REF SARSCOV2S-4P / SARSCOV2S-8P

version 0419 EN, last update 09/06/2020.

ID Screen®
SARS-CoV-2-N IgG Indirect

Indirect semi-quantitative ELISA for the detection of IgG antibodies directed against the nucleocapsid of SARS-CoV-2 in human serum and plasma.

IVD Σ 384 / 768 CE

Intended use

This diagnostic kit based on the semi-quantitative ELISA technique is intended to detect antibodies directed against the nucleocapsid of SARS-CoV-2 in human serum and plasma. It can be used in addition to direct detection of the virus by molecular biology techniques or for epidemiological survey. This kit is intended for *in-vitro* use and can be automated.

Clinical use

SARS-CoV-2, causing COVID-19 disease (Corona VIrus Disease-2019), is a single-stranded RNA virus from the *Coronaviridiae* family [1]. Comparisons of genetic sequences showed homologies with the SARS virus that appeared in 2003 [1,2]. Coronaviruses are made of several proteins [2] including envelope protein (E), spicule or spike (S), nucleocapsid (N) and matrix protein (M). SARS-CoV-2 is mainly transmitted by droplets during sneezing or coughing [3]. The incubation period of SARS-CoV-2 is around 3 to 7 days, up to a predicted maximum of 14 days [4]. Antibody detection can confirm infection in patients with evocative symptoms but also in asymptomatic patients and may be used for prevalence surveys. Analysis of two samples from the same patient can be used to demonstrate seroconversion, one being performed during the acute phase (week 1 when the symptoms are present), the other 2 to 4 weeks later [5]. Limited serological data are available for SARS-CoV-2. For SARS-CoV-1, the first appearance of IgM and IgG was observed between 3 and 42 and 5 to 47 days after exposure respectively [6]. IgGs were also shown to be the longest-lasting immunoglobulins after initial exposure [7]. These data are not yet clearly established for SARS-CoV-2. It should be noted that cross-reactions with other coronaviruses of the genus *Betacoronavirus* may exist [8].

Description and principle

Microwells are coated with the purified N protein recombinant antigen.

Samples to be tested and controls are added to the wells. Specific anti-SARS-CoV-2 antibodies, if present, form an antigen-antibody complex. After washing, a G protein conjugate marked with peroxidase (HRP), recognizing total human IgG (IgG_1, IgG_2, IgG_3, IgG_4, [9.10]), but not binding to IgA, IgM, nor IgE[9.10], is added to the wells. It fixes to anti-SARS-CoV-2 antibodies, forming an antigen-antibody-conjugate-HRP complex.

After elimination of the excess conjugate by washing, the substrate solution (TMB) is added. The resulting coloration is proportional to the quantity of specific antibodies present in the sample:

- in the presence of antibodies, a blue coloration appears which become yellow after the addition of the Stop Solution.
- in the absence of antibodies, no coloration appears.

The microplate is read at 450 nm.

Kit components

Reagents	Format		Storage conditions	
	384	768	Before opening	After opening, and until the expiry date
Coated microplate (ready-to-use) 12 x 8 well strips coated with purified recombinant antigen.	4	8	+2°C/ +26°C	After opening, immediately place the remaining strips in the ZIP bag with the desiccant sachet and seal it tightly. Keep for up to 6 months after opening at +2°C/+8°C.
Negative control (ready to use). Contains a matrix based on serum bovine albumin (BSA). Color: yellow.	1x 1mL	1x	+2°C/ +8°C	+2°C/+8°C In case of infrequent use of the kit, divide into small aliquots and store in the freezer (<-16°C) until the kit expiry date. An aliquot may undergo no more than 3 freezing-thawing cycles.
Positive control (ready to use). Contains anti-SARS-CoV-2 IgGs in a base. Color: Orange.	1x 0,5mL	2x		
Wash solution 20X (concentrated 20X). To dilute before use. See dedicated section.	2x 60 mL(*)	4x	+2°C/ +26°C	Undiluted +2°C/26°C Diluted (1X): May be stored for up to 5 days between +2°C/26°C
Concentrated conjugate 10X (concentrated 10X): preparation: see stage 5 of the instruction for use. Color: red.	1x 6 mL	2x	+2°C/ +8°C	Undiluted (10X): +2°C/8°C Diluted (1 X): may be stored for up to 24 hours between +2°C/8°C.
Dilution buffer 13 (ready-to-use) buffer for samples and conjugate. Color: pink.	3x 60 mL	5x	+2°C/ +26°C	+2°C/26°C
Substrate solution	1x 60 mL	2x	+2°C/ +8°C	+2°C/8°C. Close the bottle carefully and keep away from light. In a pipetting reservoir: up to 24h in the dark at 21°C ±5°C.
Stop solution (acid 0.5M))	1x 60 mL	2x	+2°C / +26°C	+2°C / +26°C
Instructions for use (1) Quality Control Sheet (1), Hermetic ZIP closing bag (1)				
The concentrated wash solution, substrate solution and stop solution may be used across the entire IDvet product range. Dilution buffer with the same batch numbers are interchangeable. (*) Additional liquid reagents, such as 20X washing solution, can be provided free of charge upon request.				

