VITROS Immunodiagnostic Products

Intended for Use in the United States

INSTRUCTIONS FOR USE CV2T

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack	REF	619 9953
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator	REF	619 9954

Rx ONLY
For *in vitro* Diagnostic use only

Intended Use

For *in vitro* diagnostic and laboratory professional use.

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack when used in combination with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator is a chemiluminescent immunoassay intended for the qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma (K_2-EDTA, K_3-EDTA and lithium heparin) samples collected on or after 15 days post-symptom onset using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems. The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total 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.

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator

For use in the calibration of the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 7600 Integrated Systems for the *in vitro* qualitative detection of total antibodies to SARS-CoV-2 in human serum and plasma.

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] However, the level of antibodies confers protection from re-infection is not known yet.

Principles of the Procedure

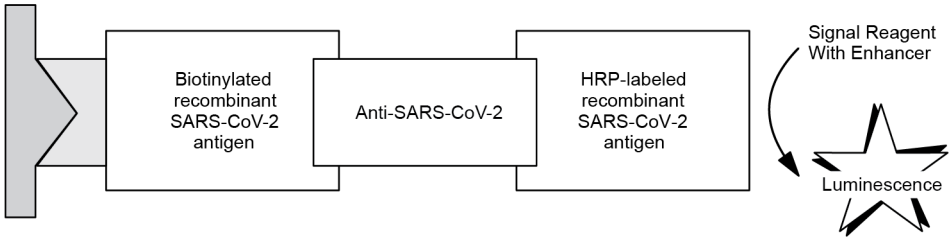
The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test is performed using the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack and the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator on the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/XT 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 spike protein S1 antigen coated on the well. Unbound sample is removed by washing. In the second stage horseradish peroxidase (HRP)-labeled recombinant SARS-CoV-2 spike protein S1 antigen is added in the conjugate reagent. The conjugate binds specifically to any anti-SARS-CoV-2 captured on the well in the first stage. Unbound conjugate is removed by the 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.

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

* Not all products and systems are available in all countries.

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]

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

WARNING: *Contains EDTA, tetrasodium, dihydrate (CAS 10378-23-1) and Mixture, 3(2H)-isothiazolone, 5-chloro-2-methyl-with 2-methyl-3(2H)-isothiazolone (CAS 55965-84-9)* [10]

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Assay Reagent contains 1.9% EDTA, tetrasodium, dihydrate and 0.03% Mixture, 3(2H)-isothiazolone, 5-chloro-2-methyl-with 2-methyl-3(2H)-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 Mixture, 3(2H)-isothiazolone, 5-chloro-2-methyl-with 2-methyl-3(2H)-isothiazolone (CAS 55965-84-9)* [10]

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total HRP Conjugate Reagent contains 0.03% Mixture, 3(2H)-isothiazolone, 5-chloro-2-methyl-with 2-methyl-3(2H)-isothiazolone. H317: May cause an allergic skin reaction. P261: Avoid breathing dust/fume/gas/mist/vapors/spray. P272: Contaminated work clothing should 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.

WARNING



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

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator contains 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 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.

Reagents

Reagent Pack Contents

1 reagent pack containing:

- 100 coated wells (streptavidin, bacterial; binds ≥3 ng biotin per well; biotin recombinant SARS-CoV-2 antigen 0.1 µg/mL)
- 6.0 mL assay reagent (buffer with bovine protein stabilizers and antimicrobial agent)

- 16.2 mL conjugate reagent (HRP-recombinant SARS-CoV-2 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 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 Calibrator (anti-SARS-CoV-2 in anti-SARS-CoV-2 negative human plasma with antimicrobial agent, 1 mL)
- Lot calibration card
- Protocol card
- 8 calibrator bar code labels

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 calibrator in original stoppered containers to avoid contamination and evaporation. To avoid evaporation, limit the amount of time the calibrator is 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

- The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator is supplied frozen.
- The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator 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 REFREEZE.**
- The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test uses 80 µL of calibrator for each determination. Transfer an aliquot of the 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 Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator is automatically processed in duplicate.

