INSTRUCTIONS FOR USE CV2TN

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Reagent Pack	REF	619 9975
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators	REF	619 9976

Rx ONLY
For *in vitro* diagnostic use only. For emergency authorization use only.

Intended Use

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Reagent Pack when used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators is a chemiluminescent immunoassay test intended for the qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma (K_2-EDTA). The VITROS Anti-SARS-CoV-2 Total N Antibody test 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. The VITROS Anti-SARS-CoV-2 Total N Antibody test should not be used to diagnose or exclude acute SARS-CoV-2 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform moderate or high complexity tests.

Results are for the detection of total SARS-CoV-2 antibodies. Total antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

The sensitivity of the VITROS Anti-SARS-CoV-2 Total N Antibody test in early infection is unknown. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for the VITROS Anti-SARS-CoV-2 Total N Antibody test may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The VITROS Anti-SARS-CoV-2 Total N Antibody test is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation of the Test

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a novel beta coronavirus that caused an outbreak of Coronavirus Disease 2019 (COVID-19), resulting in a world-wide pandemic. SARS-CoV-2 is mainly transmitted through droplets and contact routes. [1-2] People who are infected with SARS-CoV-2 may show symptoms of acute respiratory illness, such as fever, cough, shortness of breath, but can also be asymptomatic. Symptomatic, pre-symptomatic (infected but still symptom-free) and asymptomatic SARS-CoV-2 carriers all can be potential sources for viral transmission. [3] Real-time reverse transcription polymerase chain reaction (rRT-PCR) detecting the genetic material of SARS-CoV-2 genes is considered the gold standard for the diagnosis of COVID-19, and SARS-CoV-2 antigen assays have also been used to detect acute infection. [4] Individuals infected with SARS-CoV-2 start to produce antibodies to the virus 1-2 weeks post symptom onset, and most individuals achieve seroconversion in week 3-4 after symptom onset. [5-6] Patients with SARS-CoV-2 infection produce antibodies to multiple viral antigens including the spike protein and the nucleocapsid protein. [7] Notably, it is not currently known if the presence of antibodies confers protection from re-infection.

Principles of the Procedure

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody test is performed using the VITROS Anti-SARS-CoV-2 Total N Antibody Reagent Pack and the VITROS Anti-SARS-CoV-2 Total N Antibody Calibrators on VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and VITROS 5600/XT 7600 Integrated Systems. An immunometric technique is used; this involves a two-stage reaction. In the first stage antibodies to SARS-CoV-2 present in the sample bind with SARS-

CoV-2 nucleocapsid protein antigen coated on the well. Unbound sample is removed by washing. In the second stage horseradish peroxidase (HRP)-labeled recombinant SARS-CoV-2 nucleocapsid protein antigen is added in the conjugate reagent. The conjugate binds specifically to any anti-SARS-CoV-2 antibodies captured on the well in the first stage. Unbound conjugate is removed by a subsequent wash step.

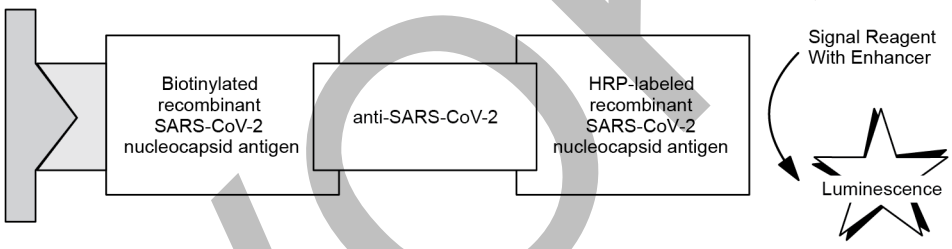
The bound HRP conjugate is measured by a luminescent reaction [8]. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. Bound HRP conjugate is indicative of the presence of SARS-CoV-2 antibody.