Precautions

1. Read the instructions carefully before use. Only use the instructions version mentioned on the box label.
2. Do not use reagents if their packaging appears to be damaged.
3. This kit is intended to be used in the laboratory by qualified personnel for the implementation of immuno-enzymatic techniques.
4. Follow Good Laboratory Practices (GLP) and safety guidelines: use a protective laboratory coat, single-use gloves and safety goggles. Contains components that can be harmful to the skin and eyes and may cause sensitization by skin contact. Avoid contact with the skin and eyes. In case of contact, rinse thoroughly with water and contact a doctor. If swallowed, contact a doctor. The stop solution (acid 0.5M) may be harmful if swallowed.
5. The substrate solution should be clear when used. Do not use it/add it on the microplate if it has a blue coloration. Do not expose the substrate solution to bright light nor to oxidizing agents.
6. The positive control of human origin was inactivated at 56°C during 30 minutes in the presence of 0.2% of Tween®20. It was found negative for the following parameters: **HbsAg, anti-HCV, anti-HIV antigen and antibody**. Positive control and samples should be considered potentially infectious and manipulated as such.
7. Eliminate reagents and waste in accordance with current regulations. Do not autoclave bleach.
8. Bring back the microplate to room temperature before opening to avoid moisture formation. Tear or cut the sachet. **In case of partial use: write down** on the traceability sheet of the test **the full identification number shown** on the side of the plate **frame**. Place the remaining strips in the supplied ZIP bag, add the desiccant sachet contained in the initial packaging and close tightly. As the strips are removable, it is advisable, in case of manual use, to identify the strips by a marker.
9. For more information, please refer to the security data sheet, available upon request at info@id-vet.com.

Wash Solution Preparation

► If crystals are present in the **20X concentrated wash solution**, do not withdraw volume to prepare the **1X solution**. Bring **the concentrated Wash Solution (20X)** to room temperature (21°C ± 5°C) or heat it (hot water bath, incubator at 37°C) and mix it thoroughly to ensure that the Wash concentrate is completely solubilized.

► Prepare the Wash Solution **(1X)** by diluting **1/20** of a volume of the Wash Solution (20X) in 19 volumes of distilled / deionized water.

► **The quality of the washing step may impact the results. Make sure the wells are completely empty between washes.** If an automatic washer is used, it is crucial to set the device properly (mode, type and suction height) to limit the residual volume. For more information, please see the "IDvet Washing Guide" available upon request.

Preparation and storage of samples

► **Sample type:** human serum collected on dry tube with or without separator, or plasma obtained on EDTA, heparin or citrate tube.

► **Sample storage** [5]: between 2 and 8 degrees, up to 5 days. For longer storage, freeze (< -16°C). Do not freeze/thaw more than 3 times.

► **Shipment conditions** [5]: between 2 and 8 degrees if the estimated shipping time is ≤ **5** days. Otherwise, at -70°C (dry ice). Do not freeze/thaw more than 3 times.

► **Diluted samples**: once diluted, samples must be tested on the same day.