Specimen Collection, Preparation and Storage

Patient Preparation

No special patient preparation is necessary.

Specimens Recommended

- Serum

- K_2-EDTA Plasma
- K_3-EDTA Plasma
- Lithium Heparin Plasma

Specimens Not Recommended

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test is intended to be used ONLY with the specimen types recommended in this document.

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 blood 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 Immunodiagnostic Products Anti-SARS-CoV-2 Total 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 15–30 °C (59–86 °F) or 7 days at 2–8 °C (36–46 °F).
- Samples that will not be tested within 24 hours at room temperature or 7 days refrigerated should be stored frozen at ≤-20 °C (≤-4 °F). Serum and plasma samples may be subjected to up to five freeze-thaw cycles.
- Thoroughly mix samples by inversion and bring to 15–30 °C (59–86 °F) before use.

Specimen Storage and Stability

Storage	Temperature	Stability
Room Temperature	15–30 °C (59–86 °F)	≤24 hours
Refrigerated	2–8 °C (36–46 °F)	≤7 days
Frozen	≤-20 °C (≤-4 °F)	≤4 weeks

Testing Procedure

Materials Provided

- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack
- VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Calibrator

Materials Required but Not Provided

- VITROS ECi/ECiQ Immunodiagnostic Systems
- VITROS 3600 Immunodiagnostic Systems
- VITROS 5600 Integrated Systems
- VITROS XT 7600 Integrated Systems
- VITROS Immunodiagnostic Products Signal Reagent
- VITROS Immunodiagnostic Products Universal Wash Reagent
- Quality control materials such as VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Controls
- 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 Signal Reagent, VITROS 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-CoV-2 Tot. The default short name that will appear on the test selection menus and laboratory reports is CV2T. 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 calibrator 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 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 volume 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 Immunodiagnostic Products Anti-SARS-CoV-2 Total 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 Immunodiagnostic Products Anti-SARS-CoV-2 Total Controls are recommended for use with the VITROS Immunodiagnostic and VITROS Integrated Systems. There are 2 VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Controls (non-reactive and reactive).

Quality Control Procedure Recommendations

- Good laboratory practice requires that controls be processed to verify the performance of the test.
- 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 the 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 Storage

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

Results

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

Result Calculation

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

Interpretation of Results

Patient sample results will be displayed with a "Non-reactive" (negative) or "Reactive" (positive) label.

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

The following table summarizes the interpretation of results obtained with the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test on the VITROS Immunodiagnostic and VITROS Integrated Systems.

VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total 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

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.
- Samples should only be tested from individuals that are 15 days or more post-symptom onset.
- The sensitivity of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test in early infection is unknown.
- At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test should not be used to diagnose acute SARS-CoV-2 infection. 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.
- The performance characteristics for that analyte were established when the original B.1 lineage of the Wuhan-Hu-1 strain was prevalent and that due to the propensity of the virus to mutate, new strains emerge over time which may affect the performance of this device and have serious public health implications.
- 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.

- There is a risk of erroneous results (i.e., negative results) due to the presence of novel emerging viral variants circulating in the intended use population.
- 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 cutoff of the assay, or the virus has undergone minor amino acid mutation(s) in the epitope recognized by the antibody detected by the test.
- A negative or non-reactive result can occur if the antibodies that are detected are not present during the stage of disease in which a sample is collected.
- A negative test result indicates that antibodies to SARS-CoV-2 were not detected in the samples. Acute infection should not be excluded based on negative antibody test results. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.
- The results obtained with this test should only be interpreted in conjunction with clinical findings, and the results from other laboratory tests and evaluations.
- 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.
- False positive results for VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test may occur due to cross-reactivity from preexisting antibodies or other possible causes.
- Positive and negative predictive values are highly dependent on prevalence.
- Accurate results are dependent on adequate specimen collection, transport, storage, and processing (as applicable). Failure to observe proper procedures in any one of these steps can lead to incorrect results.
- It is unknown at this time if the presence of antibodies to SARS-CoV-2 confers immunity to infection.
- 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.
- This test should not be used for screening of donated blood for the purpose of preventing COVID-19 transmission.