Test Type	System	Incubation Time	Time to first result	Test Temperature	Reaction Sample Volume
Immunometric	ECi/ECiQ**, 3600, 5600/XT 7600***	37 minutes	48 minutes	37 °C	80 µL

** Software version 3.9.1 or later

*** Software version 3.6.1 or later

Reaction Scheme



Warnings and Precautions

WARNING: *Potentially Infectious Material*

Treat as if capable of transmitting infection.

Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (HIV 1+2) or other infectious agents are absent. Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29). [9]

WARNING: *Contains EDTA, tetrasodium, dihydrate (CAS 10378-23-1) and 2-Methyl-3-isothiazolone (CAS 2682-20-4)* [10]

The VITROS Anti-SARS-CoV-2 Total N Antibody Assay Reagent contains 1.9% EDTA, tetrasodium, dihydrate and 0.0475% 2-Methyl-3-isothiazolone. H317: May cause an allergic skin reaction. H319: Causes serious eye irritation. P261: Avoid breathing dust/fume/gas/mist/vapors/ spray. P264: Wash face, hands and any exposed skin thoroughly after handling. P272: Contaminated work clothing must not be allowed out of the workplace. P280: Wear protective gloves and eye

protection. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do - continue rinsing. P337 + P313: If eye irritation persists: Get medical advice/attention. P363: Wash contaminated clothing before reuse. P501: Dispose of content/container to an approved waste disposal plant.

WARNING

WARNING: *Contains 2-Methyl-3-isothiazolone (CAS 2682-20-4)* [10]

The VITROS Anti-SARS-CoV-2 Total N Antibody HRP Conjugate Reagent and VITROS Anti-SARS-CoV-2 Total N Antibody Calibrators contain 0.0475% 2-Methyl-3-isothiazolone. H317: May cause an allergic skin reaction. P261: Avoid breathing dust/fume/gas/mist/vapors/ spray. P272: Contaminated work clothing must not be allowed out of the workplace. P280: Wear protective gloves. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P363: Wash contaminated clothing before reuse. P501: Dispose of content/container to an approved waste disposal plant.

Refer to www.orthoclinicaldiagnostics.com for the Safety Data Sheets and for Ortho Clinical Diagnostics contact information.

WARNING

Safe Disposal

Follow local disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

General

- For Emergency Use Authorization only.
- For *in vitro* diagnostic use only.
- For prescription use only.
- This product has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories certified under CLIA, that meet requirements to perform moderate or high complexity tests.
- This product has been authorized only for detecting total antibodies to SARS-CoV-2, not for any other viruses or pathogens.

The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food Drug and Cosmetic Act, 21 U.S.C. § 360bbb3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

Reagents

Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (streptavidin, bacterial; binds ≥ 3 ng biotin per well; recombinant SARS-CoV-2 nucleocapsid antigen 14 ng/well)
- 6.0 mL assay reagent (buffer with bovine protein stabilizers and antimicrobial agent)
- 16.2 mL conjugate reagent (HRP-recombinant SARS-CoV-2 nucleocapsid antigen) in buffer with bovine protein stabilizers and antimicrobial agent

Reagent Pack Handling

- The reagent pack is supplied ready for use.
- The reagent pack contains homogeneous liquid reagents that do not require shaking or mixing prior to loading onto the system. Handle the reagent pack with care. Avoid the following:
  - allowing condensation to form on the pack
  - causing reagents to foam
  - agitation of the pack

Reagent Pack Storage and Preparation

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8°C (36–46°F)	expiration date
Opened	On system	System turned on	≤8 weeks
Opened	Refrigerated	2–8°C (36–46°F)	≤8 weeks

- The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Reagent Pack is suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- Do not freeze reagent packs.
- Load reagent packs directly from refrigerated storage to minimize condensation.
- Opened reagent packs are moisture/humidity sensitive. Store opened refrigerated reagent packs in a sealed VITROS Immunodiagnostic Products Reagent Pack Storage Box with desiccant.

