATION

- High Control: CONTROL | H | C1q
  REF TD-42543-H — CONT 1 ml
- Low Control: CONTROL | L | C1q
  REF TD-42543-L — CONT 1 ml

The controls are human serum solutions, delipidated, filtered by 0.2 µm.
As preservatives, the controls contain <0.1% (1 g/l) Sodium Azide (NaN_3), <0.02% (0.2 g/l) Methylisothiazolone and <0.02% (0.2 g/l) Bromonitrodioxane.
The controls are ready for use and require no preparation.
Before each use it is convenient that the controls are homogenized, shaking them gently avoiding the formation of foam or bubbles.
The values of the controls are lot dependent and are indicated in the table of values of their Instructions for Use.

WARNINGS - PRECAUTIONS

- Sodium Azide is toxic. Even if at the concentrations present neither Sodium Azide nor the other preservatives are harmful, take the necessary precautions to avoid accidental ingestion or contact with the eyes.
- Sodium Azide can react with lead or copper to give explosive compounds. For disposal it is recommended to rinse with plenty of running water to avoid accumulation in drains.
- Materials of human origin have been tested and found negative for the presence of HBsAg, HCV, and anti-HIV 1 and 2 antibodies.
- Since the absence of infectious agents can not be proven with absolute certainty, components containing materials of human or animal origin must be handled with caution, as potentially infectious, following the recommended safety standards for biological risk.
- Do not mix components belonging to different lot kits.
- Clinical diagnosis should not be based on the results of a single test, but should always integrate all relevant clinical and laboratory data.

STORAGE - SHELF LIFE

- Store refrigerated at +2...+8ºC. Do not freeze, as the functionality of the controls may be altered.
- Properly stored and unopened, the controls are stable until the expiration date indicated on the label.
- Once opened, the shelf life of the controls is at least 4 weeks, provided that after each use they are stored immediately in the original containers, tightly capped and refrigerated at +2...+8ºC. This information should be taken as a guideline given that, obviously, the shelf life depends on the particular environmental and use conditions, which may differ from those of the stability studies carried out.

MATERIALS NEEDED, NOT SUPPLIED

The controls are intended to be used in conjunction with the Reagents and Calibrators:

3diag - C1q - 800	REF TD-42541
3diag - C1q - TIA	REF TD-42551
3diag - C1q - CAL SET	REF TD-42542
3diag - C1q - CAL	REF TD-42552

PROCEDURE

Follow the Instructions for Use of the analyzer used to program and calibrate an assay, with the general parameters recommended in the Instructions for Use of Reagents.
For some analyzers, in order to process the controls it may be necessary to deactivate the clot detection system.

TRACEABILITY

Values in IU/ml are referred to the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: W1032) of the *WHO* (*World Health Organization*).
For the values in mg/dl, given that certified reference materials in these units are not available, the values are referred to internal standards of highly purified proteins. Traceability is ensured by measuring the C1q in the *WHO* standard.

SYMBOLS

In addition to the harmonized symbols provided on the European Standard EN 980:2008, in the labels and instructions of use has been used the complementary symbology proposed(1) by the *EDMA* (*European Diagnostic Manufacturers Association*), whose meaning is detailed below.

(1) EDMA Labelling Task Force: "*EDMA Symbols for IVD Reagents and Components - Revision, October 2009*".

CONTROL	Control
H	High
L	Low
C1q	C1q Complement
CONT	Contents

TEXT REVISION DATE

12th June 2020.