Material required but not provided

1. Mono or multi-channel pipettes, adjustable or fixed, capable of delivering volumes of 10 µl (precision ≤ 10%), 100 µl, 200 µl, 1ml (precision ≤5%)
2. Pipettes to measure volumes of 10 ml, graduated test tubes of 25 ml, 50 ml, 100 ml and 1000 ml.
3. Disposable tips.
4. 96-well microplate reader for 450 nm reading.
5. Distilled or deionized water.
6. Manual or automatic wash system.
7. 96-wells pre-dilution microplate.
8. Vortex.
9. Individual protection equipment.
10. Absorbing paper.
11. Sodium hypochlorite (bleach).
12. Container for contaminated waste.

Testing Procedure

Allow all reagents to come to room temperature (21°C ± 5°C) by taking them out of box at least 30 min before use. **Homogenize all liquids reagents AND samples to test by inversion or vortex** before use.

1. In a 96-well pre-dilution microplate (designed for sample storage, non-adsorbent), dilute the controls and the samples to be tested at **1:21**. For example, add:
   - 200 µl of **dilution buffer 13** in all wells.
   - 10 µl of **Negative Control** in **A1** and **B1** wells.
   - 10 µl of **Positive Control** in **the C1** and **D1** wells.
   - 10 µl of each sample to be tested in the remaining wells.
2. Using a 100 µl micropipette, homogenize by suction/expulsion and transfer 100 µl of each dilution prepare in step 1 on the ELISA plate using, for example, a multichannel pipette.
3. Cover the plate and incubate **for 45 min ± 4 min** at 21°C (± 5°C).
4. Empty the wells. Wash 3 times each well with **at least** 300 µl of **Wash Solution.** Avoid drying wells between washings.
5. Prepare the **Conjugate 1X** by diluting the **Concentrated Conjugate 10X** to 1/10 in **Dilution buffer 13**.
6. Add 100 µl of **Conjugate 1X** to each well.
7. Cover the plate and incubate **30 min ± 3 min** at .21°C (±5°C)
8. Empty the wells. Wash 3 times each well with **at least** 300 µl of **Wash Solution.** Avoid drying wells between washes.
9. Add 100 µl **of Substrate Solution** to each well.
10. Cover the plate and incubate **20 min ± 2 min** at 21°C (±5°C) in the dark.
11. Add 100 µl **of Stop Solution** to each well, in the same order as in step 9, to stop the reaction.
12. Read and record OD at 450nm. After blocking, the plate should be read within 30 minutes to avoid loss of OD over time.

Validation

The test is validated if:

✓ the mean OD value of the Positive Control (OD_{PC}) is greater than 0.350.

$$\mathbf{OD_{PC} > 0,350}$$

✓ the ratio of the mean values of the Positive and Negative Controls (OD_{PC} and OD_{NC}) is greater than 3.

$$\mathbf{OD_{PC} / OD_{NC} > 3}$$

Interpretation

For each sample, calculate the S/P ratio "Sample/Positive control" express as a percentage (S/P%):

$$\mathbf{S/P\,\% = \frac{OD_{Sample} - OD_{NC}}{OD_{PC} - OD_{NC}} \times 100}$$

Samples presenting a S/P%:

- Less than or equal to 30% are considered negative.
- Between 30% and 40% are considered as doubtful.
- Greater than or equal to 40% are considered as positive.

Result	Status
S/P % ≤ 30%	NEGATIVE
30% <S/P %< 40%	DOUBTFUL
S/P % ≥ 40%	POSITIVE

Note: In case of retrospective seroprevalence study, it is advisable to use a threshold at 60% < S/P% < 70% to favor specificity and to maintain a very high PPV, even at very low prevalence.

Reference material

There is no international reference serum for quantification of antibodies directed against SARS-CoV-2. The interpretation is therefore carried out as ratios allowing a

relative measure of the concentration of antibodies in the sample tested.

Manufacturer quality control

• All products manufactured and marketed by IDvet are placed under a quality assurance system from the receipt of raw materials until the marketing of the finished products. Each batch of finished product undergoes quality control and is marketed only if it meets the acceptance criteria. The documentation relating to the production and control of each batch is kept by the manufacturer.

• Each test is validated if the validation requirements described in this notice are met. The absolute optical density values shown on the attached quality control sheet are those obtained in our Quality Control Laboratory. They are given as an indication. Indeed, certain parameters may affect these values, including temperature, incubation time, and operator. Given that the positive controls are subject to the same variations, results are expressed as sample to positive control (S/P) percentage. Results are thereby unaffected by these variations and may be standardized between runs (see "Robustness").

