Order references

Reagents

REF		CONT
CVCOL-H00	SARS-CoV-2 Reagents Kit	55 ml Reagent 1 + 25 ml Reagent 2

Other necessary products

REF		CONT
CVREK-000	SARS-CoV-2 Calibrators Kit	5 x 1 ml
CVCOK-000	SARS-CoV-2 Control Level 1 **CVCOS-002** SARS-CoV-2 Control Level 2 **CVCON-002** SARS-CoV-2 Control Level 3 **CVCOX-002**	1 x 2 ml 1 x 2 ml 1 x 2 ml

Intended Use

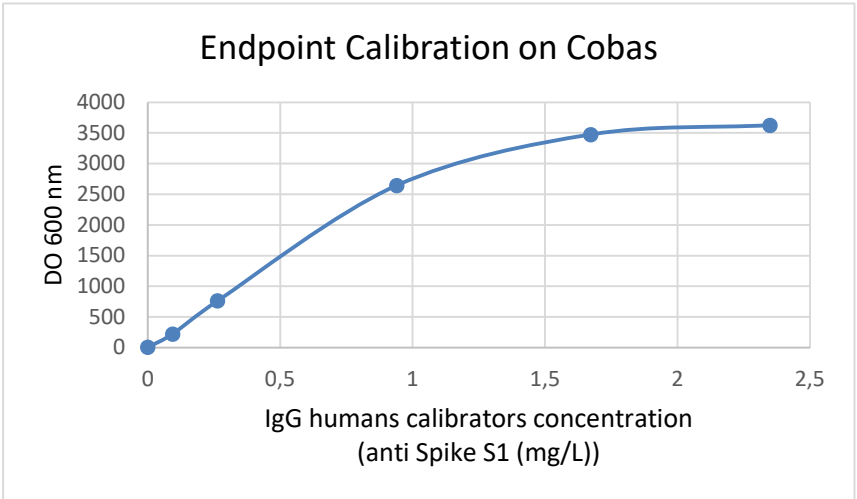
The SARS-CoV-2 serological assay is a **PETIA Homogeneous** immunoassay (Particle Enhanced Turibidimetric Immuno Assay) to be used on **automatic biochemistry analysers**.
This assay is **calibrated** with human IgG anti Spike S1 SARS-COV-2.
The SARS-CoV-2 serological assay is intended for the qualitative detection of total antibodies to SARS-CoV-2 in human serum or plasma.
The SARS-CoV-2 serological assay is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity.

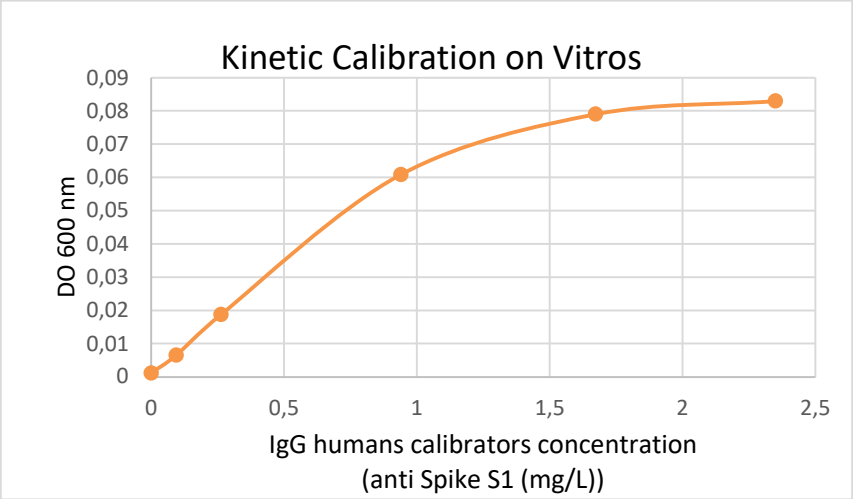
Principles of the Procedure

The SARS-CoV-2 serological assay is performed using the DiAgam SARS-CoV-2 reagents kit and the DiAgam Anti-SARS-CoV2 human IgG calibrators kit on automatic biochemistry analysers. A homogeneous immunoturbidimetric gold particle enhanced technique is used. A 2 incubations reactional steps are performed using a buffer reagent 1 and a gold colloidal probe reagent 2. The gold probe binds specifically antibodies to SARS-CoV-2 inducing a specific agglutination of the gold probe. This agglutination can be monitored at **600 nm** on biochemistry analysers or photometers using an endpoint or a kinetic protocol.

