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 - C1In - TIA

C1 (Esterase) Inhibitor for Turbidimetry

REF **TD-42591**

INTENDED USE

Quantitative determination of Complement C1 (Esterase) Inhibitor (C1In, CEI), 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 | C1In
  REF TD-42591-RA ▽ 100 test - 6 ml
  Solution of anti-human C1In antibodies.
- Reaction Buffer: BUF | C1In
  REF TD-42551-BF ▽ 100 test - 18 ml
  TRIS 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 - C1In - CAL SET — REF TD-42582
- 3diag - C1In - CONTROL — REF TD-42583

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: 72 hours - Frozen: 14 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.

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

Assay Parameters

- ①Dispense and Mix:
  - Sample/Calibrator/Control: 20 µl (diluted 1:5)
  - BUF | C1In 180 µl
- ②Incubate a fixed time between 1 and 5 minutes
- ③Dispense and Mix:
  - REAG | Ab | C1In 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 - C1In - CAL SET.
- 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 - C1In - 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

Given that certified reference materials are not available, the values are referred to internal standards of highly purified proteins.

Traceability is ensured by measuring the C1In in the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: W1032) of the *WHO* (*World Health Organization*).

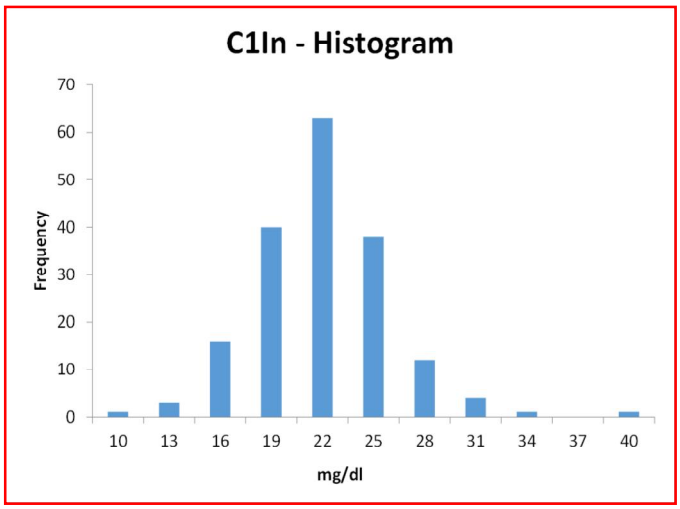
REFERENCE INTERVALS

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

The bibliography reports, depending on the method used and the population analyzed, reference values of between 19 to 37 mg/dl[(1)], 15 to 35 mg/dl[(2)] and 17.4 to 24.0 mg/dl[(3)].

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 (in mg/dl):

media	DS	rango	percentil 95	percentil 90
20.7	3.91	9.18 - 38.5	14.2 - 28.5	15.0 - 26.8



In view of the results, a concentration lower than about 15 mg/dl can be taken as a significant value, indicative of a deficiency, since high C1In values do not have an established clinical significance[(1)(3)].

CLINICAL SIGNIFICANCE

C1 inhibitor deficiency is associated with hereditary or acquired angioedema. In 85% of cases their levels are decreased (5-30% of their normal value), while in the remaining 15%, the levels are normal but the protein is not functional. The additional measurement of C1q is key to distinguish between hereditary or acquired angioedema, since it presents normal levels in the hereditary form and low levels in the acquired form.

Low levels of C1 inhibitor also predispose to autoimmune diseases, especially Lupus Erythematosus (SLE), due to its effect of consumption of C3 and C4.

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

REAG	Reagent
Ab	Antibody / Antiserum
BUF	Buffer
C1In	C1 (Esterase) Inhibitor

BIBLIOGRAPHY

(1) *Mayo Medical Laboratories* website (www.mayomedicallaboratories.com), date of consultation: 8th May 2018.
(2) Putnam F.W. - The Plasma Protein - II Edition.
(3) *"Nomenclator de Laboratorio Clinico AEFA/AEBM"* - ISBN: 84-486-0117-3.
(4) EDMA Labelling Task Force: "*EDMA Symbols for IVD Reagents and Components - Revision, October 2009*".

TEXT REVISION DATE

12th December 2019.

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INSTRUCTIONS FOR USE

Reagents for professional use,
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3diag - C1In - CAL SET

C1 (Esterase) Inhibitor
Calibrators (6 lev.)
REF **TD-42582**
(Product included in REF TD-42580)

INTENDED USE

Elaboration of the calibration curve for the quantitative determination of Complement C1 (Esterase) Inhibitor (C1In, CEI), 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 | C1In
  REF TD-42582-1 — CONT 1 ml
- Calibrator Level 2: CAL | 2 | C1In
  REF TD-42582-2 — CONT 1 ml
- Calibrator Level 3: CAL | 3 | C1In
  REF TD-42582-3 — CONT 1 ml
- Calibrator Level 4: CAL | 4 | C1In
  REF TD-42582-4 — CONT 1 ml
- Calibrator Level 5: CAL | 5 | C1In
  REF TD-42582-5 — CONT 1 ml
- Calibrator Level 6: CAL | 6 | C1In
  REF TD-42582-6 — 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 - C1In - 800 — REF TD-42581
- 3diag - C1In - TIA — REF TD-42591
- 3diag - C1In - CONTROL — REF TD-42583

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

Given that certified reference materials are not available, the values are referred to internal standards of highly purified proteins. Traceability is ensured by measuring the C1In in the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: *W1032*) de la *WHO* (*World Health Organisation*).

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)
C1In	C1 (Esterase) Inhibitor
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INSTRUCTIONS FOR USE

Reagents for professional use,
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3diag - C1In - CONTROL

C1 (Esterase) Inhibitor
Controls (2 lev.)
REF **TD-42583**
(Product included in REF TD-42580)

INTENDED USE

Internal controls, with assigned values, for the quantitative determination of Complement C1 (Esterase) Inhibitor (C1In, CEI), 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 | C1In
  REF TD-42583-H — CONT 1 ml
- Low Control: CONTROL | L | C1In
  REF TD-42583-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 - C1In- 800 — REF TD-42581
- 3diag - C1In - TIA — REF TD-42591
- 3diag - C1In - CAL SET — REF TD-42582

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

Given that certified reference materials are not available, the values are referred to internal standards of highly purified proteins.
Traceability is ensured by measuring the C1In in the *International Ref. Preparation for human serum complement Factors* (*NIBSC* code: *W1032*) de la *WHO* (*World Health Organisation*).

SYMBOLS

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

CONTROL	Control
H	High
L	Low
C1In	C1 (Esterase) Inhibitor
CONT	Contents

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23rd June 2020.