Robustness

The robustness of the kit has been evaluated and validated:

► in the optimal conditions of use of the test as defined in the instructions for use, by 3 operators in 3 independent, internal or external runs. For each run, the assay was validated as per the test validation criteria.

► internally, testing the reagent by following a protocol using the upper or lower limits of for incubation time and temperature.

Robustness was validated because:

i) regardless of test conditions, the kit validation criteria with respect to the optical densities (OD) of the positive and negative controls was achieved

ii) the S/P % of the internal reference material used as a tracer and measuring analytical sensitivity remained constant

iii) the sample status for two levels of positivity and for 2 negative samples remained unchanged.

Validation data(11)

► **Repeatability:**

Intra-test accuracy was determined by measuring the coefficient of variation (CV%) on intra-plate repetitions (n=.60 or 36) for a series of four samples for which the reactivity is distributed over the measurement range.

Sample	Negative	Positive sub-threshold	Average positive	Strong positive
n =	60	36	60	36
Average S/P%	8	33	94	154
SD	0,006	0,011	0,020	0,042
CV%	**3,5%**	**2,7%**	**3,6%**	**5,3%**

► **Accuracy:**

Of the 1331 samples tested, 1326 gave a result consistent with the data considered true (sample status), meaning an accuracy of 99,6%.

► **Detection limit/analytical sensitivity:**

In the absence of both an analytical sensitivity referential sample repository and a national or international standard, the limit of detection (LoD) was measured by end-point dilution, to determine the dilution for which there is no longer antibody detection (sub-threshold; last positive dilution), on 30 samples.

Last positive dilution	undiluted	1 :2	1 :4	1 :8	1 :16	1 :32	1 :64	>1 :128
Number of samples	2	3	7	6	9	2	1	1

► **Positivity threshold value:**

The application of the conservative formula: average + 3 standard deviations from the measurements observed on at least 30 samples of healthy subjects would have led to a threshold of: S/P: 12%.

The threshold value was determined after analysis of the observed population distribution on 1247 negative samples and 41 positive samples. The analysis of the ROC curve (Receiver Operating Characteristic curve) yielded an Area under the curve **AUC=0,968** ($IC_{95\%}$ [0,958-0,978]). For each threshold value, diagnostic sensitivity and specificity data have been established. The positioning of the chosen threshold is in the linear area of the test and allows to ensure and prioritize the specificity of the test without degrading its sensitivity.

► **Analytical specificity (exclusivity):**

• Due to the low homology of the antigen used with other pathogens that can affect humans, cross-reactions are unlikely.

• A high proportion of the population (up to 90%) have antibodies against other coronaviruses of the genus *Betacoronavirus*[8.13] affecting humans (HCoVs), such as seasonal coronaviruses (HCoV-HKU1,HCoV-OC43, HCov-NL63, HCoV-229E). Diagnostic specificity, measured on panels of samples probably containing antibodies against these HcoVs, even if their presence could not be established, suggests that cross-reactions are very unlikely.

• In addition, 92 blood samples [12] taken simultaneously along with an oropharyngeal sample on which at least one respiratory pathology was confirmed by RT-qPCR, were tested on this kit. Of these samples, 79 had a unique positivity by RT-PCR against Rhinovirus (n=47); Coronavirus 229 (n=1); Adenovirus (n=2); Bocavirus (n=1); Enterovirus (n=6); Metapneumovirus (n=2); Coronavirus NL63 (n=3); Coronavirus OC43 (n=2); Parainfluenza type 1 (n=7); or VRS (n=5). 12 samples had PCR positivity against two pathogens, of which 2 showed Coronavirus 229 positivity. 1 sample showed PCR positivity against 3 pathogenic viruses, other than coronaviruses. Although it was not possible to determine the presence of antibodies for each of the viruses identified, all **samples were found to be negative with the IDscreen® ELISA** (maximum S/P% = 32 for a Rhinovirus positive sample).

• Due to the high sequence homology of the antigen used between SARS-CoV-1 and SARS-CoV-2 (>98%), the cross-reactions are certain but could not be tested.