Test Type	Reaction Sample Volume	Buffer Reagent 1 Volume	Incubation Time	Gold Reagent 2 Volume	Incubation time	Reading OD1	Incubation Time	Reading OD2
ENDPOINT	35 µl	110 µl	5 minutes	46 µl	15-45 sec.	600 nm	5 minutes	600 nm
KINETIC	35 µl	110 µl	5 minutes	46 µl	38 sec.	600 nm	152 sec.	600 nm

The residual optical density is indicative of the amount of antibodies present in the sample.





Warning and precautions

- For in vitro diagnostic use only.
- For emergency authorization use only.
- Must be handled by qualified personnel under the responsibility of a biologist.
- Treat as if capable of transmitting infection.
- These products contain sodium azide. Products containing sodium azide must be handled with care: avoid ingestion and contact with the skin or mucous membranes.
- Sodium azide becomes explosive on contact with heavy metals such as copper or lead.

Specimen Collection, Preparation and Storage

Collection conditions

Collect specimens using standard laboratory techniques; use only suitable procedures, tubes or collection containers.

Sample type

Serum or plasma.

Storage and stability of specimens

Samples stability should be established by each laboratory.

Reagents

Composition and concentrations/Storage

Reagent kit contents (Ref: CVCOL-H00)

- 55 ml assay reagent 1 (buffer, polymer, inorganic salts, preservative).
- 25 ml gold suspended probe reagent 2 (gold particles coated with SARS-CoV2 antigen (Spike protein RBD)).

Calibrators kit contents (Ref: CVREK-000)

- SARS-CoV-2 anti-Spike S1 human IgG calibrators kit : 5x1 ml (Anti-Spike S1 human IgG in buffered stabilized diluent, with preservative).

Preparation

Ready to use.

Storage and stability

- Reagents are stable until the expiration date printed on the packaging (months passed), under the recommended storage and handling conditions.
- Unopened vial stored at temperature indicated on packaging.
- Opened vial: closed immediately after use or placed on closed analyser intended for this purpose, not contaminated by handling and stored at the temperature indicated on the packaging.
- Do not freeze the reagents.
- Nanoparticle-based reagents can settle over time. It may be necessary to delicately mix by repeated turning.

Procedure

Material provided:

- SARS-CoV-2 serological assay reagent kit.

Other materials required

Calibrators kit contents (Ref: CVREK-000)

- SARS-CoV-2 anti-Spike S1 human IgG calibrators kit.
  5x1 ml (Anti-Spike S1 human IgG in buffered stabilized diluent, with preservative).

Automatic Biochemistry Analyser

- Usual laboratory equipment including an analytical system equipped with a photometric detector.

Assay Procedure

Applications for some opened analyzers are available, please contact DiAgam if the corresponding application is not yet installed on your analyzer.
For a detailed description on how run an assay, please refer to the operating instructions for your system.

Calibration

- The calibration curve is performed by using the calibrators kit. The zero point of the calibration curve is performed with physiological saline solution.
- Calibration is lot specific; reagents kits and calibrators kit are linked by lot numbers. Reagents kits from the same lot may use the same calibration.
- When the calibration curve is proceeded, its validity is assayed against quality controls, the calibration should be used in conjunction with acceptable control values to determine the stability of calibration.
- Recalibration is required when a different reagent lot is loaded or in case of change in performance (contact the manufacturer if the changes persist) or if quality control requires it.
- Refer to the operating instructions for your system for detailed instructions on the calibration process.

Traceability

Calibration of the SARS-CoV-2 serological assay is traceable to an in-house reference calibrator.

Quality control

Quality Control Material

- CVCOK-000 controls are recommended for use with the SARS-CoV-2 serological assay CVCOL.
- The performances of other commercial control fluids should be evaluated for compatibility with the assay before they are used for quality control.
- Control material may show a difference when compared with other anti-SARS-CoV-2 methods.