Calibrator Contents

- 2 vials of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators (anti-SARS-CoV-2 in buffer with bovine serum albumin and antimicrobial agent, 1.0 mL)

Calibrator Handling

- Use only with reagent packs of the same lot number. Mix thoroughly by inversion and bring to 15–30°C (59–86°F) before use.
- Handle calibrators in original stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time the calibrators are on the system. Refer to the operating instructions for your system. Return to 2–8°C (36–46°F) as soon as possible after use, or load only sufficient volume for a single determination.

Calibrator Storage and Preparation

Calibrator	Storage Condition		Stability
Unopened	Frozen	≤-20°C (≤-4°F)	expiration date
Opened	Refrigerated	2–8°C (36–46°F)	≤24 hours

- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators are supplied frozen.
- The VITROS Anti-SARS-CoV-2 Total N Antibody Calibrators are suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- **DO NOT REFREEZE.**
- The VITROS Anti-SARS-CoV-2 Total N Antibody test uses 80 µL of calibrator for each determination. Transfer an aliquot of each calibrator into a sample container (taking account of the minimum fill volume of the container). For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.
- The VITROS Anti-SARS-CoV-2 Total N Antibody Calibrators are automatically processed in duplicate.

Specimen Collection, Preparation and Storage

Patient Preparation

No special patient preparation is necessary.

Specimens Recommended

- Serum
- K_2-EDTA Plasma

Specimens Not Recommended

No specimen limitations were identified. Refer to the Limitations of the Procedure section.

Special Precautions

IMPORTANT: *Certain collection devices have been reported to affect other analytes and tests.* [11] *Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.*

Specimen Collection and Preparation

- Collect specimens using standard procedures. [12]
- Follow the instructions provided with your specimen collection tube for use and processing of the sample. [13]
- Samples should be thoroughly separated from all cellular material. Failure to do so may lead to an erroneous result.
- The VITROS Anti-SARS-CoV-2 Total N Antibody test uses 80 µL of sample for each determination. This does not take account of the minimum fill volume of the chosen sample container. For details on minimum fill volume of sample cups or containers, refer to the operating instructions for your system.

Handling and Storage Conditions

- Handle samples in stoppered containers to avoid contamination and evaporation.
- Follow procedures within your laboratory to avoid cross contamination of patient specimens.
- The amount of time samples are on the system prior to analysis should be limited to avoid evaporation. Refer to the operating instructions for your system.
- Return to 2–8°C (36–46°F) as soon as possible after use or load sufficient volume for a single determination.
- Samples may be stored for up to 24 hours at room temperature (up to 30°C [86°F]) or 7 days at 2–8°C (36–46°F).
- Samples that will not be tested within the time frames outlined above should be stored at ≤-20°C [≤-4°F] and may be subjected to 5 freeze-thaw cycles.
- As an alternative to the above, sample stability may be established by each laboratory.

Testing Procedure

Materials Provided

- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Reagent Pack
- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators

Materials Required but Not Provided

- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls

Optional Materials Not Provided

- VITROS Immunodiagnostic Products Reagent Pack Storage Box with desiccant

Operating Instructions

Check the inventory regularly to aid the management of reagents and ensure that sufficient VITROS Immunodiagnostic Products Signal Reagent, VITROS Immunodiagnostic Products Universal Wash Reagent and calibrated reagent lots are available for the work planned. When performing panels of tests on a single sample, ensure that the sample volume is sufficient for the tests ordered.

For detailed information refer to the operating instructions for your system.

Note: Do not use visibly damaged product.

Default Test Name

The default test name which will appear on patient reports is SARS-CoV2 Tot N. The default short name that will appear on the test selection menus and laboratory reports is CV2TN. These defaults may be reconfigured, if required. For detailed information refer to the operating instructions for your system.