Performance Characteristics

Clinical Performance Characteristics

The clinical performance of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test was evaluated at three testing sites using 809 retrospective clinical samples acquired from two populations. Population 1 consisted of 296 samples collected from COVID-19 individuals with a prior SARS CoV-2 positive test result using an FDA EUA authorized RT-PCR test. Population 2 consisted of 513 samples collected prior to December 2019 (before the widespread outbreak of COVID-19).

Of the 296 samples in population 1, 31 samples were collected 0–7 days from COVID-19 symptom onset, 26 samples were collected between 8–14 days from COVID-19 symptom onset, and 239 samples were collected ≥15 days from COVID-19 symptom onset. The table below shows the sample distribution and the respective percentages from the total of samples tested per “Days post-symptoms onset” time bin.

Time bin (n= total number samples tested)	Days post-symptom onset	Percent (per time bin)
0–7 days (n=31)	0–4	77.42%
	5–7	22.58%
8–14 days (n=26)	8–11	42.31%
	12–14	57.69%
≥15 days (n=239)	15–21	11.30%
	22–30	22.18%
	31–60	44.77%
	61–90	8.79%
	91–253	12.97%

Positive Percent Agreement (PPA)

A total of 296 samples collected from individual patients confirmed to have a prior SARS-CoV-2 positive result by RT-PCR were tested. Blood samples were collected within the United States between April 2020 and April 2021. Samples were tested with the VITROS Immunodiagnostic Products Anti SARS-CoV-2 Total test on each system (except the samples that were not tested on one or more systems due to limited volume). Of the 296 samples included in the study, 70 were EDTA plasma samples, 82 were Lithium-Heparin plasma samples and 144 were serum samples.

The performance of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test and 95% Confidence Interval for each VITROS System is summarized in the tables below:

PPA performance of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test and 95% Confidence Interval by systems:
In the VITROS ECi/ECiQ Immunodiagnostic Systems:

Days from Symptom Onset	Number of Subjects Tested (with prior RT-PCR Positive)	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results		
		Reactive	PPA	95% CI (Wilson score)
0–7 days	25	9	36.00%	20.24%–55.48%
8–14 days	19	16	84.21%	62.44%–94.48%
≥15 days	238	224	94.12%	90.37%–96.46%
Total	282	–	–	–

In the VITROS 3600 Integrated Systems:

Days from Symptom Onset	Number of Subjects Tested (with prior RT-PCR Positive)	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results		
		Reactive	PPA	95% CI (Wilson score)
0–7 days	25	11	44.00%	26.66%–62.93%
8–14 days	22	17	77.27%	56.56%–89.88%
≥15 days	239	225	94.14%	90.41%–96.48%
Total	286	–	–	–

In the VITROS 5600 Integrated Systems:

Days from Symptom Onset	Number of Subjects Tested (with prior RT-PCR Positive)	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results		
		Reactive	PPA	95% CI (Wilson score)
0–7 days	27	10	37.04%	21.53%–55.77%
8–14 days	19	15	78.95%	56.67%–91.49%
≥15 days	239	225	94.14%	90.41%–96.48%
Total	285	–	–	–

In the VITROS XT 7600 Integrated Systems:

Days from Symptom Onset	Number of Subjects Tested (with prior RT-PCR Positive)	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results		
		Reactive	PPA	95% CI (Wilson score)
0–7 days	25	10	40.00%	23.40%–59.26%
8–14 days	22	17	77.27%	56.56%–89.88%
≥15 days	237	223	94.09%	90.33%–96.45%
Total	284	–	–	–

Negative Percent Agreement (NPA)