Quality Control Procedure Recommendations

- The frequency of controls and the confidence limits must be adapted to the laboratory requirements.
- Choose control levels that check the clinical relevant concentrations, the results must be within the defined confidence limits.
- Each laboratory shall establish corrective measures to be taken if results fall outside the defined limits.

- Comply with current legislation in the country and local guidelines relating to quality control.
- The calibration curve and its stability can be validated using the control materials indicated in the “Order references” section.

Results interpretation

Results are automatically calculated by the analyser and expressed in equivalent of anti-Spike S1 SARS-CoV-2 human IgG. **Note that total antibodies (including IgM and IgA) against Spike S1 SARS-CoV-2 will react with the gold probe reagent. This assay is not to be considered as a fully quantitative test.**

Cut-off determination

- Cut-off concentration between reactive specimen for anti-SARS-CoV-2 and non-reactive specimen for anti-SARS-CoV-2 specimen could be depending on the analyser, the protocol and the lot of kits used.
- Cut-off concentration will be determined by each laboratory by comparison between the results measured from patients confirmed to be SARS-CoV-2 positive by PCR and the results measured from patients presumed SARS-CoV-2 negative.
- Number of patients used for the determination of the cut-off concentration should be fixed by the laboratory in conformity with the local health authority regulation.
- By fixing the cut off concentrations, laboratories will be able to calculate the sensitivity and specificity of the test.
- Sensitivity and specificity results should be compared to the needs required by the local health authority before use, in case of not reaching the needs, the test should not be used.

Limitations of the method

The results of this test should always be interpreted in relation to the patient’s medical history, clinical signs and other findings.

Limitations

- Results that are inconsistent with clinical observations indicate the need of additional testing.
- A non-reactive result can occur if the quantity of antibodies for SARS-CoV-2 virus present in the specimen is below the detection limit of the assay or the antibodies present in the specimen are against another antigenic fraction than the S1 Spike protein.
- The results obtained with this test should only be interpreted in conjunction with clinical finding and the results from other laboratory tests and evaluation.
- This test should not be used for screening of donated blood for the purpose of preventing COVID-19 transmission.

Conditions of Authorization for the Laboratory

- All Laboratories should check with the relevant health authorities to ensure that they can use this kit for the intended uses.
- All laboratories that receive our kit will notify the relevant public health authorities of their intent to run our product prior to initiating testing.
- All laboratories using our product will have in place a process for reporting test results to healthcare providers and relevant public health authorities as appropriate.
- All laboratory personnel using our product must be appropriated trained in automated biochemistry and immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit and use our product in accordance with labelling. All laboratory personnel using the assay must be trained in and be familiar with the interpretation of results of the product.
- All laboratories will collect information on the performance of our product and report DiAgam of any suspected occurrence of false reactive or false non-reactive results and significant deviations from the established performances characteristics of our product of which they become aware.

Performances Characteristics

Clinical performances Characteristics (still in progress)

Sensitivity

31 samples collected from patients confirmed to be SARS-CoV-2 positive by PCR were tested.
The results are summarized in the table below :

Days between symptoms and serum collection	Reactive	Non-Reactive	Number tested	Positive Percent Agreement
9-17	11	0	11	100.0 %
>17	18	2	20	90.0 %
9-65	29	2	31	93.5 %

Specificity and Potential Cross-reacting Subgroups

30 samples from patients with HIV, HCV, EBV, CMV collected before the coronavirus pandemic were tested negative resulting in 100 % specificity.