Calibration

Calibration Procedure

- Calibration is lot specific; reagent packs and calibrators are linked by lot number. Reagent packs from the same lot may use the same calibration.
- A Master Calibration is established for each new reagent lot by performing multiple tests. This is the process by which a lot-specific parameter [a] which links the signal at the cutoff (cutoff value) to the calibrator signal is determined.
- Cutoff value = a_{LOT} x (Signal of Cal 1)
- Ensure that the Master Calibration for each new reagent lot is available on your system.
- Process calibrator in the same manner as samples. Load sufficient for the automatic duplicate determination. Calibration need not be programmed if bar code labels are used; calibration will be initiated automatically.
- When the calibrator is processed, the validity of the calibration is assessed against quality parameters which compare the actual signal of the calibrator with the expected signal. If the calibration is acceptable the cutoff value is calculated and stored for use with any reagent pack of that lot.
- The quality of calibration cannot be completely described by a single parameter. The calibration report should be used in conjunction with acceptable control values to determine the validity of the calibration.
- Recalibration is required after a pre-determined calibration interval, or when a different reagent lot is loaded.
- Calibration results are assessed against a range of quality parameters. Failure to meet any of the defined quality parameter ranges will be coded in the calibration report. For actions to be taken following a failed calibration refer to the operating instructions for your system.
- Refer to the operating instructions for your system for detailed instructions on the calibration process.

When to Calibrate

- Calibrate when the reagent pack and calibrator lot changes.
- Calibrate every 28 days.
- After specified service procedures have been performed.
- If quality control results are consistently outside of your acceptable range.

For additional information on when to calibrate, refer to the operating instructions for your system.

Traceability of Calibration

Calibration of the VITROS Anti-SARS-CoV-2 Total N Antibody test is traceable to an in-house reference calibrator which has been value assigned to optimize clinical sensitivity and specificity.

Calibration Model

Results are calculated as a normalized signal, relative to a cutoff value. During the calibration process a lot-specific parameter is used to determine a valid stored cutoff value for the VITROS Immunodiagnostic and VITROS Integrated Systems.

Quality Control

Quality Control Material Selection

VITROS Anti-SARS-CoV-2 Total N Controls are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. There are 2 VITROS Anti-SARS-CoV-2 Total N Controls (anti-SARS-CoV-2 Tot N Non-reactive and anti-SARS-CoV-2 Tot N Reactive). The performance of other commercial control fluids should be evaluated for compatibility with this test before they are used for quality control.

Control materials may show a difference when compared with other anti-SARS-CoV-2 Total antibody methods if they contain high concentrations of preservatives, stabilizers, or other non-physiological additives, or otherwise depart from a true human sample matrix.

Appropriate quality control value ranges must be established for all quality control materials used with the VITROS Anti-SARS-CoV-2 Total N Antibody test.

Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- Choose control levels that check the clinically relevant concentrations.

- To verify system performance, analyze control materials:
  - After calibration
  - If the system is turned off for more than 2 hours
  - After reloading reagent packs that have been removed from the MicroWell Supply and stored for later use
  - According to local regulations or at least once each day that the test is being performed
  - After specified service procedures are performed

If quality control procedures within your laboratory require more frequent use of controls, follow those procedures.

- Analyze quality control materials in the same manner as patient specimens.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- Refer to published guidelines for general quality control recommendations. [14]

For more detailed information, refer to the operating instructions for your system.

Quality Control Material Preparation and Storage

Refer to the manufacturer's product literature for preparation, storage, and stability information.

Results

Results are automatically calculated by the VITROS Immunodiagnostic and VITROS Integrated Systems.

Result Calculation

$$\text{Result} = \frac{\text{Signal for test sample}}{\text{Cutoff value}}$$

Interpretation of Results

The following table summarizes the interpretation of results obtained with the VITROS Anti-SARS-CoV-2 Total N Antibody test on the VITROS Immunodiagnostic and VITROS Integrated Systems. The magnitude of the measured result above the cutoff is not indicative of the total amount of antibody present in the sample and no clinical utility of significance has been validated for the magnitude of the measure result above the cutoff. Linearity of results has not been demonstrated (for example: an S/C result of 20 does not necessarily contain twice as much antibody as a result of 10 S/C).

