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 - C5 - TIA

C5 Complement
for Turbidimetry
REF TD-42571

INTENDED USE

Quantitative determination of C5 Complement (C5), in human serum, by turbidimetric method in automatic Clinical Chemistry Analyzers.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, 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 | C5
  REF TD-42571-RA ▽ 100 test - 6 ml
  Solution of anti-human C5 antibodies.
- Reaction Buffer: BUF | C5
  REF TD-42571-BF ▽ 100 test - 20 ml
  PBS Buffer, with PEG.

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

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 340 nm, and accessories: reagent containers, cuvettes, etc..
- 3diag - C5 - CAL SET — REF TD-42562
- 3diag - C5 - CAL-L — REF TD-42578
- 3diag - C5 - CONTROL — REF TD-42573
- 3diag - C5 - CONTROL (x3) — REF TD-42563

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: 7 days - Freezed: 60 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 93 244 86 79) for further information about applications to specific analyzers.

Assay Parameters

- ①Dispense and mix:
  - Sample/Control: 50 µl (diluted 1:10)
  - Calibrator:
    50 µl (diluted 1:10, if 3diag - C5 - CAL SET is used)
  - BUF | C5 140 µl
- ②Incubate a fixed time between 1 and 5 minutes
- ③Dispense and mix:
  - REAG | Ab | C5 60 µl
- ④Read absorbance A1 (Blank) at 340 nm
- ⑤Incubate a fixed time of about 5 minutes
- ⑥Read absorbance A2 (End Point) at 340 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 with Physiological Solution, or by programming a larger sample dilution in the analyzer, to recover a value close to the midpoint of the measurement range.

Calibration Parameters

- Use the 3diag - C5 - CAL SET or, if using the 3diag - C5 - CAL-L, program in the analyzer or prepare the necessary dilutions, and program the dilution factor of the calibrator analysis necessary, to obtain an equivalent measurement range.
- It is recommended to use Physiological Solution 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 93 244 86 79).

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 - C5 - CONTROL**.

In 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 C5 in the *WHO* standard.

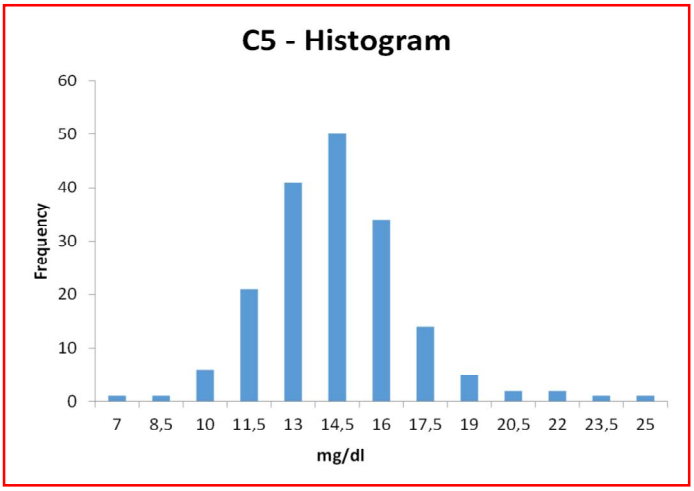
REFERENCE INTERVALS

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

The bibliography[(1)] reports reference values between 10.6 and 26.3 mg/dl.

Analyzing serum samples of 179 patients from Spanish hospital laboratories, without discarding those that presented alterations of other components of the complement, the following results have been obtained (see table and histogram):

units	mean	SD	range	95 percentile	90 percentile
IU/ml	109	20.0	49.8 - 194	77.4 - 152	79.8 - 142
mg/dl	13.8	2.53	6.30 - 24.5	9.80 - 19.3	10.1 - 18.0



In view of the results, a concentration lower than about 10 mg/dl, equivalent to about 80 IU/ml, can be taken as a significant value, indicative of a deficiency or consumption.

CLINICAL SIGNIFICANCE

Deficiency of C5 is associated with increased susceptibility to recurrent severe bacterial infections and has also been linked to susceptibility to autoimmune diseases, such as Systemic Lupus (SLE), Rheumatoid Arthritis or Liver Fibrosis.

Low levels of C5 and normal levels of C3 and C4 are consistent with C5 deficiency, while if reduced levels of C3 and C4 are also found, complement consumption is indicated.

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[(2)] by the *EDMA* (*European Diagnostic Manufacturers Association*), whose meaning is detailed below.

REAG	Reagent
Ab	Antibody / Antiserum
BUF	Buffer
C5	C5 Complement

BIBLIOGRAPHY

(1) *Mayo Medical Laboratories* website (www.mayomedicallaboratories.com), date of consultation: 7th June 2017.

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

TEXT REVISION DATE

6th February 2020.

Modifications highlighted in blue.

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INSTRUCTIONS FOR USE

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3diag - C5 - CAL SET

C5 Complement
Calibrators (6 lev.)
REF **TD-42562**
(Product included in REF TD-42560)

INTENDED USE

Elaboration of the calibration curve for the quantitative determination of C5 Complement (C5), in human serum, by immunochemical methods.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, 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 Level 1: CAL 1 C5
  REF TD-42562-1 CONT 1 ml
- Calibrator Level 2: CAL 2 C5
  REF TD-42562-2 CONT 1 ml
- Calibrator Level 3: CAL 3 C5
  REF TD-42562-3 CONT 1 ml
- Calibrator Level 4: CAL 4 C5
  REF TD-42562-4 CONT 1 ml
- Calibrator Level 5: CAL 5 C5
  REF TD-42562-5 CONT 1 ml
- Calibrator Level 6: CAL 6 C5
  REF TD-42562-6 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 - C5 - 800 REF TD-42561
- 3diag - C5 - TIA REF TD-42571
- 3diag - C5 - CONTROL REF TD-42573

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 C5 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
n	Level n (n=1..6)
C5	C5 Complement
CONT	Contents

TEXT REVISION DATE

6th May 2019.

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INSTRUCTIONS FOR USE

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3diag - C5 - CONTROL

C5 Complement
Controls (2 lev.)
REF **TD-42573**

INTENDED USE

Internal controls, with assigned values, for the quantitative determination of C5 Complement (C5), in human serum, by immunochemical methods.

PRINCIPLE OF THE METHOD

The specific antibodies (Ab) of the reagent, 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 | C5
  REF TD-42573-H — CONT 1 ml
- Low Control: CONTROL | L | C5
  REF TD-42573-L — CONT 1 ml

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 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 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 - C5 - TIA — REF TD-42571
- 3diag - C5 - CAL SET — REF TD-42562
- 3diag - C5 - CAL-L — REF TD-42578

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 C5 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
C5	C5 Complement
CONT	Contents

TEXT REVISION DATE

3rd August 2022.