Five hundred thirteen (513) presumed SARS-CoV-2 negative samples collected prior to the COVID-19 pandemic within the United States were tested. Of the 513 samples, 46 were EDTA plasma samples, 333 were lithium-heparin samples and 134 were serum samples. All samples were tested using the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and the VITROS 5600/ XT 7600 Integrated Systems (except the samples that were not tested on one or more systems due to

limited volume). The performance of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test and 95% Confidence Interval for each VITROS System is summarized in the table below:

VITROS System	Presume Negative (Collected Pre-COVID)	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results		
		Non-Reactive	NPA	95% CI (Wilson score)
ECi/ECiQ	505	502	99.41%	98.27%–99.80%
3600	511	509	99.61%	98.58%–99.89%
5600	509	508	99.80%	98.90%–99.97%
XT 7600	505	503	99.60%	98.57%–99.89%

Analytical Performance Characteristics

Analytical Sensitivity

The analytical sensitivity of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test is 0.8475 BAU/mL using the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin (human) NIBSC code: 20/136.

Potentially Cross-reacting Subgroups

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test was evaluated for potential cross-reactivity in Anti-SARS-CoV-2 negative samples from medical conditions unrelated to SARS-CoV-2 infection. The results are summarized in the table below.

Sample Category	Number of Samples Tested	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results	
		Non-reactive	Reactive
Influenza A Antibody	10	10	0
Influenza B Antibody	12	12	0
Hepatitis C Virus (HCV) Antibody	15	15	0
Anti-Nuclear Antibody (ANA)	10	10	0
Adenovirus Antibody	12	12	0
Coxsackie B Virus Antibody	10	10	0
Echovirus Antibody	10	10	0
Poliovirus Antibody	9	9	0
Respiratory Syncytial Virus (RSV) Antibody	10	10	0
Hepatitis B Virus (HBV) Antibody	12	12	0
Haemophilus influenzae Antibody	12	12	0
Human coronavirus HKU1 Antibody	11	11	0
Human coronavirus NL63 Antibody	10	10	0
Human coronavirus OC43 Antibody	21	21	0
Human coronavirus 229E Antibody	24	24	0
Human Immunodeficiency Virus (HIV) Antibody	17	17	0
Human Parainfluenza Virus (HPIV) Antibody	5	5	0
Human Metapneumovirus (HMPV) Antibody	10	10	0
Enterovirus Antibody	10	10	0
Rhinovirus Antibody	11	11	0
Epstein-Barr Virus (EBV) Antibody	11	11	0
Epstein-Barr Virus Nuclear Antigen (EBVNA) Antibody	11	11	0
Legionella pneumophila Antibody	10	10	0
Bordetella pertussis Antibody	15	15	0
Mycoplasma pneumoniae Antibody	14	14	0
Chlamydophila pneumoniae Antibody	10	10	0
Cytomegalovirus (CMV) Antibody	11	11	0
Rheumatoid Factor (RF) Antibody	11	11	0

Sample Category	Number of Samples Tested	VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test Results	
		Non-reactive	Reactive
Severe Acute Respiratory Syndrome (SARS) coronavirus Antibody	13	13	0
Middle East Respiratory Syndrome (MERS) coronavirus Antibody	14	14	0
Rubella Virus Antibody	10	10	0
Mycobacterium tuberculosis Antibody	12	12	0
Streptococcus pneumoniae Antibody	10	10	0
Streptococcus pyogenes Antibody	10	10	0
Pneumocystis jirovecii pneumonia (PJP) Antibody	10	10	0
Candida albicans Antibody	14	14	0
Pseudomonas aeruginosa Antibody	13	13	0
Staphylococcus epidermis Antibody	10	10	0
Human Anti-Mouse Antibody (HAMA)	10	10	0

Within-Laboratory Precision

The within-laboratory precision of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test was evaluated with EDTA plasma pools (PP4, PP5, and PP6), negative and positive quality control materials (PP1, PP2), and the calibrator (PP3), on the VITROS ECi/ECiQ and 3600 Immunodiagnostic Systems and the VITROS 5600 and XT 7600 Integrated Systems following the CLSI document EP05-A3. [16] A total of 3 lots of reagent packs, calibrators and controls were included in the study. For each reagent lot, operators ran two replicates of each precision panel sample on two occasions per day for twenty non-consecutive days.