VITROS Anti-SARS-CoV-2 Total N Antibody Test Result (S/C)	Interpretation
<1.00	Specimen is non-reactive (negative) for anti-SARS-CoV-2
≥1.00	Specimen is reactive (positive) for anti-SARS-CoV-2

Patient sample results will be displayed with a "Non-reactive" or "Reactive" label. Numerical results should not be reported outside the laboratory to individual patients or their physicians, rather results reported outside the laboratory should be reported as only "Non-reactive" or "Reactive" only.

Result (S/C)	<1.00	≥1.00
Result Text	Non-reactive (negative)	Reactive (positive)

Limitations of the Procedure

Known Interferences

The VITROS Anti-SARS-CoV-2 Total N Antibody test was evaluated for interference. Commonly encountered substances were tested on one lot of reagent. Of the compounds tested, none were found to interfere with the clinical interpretation of the test. Refer to "Substances that do not Interfere" for a list of compounds tested that did not show interference.

Other Limitations

- SARS-CoV-2 serology tests should not be used to diagnose acute COVID-19. An assay that directly detects the virus should be used to evaluate symptomatic individuals for acute COVID-19, particularly those who have been in contact with the virus.
- Heterophilic antibodies in serum or plasma samples may cause interference in immunoassays. [15] These antibodies may be present in blood samples from individuals regularly exposed to animals or who have been treated with animal serum products. Results that are inconsistent with clinical observations indicate the need for additional testing.

- A negative or non-reactive result can occur if the quantity of antibodies for the SARS-CoV-2 virus present in the specimen is below the detection limit of the assay, the antibodies that are detected are not present during the stage of disease in which a sample is collected, or the virus has undergone minor amino acid mutation(s) in the epitopes recognized by the antibodies detected by the test.The results obtained with this test should only be interpreted in conjunction with clinical findings, and the results from other laboratory tests and evaluations.
- Results from antibody testing should not be used to diagnose or exclude SARS-CoV-2 infection.
- It is unknown at this time if the presence of antibodies to SARS-CoV-2 confers immunity to infection.
- This test should not be used for screening of donated blood for the purpose of preventing COVID-19 transmission.
- A positive result may not indicate previous SARS-CoV-2 infection. Consider other information including clinical history and local disease prevalence, in assessing the need for a second but different serology test to confirm an immune response.
- The performance of this test has not been established in individuals that have received a COVID-19 vaccine. The clinical significance of a positive or negative antibody result following COVID-19 vaccination has not been established, and the result from this test should not be interpreted as an indication or degree of protection from infection after vaccination.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between March 2020 and January 2021 for RT-PCR positive samples at multiple sites within the USA. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

Conditions of Authorization for the Laboratory

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Reagent Pack when used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody Calibrators Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Recipients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas. Authorized laboratories using the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Antibody test (‘your product” in the conditions below) must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

- Authorized laboratories* using your product must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories using your product must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7-OIR/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Ortho-Clinical Diagnostics, Inc. (OrthoCareTechnicalSolutions@orthoclinicaldiagnostics.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.
- All laboratory personnel using your product must be appropriately trained in automated immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit, and use your product in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the product.
- Ortho-Clinical Diagnostics, Inc., authorized distributors, and authorized laboratories using your product must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

*The letter of authorization refers to, “Laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests” as “authorized laboratories.”

Performance Characteristics

Clinical Performance Characteristics

Negative Percent Agreement

1048 samples collected from apparently healthy individuals prior to December 2019 were tested on the VITROS Anti-SARS-CoV-2 Total N Antibody assay. Of the 1048 samples, 553 were serum and 495 were K_2-EDTA plasma. The results are presented in the table below. Negative percent agreement (NPA) has been calculated, along with the 95% confidence interval (95% CI).

