SARS-CoV-2 IgG

FOR USE WITH Alinity i

Read Highlighted Changes: Revised December 2021.

REF 06R9020
REF 06R9030

For use under an Emergency Use Authorization (EUA) Only
Prescription Use only.

For *In Vitro* Diagnostic Use Only.

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

For laboratory professional use only.

NAME

SARS-CoV-2 IgG (also referred to as CoV-2 IgG)

INTENDED USE

The SARS-CoV-2 IgG assay is a chemiluminescent microparticle immunoassay (CMIA) intended for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum, serum separator tube and plasma (ACD, CPD, CPDA-1, dipotassium EDTA, tripotassium EDTA, lithium heparin, lithium heparin separator tube, sodium citrate, sodium heparin). The SARS-CoV-2 IgG 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. The SARS-CoV-2 IgG assay should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) of 1988, 42 U.S.C 263a, to perform moderate or high complexity test.

Results are for the detection of SARS CoV-2 antibodies. IgG 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 SARS-CoV-2 IgG early after 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 SARS-CoV-2 IgG assay may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Due to the risk of false positive results, confirmation of positive results should be considered using a second, different IgG assay.

The SARS-CoV-2 IgG assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

SUMMARY AND EXPLANATION OF THE TEST

The SARS-CoV-2 IgG assay is designed to detect immunoglobulin class G (IgG) antibodies to the nucleocapsid protein of SARS-CoV-2 in serum and plasma from individuals who are suspected to have had coronavirus disease (COVID-19) or in serum and plasma of subjects that may have been infected by SARS-CoV-2.

COVID-19 is defined as illness caused by a novel coronavirus now called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, formerly called 2019-nCoV).[1] On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic.[2]

The incubation period of COVID-19 ranges between 1 and 14 days, with the majority of cases manifesting within 3 to 5 days. The most common symptoms of COVID-19 are fever, tiredness, dry cough, and difficulty breathing. A severe acute respiratory distress syndrome (ARDS) may develop.[3] Reported case fatality rates depend on geographic location,[4] age, and comorbidities.

The causative agent of COVID-19 is a beta coronavirus and belongs to a family of viruses that may cause respiratory symptoms ranging from common cold to severe pneumonia. These viruses are common in animals worldwide and may eventually transfer to humans, as has likely happened with SARS-CoV-2.[1]

The host immune system reacts to the infection by SARS-CoV-2 by producing specific antibodies. These antibodies have been reported to appear in serum or plasma of infected individuals after the detection of viral ribonucleic acid (RNA) in swabs[5] in as early as a few days to 2 weeks after the onset of symptoms.[6] Specific IgG antibodies to SARS-CoV-2 may be detectable in COVID-19 patients during the symptomatic phase of the disease after RNA is no longer detectable.[5, 6] The persistence of IgG antibodies allows identification of people who have been infected in the past, and likely have recovered from the illness.[7] It is unknown if IgG antibodies to SARS-CoV-2 confer immunity to infection. IgG detection and other serological assays will likely play an important role in research and surveillance.[8]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

This assay is an automated, two-step immunoassay for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Sample, SARS-CoV-2 antigen coated paramagnetic microparticles, and assay diluent are combined and incubated. The IgG antibodies to SARS-CoV-2 present in the sample bind to the SARS-CoV-2 antigen coated microparticles. The mixture is washed. Anti-human IgG acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following a wash cycle, Pre-Trigger and Trigger Solutions are added.

The resulting chemiluminescent reaction is measured as a relative light unit (RLU).

The presence or absence of IgG antibodies to SARS-CoV-2 in the sample is determined by comparing the chemiluminescent RLU in the reaction to the calibrator RLU, which is calculated by the system as an Index (S/C).

For additional information on system and assay technology, refer to the Alinity ci-series Operations Manual, Section 3.

REAGENTS

Kit Contents

SARS-CoV-2 IgG Reagent Kit 06R90

NOTE: Some kit sizes may not be available. Please contact your local distributor.

Volumes (mL) listed in the following table indicate the volume per cartridge.

REF	06R9020	06R9030
Tests per cartridge	100	500
Number of cartridges per kit	2	2
Tests per kit	200	1000
MICROPARTICLES	6.6 mL	27.0 mL
CONJUGATE	6.1 mL	26.5 mL
ASSAY DILUENT	8.3 mL	36.9 mL

MICROPARTICLES Purified SARS-CoV-2 recombinant antigen coated microparticles in TRIS buffer with surfactant. Minimum concentration: 0.045% solids. Preservatives: ProClin 950 and sodium azide.