The data presented are a representation of test performance and are provided as a guideline. Variables such as sample handling and storage, reagent handling and storage, laboratory environment, and system maintenance can affect precision of test results.

VITROS System	Panel member	Number of Obs.	Grand Mean (S/C)	Repeatability* (Within Run)		Between-Run		Between-Day		Between-Lot		Within-Laboratory**	
				SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
ECi/ ECiQ	PP1	240	0.02	0.001	N/A	0.001	N/A	0.000	N/A	0.005	N/A	0.005	N/A
	PP2	240	2.83	0.059	2.1	0.060	2.1	0.049	1.7	0.150	5.3	0.179	6.3
	PP3	240	0.94	0.016	1.7	0.023	2.4	0.023	2.4	0.000	0.0	0.036	3.8
	PP4	240	0.86	0.034	4.0	0.024	2.8	0.016	1.9	0.026	3.0	0.051	5.9
	PP5	240	3.27	0.048	1.5	0.074	2.3	0.031	0.9	0.250	7.6	0.267	8.2
	PP6	240	9.88	0.153	1.5	0.197	2.0	0.640	6.5	0.978	9.9	1.196	12.1
3600	PP1	240	0.02	0.002	N/A	0.002	N/A	0.000	N/A	0.002	N/A	0.005	N/A
	PP2	240	2.99	0.044	1.5	0.076	2.5	0.059	2.0	0.499	16.7	0.510	17.1
	PP3	240	1.00	0.021	2.1	0.031	3.1	0.031	3.1	0.134	13.4	0.142	14.2
	PP4	240	0.93	0.017	1.8	0.030	3.2	0.030	3.2	0.147	15.8	0.154	16.6
	PP5	240	3.50	0.056	1.6	0.087	2.5	0.051	1.5	0.686	19.6	0.696	19.9
	PP6	240	10.4	0.16	1.5	0.15	1.4	0.19	1.8	2.40	23.0	2.41	23.2
5600	PP1	240	0.02	0.003	N/A	0.003	N/A	0.000	N/A	0.005	N/A	0.007	N/A
	PP2	240	3.18	0.049	1.5	0.069	2.2	0.055	1.7	0.312	9.8	0.328	10.3
	PP3	240	1.06	0.021	2.0	0.041	3.9	0.008	0.8	0.030	2.8	0.055	5.2
	PP4	240	0.98	0.021	2.1	0.037	3.8	0.013	1.3	0.032	3.3	0.055	5.6
	PP5	240	3.70	0.070	1.9	0.084	2.3	0.046	1.2	0.450	12.2	0.465	12.6
	PP6	240	11.0	0.22	2.0	0.22	2.0	0.19	1.7	1.86	16.9	1.90	17.2

VITROS System	Panel member	Number of Obs.	Grand Mean (S/C)	Repeatability* (Within Run)		Between-Run		Between-Day		Between-Lot		Within-Laboratory**	
				SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
XT 7600	PP1	240	0.02	0.002	N/A	0.004	N/A	0.000	N/A	0.006	N/A	0.008	N/A
	PP2	240	3.45	0.054	1.6	0.076	2.2	0.069	2.0	0.324	9.4	0.344	10.0
	PP3	240	1.14	0.021	1.8	0.039	3.4	0.027	2.4	0.173	15.2	0.180	15.8
	PP4	240	1.06	0.021	2.0	0.039	3.7	0.021	2.0	0.152	14.3	0.160	15.1
	PP5	240	4.00	0.069	1.7	0.090	2.3	0.062	1.6	0.346	8.7	0.370	9.3
	PP6	240	11.7	0.18	1.5	0.23	2.0	0.17	1.4	0.75	6.4	0.83	7.1

* Repeatability was determined using two replicates per run.