Literature

2020 - Zhao J et al. - Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019
2020 – Haute Autorité de Santé France rapport indications tests sérologiques covid-19
2020 - SCIENCE Covid-19 : un récepteur cellulaire au centre de toutes les attentions
2020 - COVID 19 et tests sérologiques l'Institut national d'excellence en santé et en services sociaux
2020 - Test performance evaluation of SARS-CoV-2 serological assays
Jeffrey D. Whitman, M.D., M.S.1*, Joseph Hiatt, B.A.2,3,4,5,6,7*, Cody T. Mowery, B.S.2,3,5,6,7*, Brian R. Shy, M.D., Ph.D.1*, Ruby Yu, Ph.D.5,7*, Tori N. Yamamoto, Ph.D.5,6,7, Ujjwal Rathore, Ph.D.4,5,6,7, Gregory M. Goldgof, M.D., Ph.D.1, Caroline Whitty, B.S.1,5,7, Jonathan M. Woo, B.S.5,6,7, Antonia E. Gallman, B.S.2,5,8, Tyler E. Miller, M.D., Ph.D.36 , Andrew G. Levine, M.D., Ph.D.1, David N. Nguyen, M.D., Ph.D.5,6,9, Sagar P. Bapat, M.D., Ph.D.1,5,7, Joanna Balcerek, M.D., Ph.D.1, Sophia A. Bylsma, B.S.20, Ana M. Lyons, B.S.21, Stacy Li, B.S.21, Allison Wai-yi Wong, Ph.D.2, Eva Mae Gillis-Buck, M.Phil.10, Zachary B. Steinhart, Ph.D.5,7, Youjin Lee, Ph.D.5, Ryan Apathy, B.S.5,6,7, Mitchell J. Lipke, B.S.5,7, Jennifer Anne Smith, Ph.D.7,11, Tina Zheng, B.S.2,3,12,13, Ian C. Boothby, B.A.2,14, Erin Isaza, B.S.2,15, Jackie Chan, B.S.5, Dante D. Acenas II, B.A.5, Jinwoo Lee, Ph.D.2,16, Trisha A. Macrae, Ph.D.2,16, Than S. Kyaw, B.S.2,5, David Wu, B.S.2,3, Dianna L. Ng, M.D.13,17, Wei Gu, M.D., Ph.D.1, Vanessa A. York, B.S.18, Haig Alexander Eskandarian, Ph.D.18, Perri C. Callaway, B.A.18,19, Lakshmi Warrier, B.S.18, Mary E. Moreno, B.S.18, Justine Levan, Ph.D.18, Leonel Torres, B.S.18, Lila A. Farrington, Ph.D.18, Rita Loudermilk, B.S.22, Kanishka Koshal, M.P.H.22, Kelsey C. Zorn, M.H.S.23, Wilfredo F. Garcia-Beltran, M.D., Ph.D.36, Diane Yang, Ph.D.36, Michael G. Astudillo, M.D.36, Bradley E. Bernstein, M.D., Ph.D.36, Jeffrey A. Gelfand, M.D.37, Edward T. Ryan, M.D.37, Richelle C. Charles, M.D.37, A. John Iafrate, M.D., Ph.D.36, Jochen K. Lennerz, M.D., Ph.D.36, Steve Miller, M.D., Ph.D.1, Charles Y. Chiu, M.D., Ph.D. 1,9,24, Susan L. Stramer, Ph.D.25, Michael R. Wilson, M.D. 3,22, Aashish Manglik, M.D., Ph.D.27, Chun Jimmie Ye, Ph.D.28,29,30,31,32,33, Nevan J. Krogan, Ph.D.4,34,35, Mark S. Anderson, M.D., Ph.D.7, Jason G. Cyster, Ph.D.5,8, Joel D. Ernst, M.D.18, Alan H. B. Wu, Ph.D.1, Kara L. Lynch, Ph.D.1, Caryn Bern, M.D., M.P.H.33**, Patrick D. Hsu, Ph.D.6,20**, Alexander Marson, M.D., Ph.D Test performance evaluation of SARS-CoV-2 serological assays

Symbols legend

The following symbols may appear on the packaging and the label:

LOT	*Batch code*	BUF	*Buffer*
	Use until	CAL	*Calibrator*
	Manufacturer	H	*High*
IVD	*In vitro diagnostic medical device*	M	*Moderate*
	Temperature (Storage at)	L	*Low*
REF	*Catalogue reference*	4 LEV	*4 levels*
	Read the usage instructions	5 LEV	*5 levels*
REAG	*Reagent*	6 LEV	*6 levels*
KIT	*Kit*	CONTROL	*Control*
CONT	*Content*		
Ab	*Antibody or Antisera*		

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