CONJUGATE Anti-human IgG (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with surfactant and protein (bovine) stabilizer. Minimum concentration: 4 ng/mL. Preservatives: ProClin 300 and antimicrobial agents.

ASSAY DILUENT TRIS buffer and detergent. Preservatives: ProClin 950 and sodium azide.

Warnings and Precautions

For Use Under An Emergency Use Authorization Only.

This assay is only for *in vitro* diagnostic use under the FDA Emergency Use Authorization.

- IVD
- For *In Vitro* Diagnostic Use
- Rx ONLY
- This test has not been FDA cleared or approved; this test has been authorized by FDA under an EUA for use by laboratories certified under CLIA, that meet requirements to perform moderate or high complexity tests.
- This test has been authorized only for the presence of IgG antibodies against SARS-CoV-2, not for any other viruses or pathogens.
- This test 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 Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

Safety Precautions

CAUTION: This product requires the handling of human specimens. It is recommended that all human-sourced materials and all consumables contaminated with potentially infectious materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate regional, national, and institutional biosafety practices should be used for materials that contain, are suspected of containing, or are contaminated with infectious agents.[9-12]

The following warnings and precautions apply to: MICROPARTICLES and ASSAY DILUENT	
	
WARNING	Contains methylisothiazolone and sodium azide.
H317	May cause an allergic skin reaction.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: CONJUGATE	
H402	Harmful to aquatic life.
H412	Harmful to aquatic life with long lasting effects.
Prevention	
P273	Avoid release to the environment.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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

For the most current hazard information, see the product Safety Data Sheet.

Safety Data Sheets are available at www.corelaboratory.abbott or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 8.

Reagent Handling

- Reagents are shipped on wet ice.
- Upon receipt, gently invert the unopened reagent kit by rotating it over and back for a full 180 degrees, 5 times with green label stripe facing up and then 5 times with green label stripe facing down. This ensures that liquid covers all sides of the bottles within the cartridges. During reagent shipment, microparticles can settle on the reagent septum.
  - Place a check in the square on the reagent kit to indicate to others that the inversions have been completed.
- After mixing, place reagent cartridges in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.
- When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human IgG will result in a neutralized conjugate.

For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 7.

Reagent Storage

- Do not freeze.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright, gently invert the cartridge 10 times and place in an upright position for 1 hour before use.

Abbott

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Onboard	System Temperature	7 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright during storage off the system, discard the cartridge. Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 8°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, refer to the Alinity ci-series Operations Manual, Section 5.

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when a calibration error occurs or a control value is out of the specified range. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The SARS-CoV-2 IgG assay file must be installed on the Alinity i system prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the Alinity ci-series Operations Manual, Section 2.

For information on printing assay parameters, refer to the Alinity ci-series Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity ci-series Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below may be used with this assay.

Specimen Types	Collection Tubes
Serum	Serum
	Serum separator
Plasma	ACD
	CPD
	CPDA-1
	Dipotassium EDTA
	Tripotassium EDTA
	Lithium heparin
	Lithium heparin separator
	Sodium heparin
	Sodium citrate

- Each laboratory is responsible for following their own procedures to establish the use of additional tube or collection types.
- Performance has not been established for the use of cadaveric specimens or the use of bodily fluids other than human serum/plasma.
- Liquid anticoagulants may have a dilution effect resulting in lower Index (S/C) values for individual specimens.

The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use:
  - heat-inactivated specimens
  - pooled specimens
  - grossly hemolyzed specimens
  - specimens with obvious microbial contamination
  - specimens with fungal growth
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed vortex or by inverting 10 times prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly by low speed vortex or by inverting 10 times.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Recentrifuge specimens.

Recentrifugation of Specimens

- Transfer specimens to a centrifuge tube and centrifuge.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time
Serum/Plasma	Room temperature (15 to 30°C)	2 days
	2 to 8°C	7 days

If testing will be delayed more than 7 days, it is recommended to store frozen.

It is the responsibility of the individual laboratory to determine specific specimen stability criteria for their laboratory per their laboratory workflow.

For additional information on sample handling and processing, refer to CLSI GP44-A4.[13] The storage information provided here is based on data maintained by the manufacturer.

Frozen specimens subjected to up to 2 freeze/thaw cycles have been evaluated.

Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

06R90 SARS-CoV-2 IgG Reagent Kit

Materials Required but not Provided

- SARS-CoV-2 IgG assay file
- 06R9001 SARS-CoV-2 IgG Calibrator Kit
- 06R9010 SARS-CoV-2 IgG Control Kit or other control material containing IgG antibodies to SARS-CoV-2
- Alinity Pre-Trigger Solution
- Alinity Trigger Solution
- Alinity i-series Concentrated Wash Buffer

For information on materials required for operation of the instrument, refer to the Alinity ci-series Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the Alinity ci-series Operations Manual, Section 9.

Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity ci-series Operations Manual, Section 5.

- If using primary or aliquot tubes, refer to the Alinity ci-series Operations Manual, Section 4 to ensure sufficient specimen is present.
- Minimum sample cup volume is calculated by the system and printed on the Order List report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
- Maximum number of replicates sampled from the same sample cup: 10
  - Priority:
    - Sample volume for first test: 75 µL
    - Sample volume for each additional test from same sample cup: 25 µL
  - ≤ 3 hours on the reagent and sample manager:
    - Sample volume for first test: 150 µL
    - Sample volume for each additional test from same sample cup: 25 µL
  - > 3 hours on the reagent and sample manager:
    - Replace with a fresh aliquot of sample.
- Refer to the SARS-CoV-2 IgG calibrator package insert REF 06R9001 and/or SARS-CoV-2 IgG control package insert REF 06R9010 for preparation and usage.
- For general operating procedures, refer to the Alinity ci-series Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity ci-series Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Sample Dilution Procedures

Do not use diluted samples for the SARS-CoV-2 IgG assay.

Calibration

For instructions on performing a calibration, refer to the Alinity ci-series Operations Manual, Section 5.

Calibrator is tested in triplicate.

A single sample of each control level must be tested to evaluate the assay using the ratio of the sample RLU to the cutoff RLU (S/C) for assay calibration.

Ensure that assay control values are within the S/C ranges specified in the control package insert.

Each assay control must be tested to evaluate the assay calibration.

Once a calibration is accepted and stored, it may be used for 30 days. During this time, all subsequent samples may be tested without further calibration unless:

- A reagent kit with a new lot number is used.
- Daily quality control results are outside of quality control limits used to monitor and control system performance.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

The recommended control requirement for the SARS-CoV-2 IgG assay is that a single sample of each control level be tested once every 24 hours each day of use.

Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

To establish statistically-based control limits, each laboratory should establish its own concentration target and ranges for new control lots at each clinically relevant control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days and using the reported results to establish the expected average (target) and variability about this average (range) for the laboratory. Sources of variation that should be included in this study in order to be representative of future system performance include:

- Multiple stored calibrations
- Multiple reagent lots
- Multiple calibrator lots
- Multiple processing modules (if applicable)
- Data points collected at different times of the day

Refer to published guidelines for information or general control recommendation, for example Clinical and Laboratory Standards Institute (CLSI) Guideline C24, 4th ed., or other published guidelines, for general quality control recommendations.[14]

- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, sample results may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary. For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Controls should be used according to the guidelines and recommendations of the control manufacturer. Concentration ranges provided in the control package insert should be used only for guidance.

For any control material in use, the laboratory should ensure that the matrix of the control material is suitable for use in the assay per the assay package insert.

Quality Control Guidance

Refer to "Basic QC Practices" by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[15]

Verification of Assay Claims

For protocols to verify package insert claims, refer to Verification of Assay Claims in the Alinity ci-series Operations Manual.

For protocols to verify package insert claims, follow CLIA recommendations or internal laboratory procedures.

RESULTS

Calculation

The Alinity i system calculates the calibrator mean chemiluminescent signal from 3 calibrator replicates and stores the result. Results are reported by dividing the sample result by the stored calibrator result. The default result unit for the SARS-CoV-2 IgG assay is Index (S/C).

Interpretation of Results

The cutoff is 1.40 Index (S/C).

As with all analyte determinations, the result should be used in conjunction with information available from clinical evaluation and other diagnostic procedures.

Index (S/C)	Interpretation
< 1.40	Negative
≥ 1.40	Positive

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the Alinity ci-series Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- **For use under an Emergency Use Authorization only.**
- This assay is for *in vitro* diagnostic use under FDA Emergency Use Authorization only.
- This test is for clinical laboratory use only. It is not for home use.
- Results should be used in conjunction with other data; e.g., symptoms, results of other tests, and clinical impressions.
- Immunocompromised patients who have COVID-19 may have a delayed antibody response and produce levels of antibody which may not be detected as positive by the assay.
- 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.
- Negative results do not rule out SARS-CoV-2 infection, particularly in those who have been in contact with the virus. Testing with a molecular diagnostic should be considered to evaluate for active infection in these individuals.
- Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
- Pedigreed specimens with direct evidence of antibodies to non-SARS-CoV-2 coronavirus (common cold) strains such as HKU1, NL63, OC43, or 229E have not been evaluated with this assay.
- Not to be used to screen units of blood for SARS-CoV-2 infection.
- Potentially interfering disease states and other cross reactants have been evaluated and are represented in the SPECIFIC PERFORMANCE CHARACTERISTICS section of this package insert.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as SARS-CoV-2 IgG that employ mouse monoclonal antibodies.[16, 17]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference, and anomalous values may be observed.[18]
- Rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[18]
- The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with 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 at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

