CRP-CHECK-1

Quantitative determination of C-Reactive Protein in whole blood

- FOR EASY READER® OR EASY READER+®USE ONLY -

Ref. 34191-3L (Doctor's office version)

- PATENTED TEST -

I- PRINCIPLE

C-Reactive Protein (CRP) is a non specific, acute-phase reactant used to diagnose bacterial infectious disease and inflammatory disorders, such as acute rheumatic fever and rheumatoid arthritis (1, 2). CRP levels do not consistently rise with viral infections. CRP is an abnormal protein produced primarily by the liver during an acute inflammatory process (3). A positive test result indicates the presence, but not the cause, of an acute inflammatory reaction (4). The synthesis of CRP is initiated by antigen-immune complexes, bacteria, fungi, and trauma.

The CRP test is a more sensitive and rapidly responding indicator than the erythrocyte sedimentation rate (5, 6) and could be helpful for an antibiotic treatment decision (7).

This test is also useful in evaluating patients with an acute myocardial infarction. The level of CRP correlates with peak levels of the MB isoenzyme of creatine kinase, but CRP peaks occur 1 to 3 days later. Failure of CRP to normalise may indicate ongoing damage to the heart tissue. Levels are not elevated in patients with angina.

CRP is classically measured using latex agglutination and nephelometric or turbidimetric methods. CRP-CHECK-1 is a rapid quantitative screening test for the detection of CRP in whole blood samples.

Depending on the CRP concentration, different lines will appear in the reading window, allowing the quantitative measurements of CRP in whole blood samples, when used in combination with the EASYREADER® or EASYREADER+® rapid test readers.

II- CRP-CHECK-1 KIT COMPONENTS

Each kit contains everything needed to perform 10 or 20 tests.

1- CRP-CHECK-1 test devices	10	20
2- Disposable plastic capillaries (20 µL) with a level indicator (black line)	10	20
3- Plastic dropper bottle containing 3.5 mL diluent	10	20
4- Instruction leaflet	1	1

5- Controls (Optional):

Positive control (ref. V340) and Negative control (ref. V341): a freeze-dried preparation of a non-infectious compound in diluted human serum, tested and found negative for anti-HIV, anti-HCV and HBs antigen, containing 0.05 % sodium azide is optionally available as a positive and negative control (1x 0.125 mL). The concentration range is indicated on the vial label.

III- MATERIAL REQUIRED BUT NOT PROVIDED

-Timer

- Automatic precision pipette for sampling 10 and 20µL

IV- STORAGE AND STABILITY

1- All CRP-CHECK-1 kit components, including optional control before reconstitution with distilled water, should be stored at any temperature between +4°C and +30°C in the sealed pouch.

2- **Do not freeze the test kit**.

3- The CRP-CHECK-1 kit is stable until the expiry date stated on the package label.

V- PRECAUTIONS

1- This test is designed for *in vitro* diagnostic use and professional use only.

2- Read carefully the instructions before using this test.

3- Handle all specimens as if they contained infectious agents. When the assay procedure is completed, dispose of specimens carefully after autoclaving them for at least one hour. Alternatively, they can be treated with 0.5% to 1% solution of sodium hypochlorite for one hour before disposal.

4- Wear protective clothing such as laboratory coats and disposable gloves while assaying samples.

5- Do not eat, drink or smoke in the area where specimens and kit reagents are handled.

6- Avoid any contact between hands and eyes or nose during specimen collection and testing.

7- Do not use beyond the expiry date which appears on the package label.

8- Do not use a test from a damaged protective wrapper.

VI- SPECIMEN COLLECTION AND PREPARATION

a) Whole blood collection

1- CRP-CHECK-1 test is performed on whole blood.

2- The specimen should be collected under the standard laboratory conditions (aseptically in such a way as to avoid hemolysis).

3- Each specimen should be treated as if potentially infectious.

4- The test must be performed with fresh whole blood samples (< 4 hours). Finger prick samples should be assayed just after collection.

b) Whole blood dilution

1- Label one dropper bottle containing the diluent with patient's name.

2- Unscrew the dropper bottle.

3- Fill one plastic capillary with whole blood sample up to the black line (level indicator corresponding to 20 µL).

4- Add the whole blood sample into the diluent by pressing the bulb of capillary.

5- Replace the screw cap on the dropper bottle.

6- Mix well by inverting upside-down the bottle several times.

VII- ASSAY PROCEDURE

a) Controls preparation and testing

1- Reconstitute the vial with **0.125 mL** of distilled water or tap water using a lab pipette. Wait for 15 minutes for freeze-dried dissolving.

2- Fill one disposable capillary with CRP control up to the black line (level indicator corresponding to 20µL).

3- Add the CRP control sample into **the sample well of the test device (▷)**.