• Due to the low sequence homology (<50%) of the antigen used between SARS-CoV-1 and -2, and the Middle East Respiratory Syndrome virus (MERS), cross-reactions are unlikely but could not be tested.

► **Seroconversion kinetics [14]**

• External study [14]: the onset of symptoms was followed at the CHU de Montpellier in 4 patients tested positive for COVID-19 by RT-PCR.

	Time after onset of symptoms (j)										
Patient	**1**	**2**	**3**	**5**	**6**	**7**	**9**	**11**	**13**	**15**	**18**
1	3	-	17	61	121	-	153	151	-	-	-
2	-	3	-	-	-	3	5	39	160	258	318
3	-	-	-	- 2	-	120	-	-	-	332	-
4	-	-	-	-	86	186	236	-	317	309	-

- : not tested ; resuts express as S/P% ratio ;
positivity threshold : 70%

For the patients tested, IgG antibodies were detected between 5 and 13 days after the onset of symptoms.

► **Diagnostic/clinical specificity**

Diagnostic specificity (DSp) was assessed by IDvet through the analysis of 1247 samples (100 sera and 1147 plasmas from healthy blood donors) taken in France before the appearance of the SARS-CoV-2 virus (2010, 2016, 2017*). **At the threshold of S/P=30%, the measured DSp is 99,6% ($IC_{95\%}$: 99,1-99,8) ; 99,9% ($IC_{95\%}$: 99,6%-100%). at the threshold of S/P=60%.**

Age group	Years	Type	N=	Pos.	Neg.	Sp (%)
20-33	2016	plasma	51	0	51	100
18-70	2017	plasma	48	0	48	100
18-70	2010	serum	100	0	100	100
18-70	2010	plasma	88	0	88	100
18-70	2017	plasma*	960	5	955	99,5
TOTAL			**1247**	**5**	**1242**	**99,6 [99,1–99,8]**

**Samples provided by EFS (Etablissement Français du Sang) Occitanie*

• External study [14]: The specificity was assessed by the CHU of Montpellier through the analysis of samples from healthy patients (n=20). The measured specificity was **100% ($IC_{95\%}$ 83,9% - 100%).**

► **Diagnostic/clinical sensitivity [12]**

• Diagnostic Sensitivity (DSe) was determined by IDvet through the analysis of 41 plasma samples from 41 patients tested positive for COVID-19 RNA by RT-qPCR in respiratory samples. For each sample, the date of blood sampling in relation to the onset of symptoms is known. Blood samples were provided by the Biological Resource of Montpellier hospital (CHU Montpellier) (COVIDotheque collection, n°. 2020-A00935-34) [12].

Groups	N=	Positive	Negative	Average S/P%	Se
0-4 days	1	1	0	3	0
5-9 days	2	1	1(*)	42	50
10-14 days	8	7	1	169	87,5
15 - 19 days	20	19	1(*)	195	95,0
> 19 days	10	9	1(*)	175	90,0

(*) Non-reactive samples on different prototypes based on the detection of the N protein of SARS-CoV-2 using an anti IgG-A-M conjugate, and tested negative on commercially available SARS-CoV-2 IgG and IgA ELISA

The diagnostic sensitivity measured on the samples collected > 15 days after the onset of symptoms on this sample panel was estimated at **95,2% ($IC_{95\%}$ 78,8 – 98,2%), n=30.**

• Sensitivity was assessed through an external study [14] at the CHU of Montpellier by the analysis of samples from different patients tested positive for the COVID-19 RNA by RT-qPCR at different days after the onset of symptoms.

Groups	N=	Positive	Negative	Average S/P%	Se
0-4 days	10	0	10	7	0
5-9 days	9	1	8	14	11,1
10-14 days	20	15	5	187	75,0
15 - 19 days	22	21	1	279	95,5
>19 days	32	31	1	280	96,9

The diagnostic sensitivity measured on the samples collected > 15 days after the onset of. symptoms was estimated on this sample panel at **96,3% ($IC_{95\%}$ 87,5 – 99,0%), n=54.**

In total, the sensitivity measured on the samples collected >15 days after the onset of symptoms was therefore estimated at **95,2% (IC95% 88,4 – 98,1%), n=84.** In external studies (Kremlin Bicêtre, France) the sensitivity on samples taken 10-14 days after the onset of symptoms was increased by 6% (n=85) by using the 30% cut-off instead of 60%.