CONDITIONS OF AUTHORIZATIONS FOR THE LABORATORIES

The SARS-CoV-2 IgG Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients, 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 or at https://www.corelaboratory.abbott/us/en/offerings/segments/infectious-disease/sars-cov-2.

Authorized laboratories using the SARS-CoV-2 IgG ("your product" in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

A. Authorized laboratories* using your product will include with result reports of your product, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

B. Authorized laboratories using your product will use your product as outlined in the Instructions for Use. 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.

C. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.

D. Authorized laboratories using your product will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.

E. Authorized laboratories will 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 Abbott Laboratories at https://www.corelaboratory.abbott/us/en/offerings/segments/infectious-disease/sars-cov-2 any suspected occurrence of false reactive or false non-reactive results and significant deviations from the established performance characteristics of your product of which they become aware.

F. 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.

G. Abbott Laboratories, authorized distributors, and authorized laboratories using your product will 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, to perform moderate and high complexity tests" as "authorized laboratories."

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

The Alinity i system and the ARCHITECT i2000SR System utilize the same reagents and sample/reagent ratios.

Some performance characteristics for the Alinity i assay were established using the ARCHITECT i System.

Precision

Within-Laboratory Precision

This study was conducted using the Alinity i analyzer. Testing was conducted using 1 lot of the SARS-CoV-2 IgG Reagent Kit, 1 lot of the SARS-CoV-2 IgG Calibrator Kit, and 1 lot of the SARS-CoV-2 IgG Control Kit and 1 instrument. Two controls and 1 human serum panel were assayed in a minimum of 3 replicates at 2 separate times per day on 5 different days.

			Repeatability (Within-Run)		Within-Laboratory[a]	
Sample	n	Mean (Index [S/C])	SD	%CV	SD	%CV
Negative Control	30	0.05	0.000	N/A[b]	0.000	N/A[b]
Positive Control	30	3.11	0.047	1.5	0.047	1.5
Positive Panel	30	2.15	0.035	1.6	0.036	1.7

[a] Includes repeatability (within-run), between-run, and between-day variability.

[b] Not applicable

Analytical Specificity

This study was performed on the ARCHITECT i2000SR System.

Potentially Cross-Reacting Antibodies

The SARS-CoV-2 IgG assay was evaluated for potentially cross-reacting antibodies. A total of 112 specimens from 23 different categories were tested. One hundred eleven (111) specimens were negative and 1 specimen was positive by the SARS-CoV-2 IgG assay. The data are summarized in the following table.

Category	n	Positive	Negative
Antinuclear Antibody (ANA)	5	0	5
Cytomegalovirus (CMV) IgG	5	1*	4
CMV Immunoglobulin Class M (IgM)	5	0	5
Double-Stranded Deoxyribonucleic Acid (dsDNA) Antibody	5	0	5
Epstein-Barr Virus (EBV) IgG	5	0	5
EBV IgM	5	0	5
Escherichia coli (E. coli) Antibody	5	0	5
HAMA	5	0	5
Anti-Hepatitis A Virus (HAV)	5	0	5
Hepatitis B Core (HBc) IgM	4	0	4
Anti-Hepatitis C Virus (HCV)	5	0	5
Anti-Hepatitis D Virus (HDV)	5	0	5
Anti-Herpes Simplex Virus (HSV)	5	0	5
Heterophilic Antibody Positive	5	0	5
Anti-Human T-Lymphotropic Virus (HTLV) Type 1	5	0	5
Anti-HTLV Type 2	5	0	5
Monoclonal Hyper IgG	5	0	5
Polyclonal Hyper IgG	3	0	3
Anti-Respiratory Syncytial Virus (RSV)	5	0	5
RF	5	0	5
Rubella IgG	5	0	5
Toxoplasmosis IgG	5	0	5
Anti-Varicella Zoster Virus	5	0	5
Total	112	1	111

* Testing was performed on an additional 199 specimens collected prior to September 2019 from subjects who were reactive for total (IgG/IgM) antibodies to CMV. Of those 199 specimens, 1 was positive on the SARS-CoV-2 IgG assay.