** Within-Laboratory precision variability contains the Within Run, Between Run, Between Day and Between Lot variance components using three individual reagent lots with a single calibration for each reagent lot.

N/A = Not Applicable, %CV is not meaningful for S/C results <0.5.

Reproducibility

The reproducibility of the VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test was determined with EDTA plasma pools (TRP4, TRP5, and TRP6), quality controls (TRP1 and TRP2) and calibrator (TRP3) using the VITROS ECi/ECiQ and 3600 Immunodiagnostic Systems, and the VITROS 5600 and XT 7600 Integrated Systems. Samples were measured in triplicate using 3 reagent lots, in 2 runs per day over 5 days at 3 sites, according to CLSI EP05-A3. [16] Variance components were calculated, and the following results were observed per system:

Reproducibility of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test evaluated on VITROS ECi/ECiQ Immunodiagnostic Systems

Panel Member	Number of Obs.	Grand Mean (S/C)	Repeatability (Within Run)		Between-Run		Between-Day		Between-Lot[a]		Within-Laboratory[b]		Between-Site[c]		Reproducibility (Overall)[d]	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
TRP1	270	0.02	0.007	N/A+	0.000	N/A+	0.002	N/A+	0.000	N/A+	0.007	N/A+	0.006	N/A+	0.010	N/A+
TRP2	270	3.17	0.153	4.8	0.000	0.0	0.044	1.4	0.000	0.0	0.159	5.0	0.128	4.0	0.239	7.5
TRP3	270	1.05	0.066	6.3	0.000	0.0	0.000	0.0	0.036	3.4	0.075	7.1	0.017	1.6	0.088	8.4
TRP4	270	0.97	0.046	4.7	0.019	1.9	0.018	1.8	0.035	3.6	0.063	6.5	0.000	0.0	0.077	7.9
TRP5	270	3.70	0.130	3.5	0.000	0.0	0.053	1.4	0.151	4.1	0.206	5.6	0.112	3.0	0.263	7.1
TRP6	270	11.1	0.39	3.5	0.00	0.0	0.18	1.6	0.80	7.2	0.90	8.1	0.48	4.3	1.10	9.9

[a] Between lot: Variability of the test performance from lot to lot.

[b] Within-Laboratory variability contains the Within Run, Between Run, Between Day and Between Lot variance components.

[c] Between site: Variability of the test performance from site to site.

[d] Reproducibility: Variability of the test incorporating factors of site, lot, run and day.

+ %CVs are not meaningful for S/C results <0.50.

Reproducibility of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test evaluated on VITROS 3600 Immunodiagnostic Systems

Panel Member	Number of Obs.	Grand Mean (S/C)	Repeatability (Within Run)		Between-Run		Between-Day		Between-Lot[a]		Within-Laboratory[b]		Between-Site[c]		Reproducibility (Overall)[d]	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
TRP1	270	0.03	0.027	N/A+	0.004	N/A+	0.006	N/A+	0.000	N/A+	0.028	N/A+	0.005	N/A+	0.030	N/A+
TRP2	270	3.31	0.135	4.1	0.000	0.0	0.098	3.0	0.000	0.0	0.166	5.0	0.276	8.3	0.391	11.8
TRP3	270	1.09	0.086	7.9	0.041	3.7	0.020	1.9	0.046	4.2	0.107	9.9	0.024	2.2	0.152	14.0
TRP4	270	1.02	0.039	3.9	0.014	1.3	0.024	2.4	0.043	4.2	0.065	6.4	0.045	4.5	0.093	9.1
TRP5	270	3.88	0.144	3.7	0.000	0.0	0.097	2.5	0.054	1.4	0.182	4.7	0.347	8.9	0.472	12.2
TRP6	270	11.5	0.33	2.9	0.00	0.0	0.18	1.6	0.67	5.8	0.77	6.7	0.99	8.6	1.49	13.0

[a] Between lot: Variability of the test performance from lot to lot.