• Prior to analysis, and for safety purposes, the plasmas used in the diagnostic sensitivity study were inactivated at 56°C for 30 minutes in the presence of a non-ionic detergent (0.2%Tween20®). The following results were obtained:

		Inactivated samples		
		Positive	Negative	TOTAL
Non-inactivate samples	Positive	36	0	36
	Negative	0	5	5
	TOTAL	36	5	41

On the panel tested, the pre-treatment of the samples had no impact on the results. However, this process does not constitute a recommendation for pre-treatment of the samples before using this kit.

Correlation/agreement

Results obtained for 41 samples from the diagnostic sensitivity study panel, as well as for 8 samples from the diagnostic specificity study panel, were compared with those obtained with commercially available ELISA kits based on the S protein, specifically detecting IgG or IgA.

	PCR positives		Free of disease	
	Positive	Negative	Positive	Negative
ID screen® SARS-CoV-2-N IgG Indirect	36	5	0	8
Kit A, ELISA IgG	36	5	0	8
Kit B, ELISA IgA	38	3	2	6

Positive / Negative Predictive Values

The HAS guide [11] states that NPVs and PPVs "are not relevant due to the lack of robust data on the prevalence of COVID-19 infection." Nevertheless, they may be useful to interpret seroprevalence survey measurement results in relation to the diagnostic performance of the test. PV was calculated based on DSe: 95.2% and DSp:99.6%.

	PV (Sp : 99,6% ; Se : 95,2%) for different seroprevalences						
	1%	5%	10%	15%	25%	30%	35%
PPV	70,6%	92,6%	97,5%	98,3%	98,8%	99,2%	99,4%
NPV	100,0%	99,7%	99,5%	98,8%	98,0%	96,9%	95,4%

Use of a robot

The stability of the reagents allows partial or complete adaptation of the test on automated systems. However, this adaptation can lead to differences between the results obtained manually and those obtained by a robot. It is the responsibility of the user to validate the instruments used in order to ensure that they give reliable results.

Limits of use

• This test is only indicated for semi-quantitative detection and cannot be the only basis for the diagnosis or treatment of COVID-19.

• The diagnosis of infection with the SARS-CoV-2 virus can only be definitively established using a set of clinical and biological data (from an RT-qPCR test, for example). A negative serological test result does not exclude the presence of the disease.

• The result of a single anti-SARS-CoV-2 IgG antibody assay test is not in itself enough evidence to diagnose a recent infection with the SARS-CoV-2 virus.

• Only one set of clinical and biological data (significant increase in the anti-SARS-CoV-2 IgG titer between two samples from the same patient taken 2 to 3 weeks apart and tested during a single assay; presence of anti-SARS-CoV-2 IgM or recent RT-qPCR results) suggests a recent infection with the virus.

• If the sample is taken too early during an initial primary infection, the anti-SARS-CoV-2 IgG antibodies may not yet be present. In case of doubt, a second sample [5] must be taken 2 to 3 weeks later, for which the search for IgG and / or IgM will be repeated.

• Bacteriological or fungal contamination of samples or reagents, or cross-contamination between reagents can lead to erroneous results.

• **Washing** the wells is an **essential step** in handling: respect the prescribed number of washing cycles, and ensure that all the wells are completely filled, then completely emptied (<10µl). **Improper washing can lead to incorrect results** (abnormally high OD, false positive results, problems of repeatability or reproducibility of the test).

• **Preferably use disposable equipment.** Otherwise, **use glassware that has been thoroughly washed and rinsed** with running water and then distilled. Contact IDvet for more information.

• Never use the same container to dispense the conjugate and the substrate solution.

• **Do not carry out the test in the presence of reactive vapors** (acids, alkaline, aldehydes), which could alter the enzymatic activity of the conjugate.

• Do not allow the microplate to dry between washes and / or dispensing of reagents.

• The enzymatic reaction is very sensitive to all metals or metal ions. Consequently, no metallic element should come into contact with the various solutions containing the conjugate or the substrate. IDvet is able to provide a document specifying the minimum recommendations concerning water quality.

• Use a new distribution cone for each sample.