Sample Matrix	Subjects (n)	Reactive Results	Non-Reactive Results	NPA	95% CI
Serum	553	5	548	99.1%	97.9–99.6%
K_2-EDTA	495	4	491	99.2%	97.9–99.7%
Combined	1048	9	1039	99.1%	98.4–99.5%

Positive Percent Agreement

176 samples were collected from subjects determined to be positive for the SARS-CoV-2 virus by an EUA RT-PCR method. The 176 samples consisted of 131 serum samples and 45 K_2-EDTA plasma samples. The results are summarized in the tables below, with samples classified based on the number of days after onset of symptoms. Positive percent agreement (PPA) has been calculated, along with the 95 % confidence interval (95% CI).

Matrix	Symptom Onset (days)	Subjects (n)	Reactive Results (n)	Non-Reactive Results (n)	PPA	95% CI
Serum	0–7	22	18	4	81.8%	61.5–92.7%
	8–14	39	36	3	92.3%	79.7–97.4%
	≥15	70	63	7	90.0%	80.8–95.1%

Matrix	Symptom Onset (days)	Subjects (n)	Reactive Results (n)	Non-Reactive Results (n)	PPA	95% CI
K_2-EDTA	0–7	0	N/A	N/A	N/A	N/A
	8–14	0	N/A	N/A	N/A	N/A
	≥15	45	44	1	97.8%	88.4–99.6%

Potentially Cross-reacting Subgroups

76 samples from the following potentially cross-reacting sub-groups were tested and none were found to be reactive in the VITROS Anti-SARS-CoV-2 Total N Antibody test.

Sample Category	Number Tested	Samples Non-reactive	Samples Reactive
anti-influenza A IgG	5	5	0
anti-influenza A IgM	19	19	0
anti-influenza B IgG	17	17	0
anti-influenza B IgM	15	15	0
anti-HCV	5	5	0
anti-HBV	9	9	0
anti-Haemophilus influenzae	25	25	0
anti-229E (alpha coronavirus)	24	24	0
anti-NL63 (alpha coronavirus)	10	10	0
anti-OC43 (beta coronavirus)	21	21	0
anti-HKU1 (beta coronavirus)	11	11	0
anti-nuclear antibodies	5	5	0
anti-respiratory syncytial virus	20	20	0
anti-HIV	5	5	0

Specificity

Substances that do not Interfere

The VITROS Anti-SARS-CoV-2 Total N Antibody test was evaluated for interference consistent with CLSI document EP07. [16] Of the compounds tested, none were found to interfere with the clinical interpretation of the test at the concentrations indicated at a VITROS Anti-SARS-CoV-2 Total N Antibody result of approximately 0, 1.5-3, and 10-20 S/C.

Compound	Concentration
Hemoglobin	1000 mg/dL
Bilirubin (unconjugated)	40.0 mg/dL
Bilirubin (conjugated)	40.0 mg/dL
Intralipid	2000 mg/dL
Biotin	3510 ng/mL
Total Protein	15 g/dL

References

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Glossary of Symbols

The following symbols may have been used in the labeling of this product.

Do Not Reuse	Upper Limit of Temperature	Range
Use by or Expiration Date (Year-Month-Day)	Lower Limit of Temperature	Range of Means
LOT Batch Code or Lot Number	Temperature Limitation	Midpoint
SN Serial Number	Consult Instructions for Use	Revised
REF Catalog Number or Product Code	Attention: The Instructions for Use (IFU) has been updated	Supersedes
Caution	S1 For use in Slide Supply 1	Σ Contains Sufficient for "n" Tests
Keep Dry (Protect from Moisture/Humidity)	S2 For use in Slide Supply 2	IVD *in vitro* Diagnostic Medical Device
Manufacturer	SI SI Units	Der Grüne Punkt (the Green Dot). Manufacturer follows certain packaging material waste disposal management regulations
Date of Manufacture	CONV Conventional Units	σ Estimated within-lab SD
EC REP Authorized Representative in the European Community	Value	
Corrosive	Flammable	Serious Health Hazards
Health Hazards	Acute Toxicity	Environmental or Aquatic Toxicity