[b] Within-Laboratory variability contains the Within Run, Between Run, Between Day and Between Lot variance components.

[c] Between site: Variability of the test performance from site to site.

[d] Reproducibility: Variability of the test incorporating factors of site, lot, run and day.

+ %CVs are not meaningful for S/C results <0.50.

Reproducibility of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test evaluated on VITROS 5600 Integrated Systems

Panel Member	Number of Obs.	Grand Mean (S/C)	Repeatability (Within Run)		Between-Run		Between-Day		Between-Lot[a]		Within-Laboratory[b]		Between-Site[c]		Reproducibility (Overall)[d]	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
TRP1	270	0.02	0.008	N/A+	0.001	N/A+	0.002	N/A+	0.000	N/A+	0.008	N/A+	0.003	N/A+	0.009	N/A+
TRP2	270	3.17	0.086	2.7	0.022	0.7	0.000	0.0	0.000	0.0	0.089	2.8	0.255	8.0	0.318	10.0
TRP3	270	1.05	0.046	4.4	0.025	2.4	0.000	0.0	0.019	1.8	0.056	5.3	0.055	5.2	0.101	9.6
TRP4	270	0.97	0.032	3.2	0.029	3.0	0.020	2.1	0.043	4.5	0.064	6.6	0.044	4.6	0.085	8.8
TRP5	270	3.65	0.249	6.8	0.081	2.2	0.000	0.0	0.166	4.6	0.310	8.5	0.265	7.3	0.494	13.5
TRP6	270	10.9	0.48	4.4	0.09	0.9	0.00	0.0	0.87	8.0	0.99	9.1	0.97	8.9	1.54	14.2

[a] Between lot: Variability of the test performance from lot to lot.

[b] Within-Laboratory variability contains the Within Run, Between Run, Between Day and Between Lot variance components.

[c] Between site: Variability of the test performance from site to site.

[d] Reproducibility: Variability of the test incorporating factors of site, lot, run and day.

[+] %CVs are not meaningful for S/C results <0.50.

Reproducibility of VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test evaluated on VITROS XT 7600 Integrated Systems

Panel Member	Number of Obs.	Grand Mean (S/C)	Repeatability (Within Run)		Between-Run		Between-Day		Between-Lot[a]		Within-Laboratory[b]		Between-Site[c]		Reproducibility (Overall)[d]	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
TRP1	270	0.02	0.006	N/A+	0.001	N/A+	0.001	N/A+	0.000	N/A+	0.006	N/A+	0.005	N/A+	0.009	N/A+
TRP2	270	3.21	0.199	6.2	0.077	2.4	0.119	3.7	0.029	0.9	0.246	7.7	0.048	1.5	0.289	9.0
TRP3	270	1.06	0.062	5.9	0.024	2.2	0.029	2.8	0.038	3.6	0.082	7.8	0.000	0.0	0.110	10.4
TRP4	270	1.00	0.036	3.6	0.000	0.0	0.019	1.9	0.058	5.9	0.071	7.2	0.000	0.0	0.090	9.0
TRP5	270	3.78	0.104	2.8	0.000	0.0	0.036	1.0	0.188	5.0	0.218	5.8	0.105	2.8	0.280	7.4
TRP6	270	11.2	0.30	2.7	0.07	0.7	0.00	0.0	0.88	7.9	0.94	8.3	0.33	2.9	1.06	9.5

[a] Between lot: Variability of the test performance from lot to lot.

[b] Within-Laboratory variability contains the Within Run, Between Run, Between Day and Between Lot variance components.

[c] Between site: Variability of the test performance from site to site.

[d] Reproducibility: Variability of the test incorporating factors of site, lot, run and day.