4- Break the tip of one dropper bottle containing the diluent and add 5 drops (150µL) of diluent onto the sample well (▷). Read the test result after exactly 5 minutes.

5- The reconstituted vial should be kept between +2°C and +8°C and should be used within 7 days after reconstitution.

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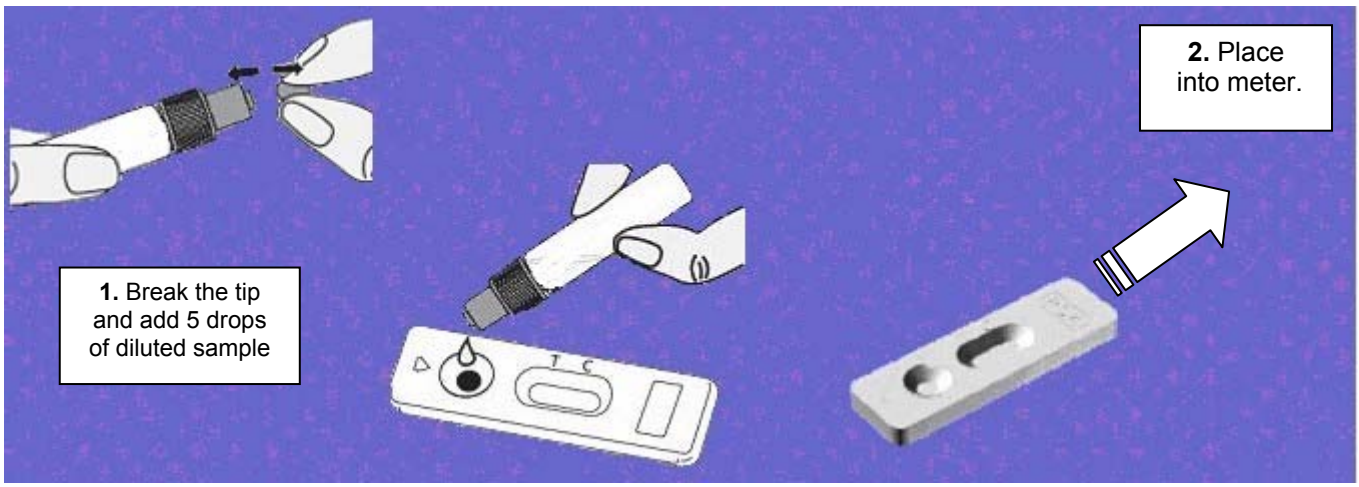
b) Samples testing

Follow the instructions below or refer to the picture n°1.

1- Allow samples and CRP-CHECK-1 test devices to come to room temperature prior to testing.
2- Remove the reaction device from its protective wrapper by tearing along the split.
3- Label device with the patient's name or control number.
4- Break the tip of the dropper bottle containing the sample. Add 5 drops (150µL) of diluted sample into the sample well (▷).
5- Read the result **(in µg/mL**) after 5 minutes, either using the immediate or countdown reading mode (See corresponding leaflet).
For general instructions describing how to use the EASYREADER® or EASYREADER+® meter, refer to the corresponding leaflet.

BE CAREFUL: **IF VISUAL INTERPRETATION OF THE TEST RESULT IS PREFERRED, PLEASE GO TO CHAPTER "QUALITATIVE READING".**



Picture n°1

VIII- PERFORMANCES CHARACTERISTICS

a) Linearity

The measuring range is 2.5 to 400 µg/mL and results will be given as per the table hereunder.

CRP concentration (µg/mL)	Reader results (µg/mL)
0 - 2.5	"< 2.5 µg/mL"
2.5 - 100	Quantitative results
100 - 200	"100 – 200 µg/mL"
200 - 400	"200 – 400 µg/mL"
400 and over	"> 400 µg/mL"

b) Accuracy

A study has been performed using a range of standards prepared by dilution of international W.H.O. standard Nr 8-506 in a serum depleted in CRP and covering a range of 0 to 400 µg/mL. Optical densities expressed as a function of CRP concentrations are described by following curve:

$$Y = \frac{570\ x}{(37.8+x)} \quad (r = 0.96).$$

c) Sensitivity

The CRP-CHECK-1 is allowing to detect CRP concentration of 2.5µg/mL, according to WHO 1st CRP International Standard Nr 85-506.
Levels higher than 8µg/mL are generally considered as abnormal values.

d) Precision

A panel of 33 human sera pre-assayed on BECKMAN analyser has been evaluated using the CRP-CHECK-1 quantitative rapid device. Results are read with theVEDALAB4s reader and reported in table I. Three samples identified in bold typo are showing discrepant results when compared to the reference method.
But in the three cases, both methods lead to the same clinical diagnosis profile (positive).
Therefore negative, borderline and positive samples are all correctly identified (a correlation of 98.2% has been established between VEDALAB rapid test and BECKMAN) using CRP-CHECK-1.