Revision History

Date of Revision	Version	Description of Technical Changes*
2023-08-01	2.0	• Warnings and Precautions: Updated Hazard and Precaution statements to align with the new Safety Data Sheets • Materials Required but Not Provided: Updated "Anti-SARS-CoV-2 Total Controls" to "Anti-SARS-CoV-2 Total N Controls" • Quality Control Material Selection: – Updated "Anti-SARS-CoV-2 Total Controls" to "Anti-SARS-CoV-2 Total N Controls" – Updated "Anti-SARS-CoV-2 Tot Non-reactive" to "Anti-SARS-CoV-2 Tot N Non-reactive" – Updated "Anti-SARS-CoV-2 Tot Reactive" to "Anti-SARS-CoV-2 Tot N Reactive" • Corrected the legal manufacturer from Rochester to Pencoed

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

_____ _____

Signature Obsolete Date

Conditions of supply: all supplies are made subject to the standard terms and conditions of Ortho Clinical Diagnostics or its distributors. Copies of these are available on request.

Distributed in the US by:
Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, NY 14626

Ortho-Clinical Diagnostics
Felindre Meadows
Pencoed
Bridgend
CF35 5PZ
United Kingdom

To obtain a paper copy free of charge contact:
OrthoCareTechnicalSolutions@
orthoclinicaldiagnostics.com
1 800 421 3311

Ortho Clinical Diagnostics

INSTRUCTIONS FOR USE CV2TN

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls

REF 617 4442

Rx ONLY

Intended Use

For use under Emergency Use Authorization (EUA) only
For *in vitro* diagnostic and laboratory professional use.
For use in monitoring the performance of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N test when used on the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems.

Warnings and Precautions

WARNING: *Potentially Infectious Material*

Treat as if capable of transmitting infection.

Use caution when handling material of human origin. Consider all samples potentially infectious. No test method can offer complete assurance that hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (HIV 1+2) or other infectious agents are absent. Handle, use, store and dispose of solid and liquid waste from samples and test components, in accordance with procedures defined by appropriate national biohazard safety guideline or regulation (e.g. CLSI document M29).[1]

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls 1 and 2 contain: SARS-CoV-2 antibody negative plasma obtained from donors who were tested individually and who were found to be negative for hepatitis B surface antigen, and for antibodies to hepatitis C virus (HCV) and HIV, using approved methods (enzyme immunoassays).

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Control 2 in addition contains: SARS-CoV-2 antibody. Handle as if capable of transmitting infection.

WARNING: *Contains 2-Methyl-3-isothiazolone (CAS 2682-20-4)*[2]

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls contain 0.0475% 2-Methyl-3-isothiazolone. H317: May cause an allergic skin reaction. P261: Avoid breathing dust/fume/gas/mist/vapors/spray. P272: Contaminated work clothing must not be allowed out of the workplace. P280: Wear protective gloves. P302 + P352: IF ON SKIN: Wash with plenty of soap and water. P333 + P313: If skin irritation or rash occurs: Get medical advice/attention. P363: Wash contaminated clothing before reuse. P501: Dispose of contents/container to an approved waste disposal plant.

Refer to www.orthoclinicaldiagnostics.com for the Safety Data Sheets and for Ortho contact information.

WARNING

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
- This product has been authorized for use with a test authorized only for detecting total antibodies to SARS-CoV-2, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

Materials Provided

3 sets of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls 1 and 2 (defibrinated human plasma with anti-microbial agent, 2 mL). Control 1 is non-reactive and Control 2 is reactive.

Materials Required but Not Provided

Pipette, sample containers.