[+] %CVs are not meaningful for S/C results <0.50.

Interference

Interferents

The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test was evaluated for potential interference consistent with CLSI document EP07. [17]Commonly encountered substances were tested on one lot of reagent using the VITROS 3600 Immunodiagnostic System or the VITROS 5600 Integrated System in 3 reactive (low positive) and 3 non-reactive (negative) samples. All potentially interfering substances have been shown to not interfere (<10% bias for low reactive samples and bias <0.22 S/C for non-reactive samples) with the test performance at the concentration listed in the table below.

Endogenous interferents evaluated with VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test

Substance	Test Concentration	
	Conventional Units	SI Units
Anti-Nuclear Antibody (ANA)	>8 AI	N/A
Bilirubin, conjugated	40 mg/dL	475 µmol/L
Bilirubin, unconjugated	40 mg/dL	684 µmol/L
Cholesterol	400 mg/dL	10.3 mmol/L
Hemoglobin	1000 mg/dL	10 g/L
Human Anti-Mouse Antibody (HAMA)	3600 ng/mL	0.024 µmol/L
Rheumatoid Factor (RF)	35.7–61.7 IU/mL	N/A
Total Protein	9.37 g/dL	93.7 g/L
Triglycerides	1500 mg/dL	16.94 mmol/L

N/A = Not Applicable (alternate units are not provided)

Exogenous interferents evaluated with VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total test

Substance	Test Concentration	
	Conventional Units	SI Units
Abacavir	1.27 mg/dL	44.4 µmol/L
Acetaminophen	15.6 mg/dL	1.03 mmol/L
Amlodipine	7.5 µg/dL	0.183 µmol/L
Amoxicillin	5.4 mg/dL	148 µmol/L
Aspirin	3 mg/dL	0.167 mmol/L
Atorvastatin	75 µg/dL	1.34 µmol/L
Azithromycin	1.1 mg/dL	14.8 µmol/L
Biotin	3510 ng/mL	14.3 µmol/L
Cefoxitin	660 mg/dL	15.5 mmol/L
Ceftriaxone	84 mg/dL	1.51 mmol/L
Dextromethorphan	1.56 µg/dL	0.0575 µmol/L
EDTA	0.099 mg/dL	3.39 µmol/L
Gentamicin	3.0 mg/dL	62.8 µmol/L
Guaifenesin	450 µg/dL	22.7 µmol/L
Heparin	330 units/dL	330 units/dL
Ibuprofen	21.9 mg/dL	1.06 mmol/L
Intralipid	2000 mg/dL	NA
Levofloxacin	0.9 mg/dL	24.9 µmol/L
Levothyroxine	429 µg/dL	0.552 µmol/L
Lisinopril	24.6 µg/dL	0.607 µmol/L
Lopinavir	57.17 µg/mL	90.89 µmol/L
Loratadine	8.7 µg/dL	0.271 µmol/L
Losartan	1155 ng/mL	2.505 µmol/L
Meropenem	33.9 mg/dL	884 µmol/L
Metformin	1.2 mg/dL	92.9 µmol/L
Metoprolol	150 µg/dL	5.61 µmol/L
Naproxen	36.0 mg/dL	1.56 mmol/L
Omeprazole	840 µg/dL	24.3 µmol/L
Oseltamivir	39.9 µg/dL	1.28 µmol/L
Peramivir	183,600 ng/mL	559 µmol/L
Prednisone	10 µg/dL	0.276 µmol/L
Ritonavir	10.98 mg/dL	126.42 mmol/L
Theophylline	6.0 mg/dL	333 µmol/L
Vancomycin	12.0 mg/dL	82.8 µmol/L
Zanamivir	1089 ng/mL	3.28 µmol/L

N/A = Not Applicable (alternate units are not provided)
When Levofloxacin was tested at a concentration of 1.8 mg/dL, a positive bias (+12.03% change of the S/C value) was observed in reactive samples.

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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	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	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*
2023-08-25	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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