• Check the accuracy of the pipettes and the proper functioning of the devices used.

Technical assistance and customer service

In case of question or technical issue, you can get help and assistance from IDvet (E-mail: info@id-vet.com) or its local representative.

Bibliography

(1) Zhou, Peng & Yang, et al. (2020). Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. doi :10.1101/2020.01.22.914952.

(2) Chan, Jasper Fuk-Woo et al. "Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan." Emerging microbes & infections vol. 9,1 221-236. 28 Jan. 2020, doi:10.1080/22221751.2020.1719902

(3) Fehr, A. R., & Perlman, S. (2015). Coronaviruses: An Overview of Their Replication and Pathogenesis. Coronaviruses Methods in Molecular Biol

(4) Wang G, JinX. The progress of 2019 Novel Coronavirus (2019-nCoV) event in China. J Med Virol. doi: 10.1002/jmv.25705

(5) Laboratory testing for coronavirus disease (COVID-19) in suspected human cases, Interim Guidance, WHO,19 March 2020

(6) Chen X et al. Serology of severe acute respiratory syndrome: implications for surveillance and outcome. J Infect Dis. 2004 ;189(7):1158-63.

(7) Wu, L.-P., et al. (2007). Duration of Antibody Responses after Severe Acute Respiratory Syndrome. Emerging Infectious Diseases, 13(10), 156210.3201/eid1310.070576

(8) Okba N, et al. Sensitive and Specific Detection of Low-Level Antibody Responses in Mild Middle East Respiratory Syndrome Coronavirus Infections. Emerging Infectious Diseases. 2019;25(10):1868-1877. doi:10.3201/eid2510.190051

(9) Harlow, Ed. Lane, D. Antibodies: a laboratory manual. 1998.

(10) Antibody binding affinities of Protein A, Protein G, Protein L. URL: [www.abcam.com/kits/antibody-binding-affinities-of-protein-a-protein-g-protein-l-and-jacalin]. Consulted online, April 11th, 2020.

(11) Cahier des charges définissant les modalités d'évaluation des performances des tests sérologiques détectant les anticorps dirigés contre le SARS-CoV-2 en France, Haute autorité de santé (HAS) - avril 2020.

(12) Centre de Ressources Biologiques du CHU de Montpellier, https://www.chu-montpellier.fr/fr/crb.

(13) Meyer B, Müller MA, Corman VM, Reusken CB, Ritz D, Godeke GJ, et al. Antibodies against MERS coronavirus in dromedary camels, United Arab Emirates, 2003 and 2013. Emerg Infect Dis. 2014 ;20 :552–9.

(14) Communication personnelle de résultats, Dr E. TUAILLON, CHU de Montpellier ; UMR PCCI 1058 Inserm/Université de Montpellier/EFS (Dr E. TUAILLON, Pr P. VANDE PERRE, Mme K. BOLLORE (UM), Mme S. DEBIESSE (Inserm).

IDvet
310, rue Louis Pasteur
34790 GRABELS
FRANCE
www.id-vet.com
E-mail: info@id-vet.com

Meaning of the symbols

EN 980/ISO 15223


Possible biological hazard


Keep away from light


Conform to the CE essentials requirements


Read the instructions before use


Storage temperature limits

In vitro diagnostic device

Batch number


Expiration date


Manufacturer

Reference – product code

History of revision

Any major changes to the manual will be clearly described on the front page in a red frame. Bullets are arranged in the instruction for use to alert the user of the changes made.

Type of modification	Modification	Change of version	Revision update and references
Correction of anomalies in the document (writing, typography, layout, providing details on implementation	Minor	No	Yes
Update: Add/changes of the validation data	Minor	No	Yes
Technical modification: technical modification of the reagent, composition, modus operandi	Major	Yes	Yes

Version	Edition date	Reference	Type	Modification description
0419	29/04/2020	DOC10582	First version	N/A
0419	30/04/2020	DOC10584	Update	Addition of specificity data
0419	05/05/2020	DOC10590	Update	Addition of the CE symbol
0419	12/05/2020	DOC10616	Correction of anomalies in the document	Correction in the number of vials provided for the Negative control and the Wash Solution 20X
0419	09/06/2020	DOC10692	Update	Threshold modification depending intent of use