Control Storage and Handling

Control	Storage Condition		Stability
Unopened	Frozen	≤-20 °C (≤-4 °F)	expiration date
Opened	Refrigerated	2–8 °C (36–46 °F)	≤7 days

- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls are supplied frozen.
- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Controls are suitable for use until the expiration date on the carton when stored and handled as specified. Do not use beyond the expiration date.
- **DO NOT REFREEZE.**
- Thoroughly mix controls by inversion and bring to 15–30 °C (59–86 °F) before use.
- Handle controls in stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time controls are on the system. Refer to the operating instructions for your system.
- Return to 2–8 °C (36–46 °F) as soon as possible after use, or load only sufficient for a single determination.
- Baseline statistics for controls should be entered onto the system. For further information, refer to the operating instructions for your system.
- The expiration date for the controls must be entered onto the system. For further information, refer to the operating instructions for your system.

Testing Procedure

Load each control onto the system by transferring an aliquot into a sample container (taking account of the volume required by the test and the minimum fill volume of the container). Process in the same manner as samples, according to the instructions in the appropriate VITROS Immunodiagnostic Products Reagent Pack and Calibrator instructions for use.

Note: Do not use visibly damaged product.

For further information on quality control procedures refer to the operating instructions for your system.
Not all products and systems are available in all countries.

Baseline Statistics

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Control 1 should generate Non-reactive (negative) results.
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total N Control 2 should generate Reactive (positive) results. If a control result is out of its specified range, <1.00 S/C for the negative control and ≥1.00 S/C for the positive control,

investigate the cause before reporting patient results. When the condition is corrected, retest the controls and confirm that results are within acceptable limits. Repeat all patient specimens before reporting results for this run.

References

1. CLSI. *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline - Fourth Edition.* CLSI document M29-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
2. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

Glossary of Symbols

The following symbols may have been used in the labeling of this product.

Do Not Reuse	Upper Limit of Temperature	Range
Use by or Expiration Date (Year-Month-Day)	Lower Limit of Temperature	Range of Means
LOT Batch Code or Lot Number	Temperature Limitation	Midpoint
SN Serial Number	Consult Instructions for Use	Revised
REF Catalog Number or Product Code	Attention: The Instructions for Use (IFU) has been updated	Supersedes
Caution	S1 For use in Slide Supply 1	Σ Contains Sufficient for "n" Tests
Keep Dry (Protect from Moisture/Humidity)	S2 For use in Slide Supply 2	IVD *in vitro* Diagnostic Medical Device
Manufacturer	SI SI Units	Der Grüne Punkt (the Green Dot). Manufacturer follows certain packaging material waste disposal management regulations
Date of Manufacture	CONV Conventional Units	σ Estimated within-lab SD
EC REP Authorized Representative in the European Community	Value	
Corrosive	Flammable	Serious Health Hazards
Health Hazards	Acute Toxicity	Environmental or Aquatic Toxicity

Revision History

Date of Revision	Version	Description of Technical Changes*
2023-09-20	1.0	Initial version of Instructions for Use

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

Signature

Obsolete Date

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Distributed in the US by:
Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, NY 14626 USA

Ortho-Clinical Diagnostics
Felindre Meadows
Pencoed
Bridgend
CF35 5PZ
United Kingdom

To obtain a paper copy free of charge contact:
OrthoCareTechnicalSolutions@
orthoclinicaldiagnostics.com
1 800 421 3311

Ortho Clinical Diagnostics

Rx Only

For EUA Only

IVD

Printed Instructions for Use may be requested at no charge at 1 800 421 3311.

This is not the full Instructions for Use. The full Instructions for Use are available on https://techdocs.orthoclinicaldiagnostics.com/TechDocs/TechDocSearch.aspx?tID=0

This product has not been US FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.

This product has been authorized for use with a test authorized only for detecting total antibodies to SARS-CoV-2, not for any other viruses or pathogens.

The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the US Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3 (b)(1), unless the declaration is terminated or authorization is revoked sooner.

Product code: 6174442

Issued September 2023
PIGEM5505EUA/J71779

Rx Only

For EUA Only

IVD

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This is not the full Instructions for Use.
The full Instructions for Use are available on https://techdocs.orthoclinicaldiagnostics.com/TechDocs/TechDocSearch.aspx?tID=0

This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.

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Issued July 2021
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Product codes: 6199975, 6199976