Table I

Human sera identification	[CRP] in µg/mL Expected values BECKMAN	[CRP] in µg/mL Obtained values CRP-CHECK-1
1	<1	<2.5
2	4.2	5.02
3	10.7	9.14
4	58	57.58
5	132	100-200
6	1.6	<2.5
7	2	<2.5
8	7.3	8.7
9	17.9	18.69
10	34.1	38.12
11	74.3	64.25
12	91	100-200
13	113	93.85
14	227	200-400
15	397	200-400
16	3.7	3.36
17	**9.9**	**7.4**
18	13.9	12.7
19	**29.4**	**22.27**
20	74	75
21	80	89.21
22	81	76.4
23	82	79.1
24	88	89.9
25	90	90.5
26	91	90.9
27	93	97.1
28	**93**	**72**
29	130	100-200
30	134	100-200
31	163	100-200
32	166	100-200
33	193	200-400

e) Hook effect
A sample containing 3,010 µg/mL gave a result of ">400 µg/mL" on the VEDALAB's meter indicating that no hook effect has been observed up to rather 500 times the normal values.

f) Intra-assay reproducibility
Within run precision was evaluated by using 35 replicates of two commercially available sera containing 10.97 and 50.65 µg/mL of CRP as determined with quantitative CRP-CHECK-1 for VEDALAB's reader.
The obtained CVs (coefficient of variation) were respectively equal to 12.55% and 11.20%.

IX- VISUAL (QUALITATIVE) RESULT INTERPRETATION

The CRP test could also be visually interpreted semi quantitatively, using the below pictures. The test result should be interpreted 5 minutes after having added the diluted sample into the sample well.

1/ < 8 µg/mL: No infection

2/ 8 to 40 µg/mL: Viral infection

3/ 40 to 100 µg/mL: Doubtful. Viral or a bacterial infection.

4/ > 100 µg/mL: Bacterial infection.

Depending on the CRP concentration in the sample, antibiotic treatment could or not be prescribed.
It is generally admitted (7) that:
- A CRP concentration of up to 40 µg/mL is due to viral infections for which there is no need of antibiotic treatment.
- A CRP concentration of 40 µg/mL to 100µg/mL could be due either to viral or bacterial infection. Therefore antibiotic treatment could be prescribed.
- A CRP concentration over 100µg/mL is due to bacterial infectious for which antibiotic treatment must be prescribed.

X- LIMITATIONS

1- An equivocal result could indicate the beginning of an immune response.
2- A questionable result can also be observed after therapy and an overcome infection.
3- As for any diagnostic procedure, the physician should evaluate the data obtained using this kit in the light of the other clinical available information.
<u>4- Use only fresh whole blood samples (< 4 hours) to perform the test. Finger prick samples should be assayed just after collection.</u>
5- This format of test is to be used only with VEDALAB rapid test readers (EASYREADER® or EASYREADER+®) when quantitative results are to be obtained.
6- If the reading time (5 minutes) is not strictly respected, wrong results will be obtained.
7- As it is true for any diagnostic method or for any measurements through analysers, there is a variability of the obtained result. Therefore, a confidence range of +/- 25% should be considered for the final value and for the clinical significance of the result.

XI- BIBLIOGRAPHY

1- **Van Lente F**, "The Diagnostic Utility of C-Reactive Protein", Hum Pathol, 1982 13(12) : 1061-3.
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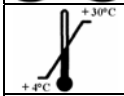
3- **Dowton SR and Colten HR**, "Acute Phase Reactants in Inflammation and Infection", Semin Hematol, 1988, 25(2):84-90.
4- **Shaw AC**, "Serum C-Reactive Protein and Neopterin Concentrations in Patients with Viral or Bacterial Infection", J Clin Pathol, 1991, 44(7): 596-9.
5- **Wu TT, Lee YH, Tzeng WS, et al** "The Role of C-Reactive Protein and Erythrocyte Sedimentation Rate in the Diagnosis of Infected Hydronephrosis and Pyonephrosis", J Urol, 1994, 152(1): 26-8.
6- **Gambino R.** "C-Reactive Protein (CRP) - How much Proof do we need?" Lab Rep, 1994, 16(11) : 83-5.
7- **Korppi, M. and Kröger, L.** C-Reactive protein in viral and bacterial respiratory infection in children. Scan. J. of Infectious Diseases. 1993, 25(2): 207-213.

	Read the instructions before use		For *in vitro* diagnostic use
	Temperature limitations		Do not reuse
	Manufacturer		

Manufactured by VEDALAB - France