Potentially Interfering Medical Conditions and Respiratory Illnesses

The SARS-CoV-2 IgG assay was evaluated for potential cross-reactivity from individuals with potentially interfering medical conditions and respiratory illnesses. A total of 65 specimens from 12 different categories were tested. Sixty-five (65) specimens were negative by the SARS-CoV-2 IgG assay. The data are summarized in the following table.

Category	n	Positive	Negative
Adenovirus	5	0	5
Autoimmune Hepatitis	5	0	5
Hepatitis B Virus (HBV)	5	0	5
Human Immunodeficiency Virus (HIV)	5	0	5
Influenza A	7	0	7
Influenza B	5	0	5
Influenza (Type Unknown)	8	0	8
Influenza Vaccine	5	0	5
Lupus	5	0	5
Picornavirus	5	0	5
Pregnant Females	5	0	5
Pregnant Females, Multiparous	5	0	5
Total	65	0	65

Interference

These studies were performed on the ARCHITECT i2000SR System.

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.[19] Each substance was tested at 2 levels of the analyte (high negative and low positive levels, approximately 1.25 Index and 2.75 Index) in replicates of ten. The observed interference was within ± 0.14 Index or ± 10% at the following concentrations and therefore, the study showed no interference from these endogenous substances:

Potentially Interfering Endogenous Substance	Interferent Level
Unconjugated Bilirubin	40 mg/dL
Conjugated Bilirubin	40 mg/dL
Hemoglobin	1000 mg/dL
Triglyceride (Intralipid)	2000 mg/dL
Total Protein	15 g/dL

Potentially Interfering Exogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.[19] Each substance was tested at 2 levels of the analyte (approximately 1.25 Index and 2.75 Index) in replicates of ten. The observed interference was within ± 0.14 Index or ± 10% at the following concentrations and therefore, the study showed no interference from these exogenous substances:

Potentially Interfering Exogenous Substance	Interferent Level
Acetaminophen	1030 µmol/L
Alprazolam	0.835 µmol/L
Ascorbic Acid	298 µmol/L
Biotin	4250 ng/mL
Captopril	12.1 µmol/L
Fluoxetine	4.59 µmol/L
Guaifenesin	22.7 µmol/L
Hydroxychloroquine	388.8 ng/mL

Clinical Performance

This study was performed on the ARCHITECT i2000SR System.

A study was performed to determine the clinical performance of the SARS-CoV-2 IgG assay.

To estimate the positive percent agreement (PPA) between the SARS-CoV-2 IgG assay and the polymerase chain reaction (PCR) comparator, 122 serum and plasma specimens were collected at different times from 31 subjects who tested positive for SARS-CoV-2 by a PCR method and who also presented with COVID-19 symptoms. Each specimen was tested using the SARS-CoV-2 IgG assay. The PPA and the 95% confidence interval (CI) were calculated.

To estimate the negative percent agreement (NPA), 1070 serum and plasma specimens from subjects assumed to be negative for SARS-CoV-2 were tested. Of the 1070 specimens, 997 specimens were collected prior to September 2019 (pre-COVID-19 outbreak). An additional 73 specimens were collected in 2020 from subjects who were exhibiting signs of respiratory illness but tested negative for SARS-CoV-2 by a PCR method. All 1070 specimens were tested using the SARS-CoV-2 IgG assay. The NPA and the 95% CI were calculated.

The results of both groups are presented in the following 2 tables.

Positive Agreement by Days Post-Symptom Onset

Days Post-Symptom Onset	n	Positive	Negative	PPA (95% CI)
< 3	4	0	4	0.00% (0.00, 60.24)
3 - 7	8	2	6	25.00% (3.19, 65.09)
8 - 13	22	19	3	86.36% (65.09, 97.09)
≥ 14	88[a]	88	0	100.00% (95.89, 100.00)

[a] Five specimens from 1 immunocompromised patient were excluded from the study. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information. When the results from these specimens were included, the PPA at ≥ 14 days post-symptom onset was 96.77% (95% CI: 90.86, 99.33).

Negative Agreement by Category

Category	n	Positive	Negative	NPA (95% CI)
Pre-COVID-19 Outbreak	997	4	993	99.60% (98.98, 99.89)
Other Respiratory Illness	73	0	73	100.00% (95.07, 100.00)
Total	1070	4	1066	99.63% (99.05, 99.90)

Class Specificity

A study was performed to support class specificity for both the ARCHITECT i System and the Alinity i system. The anti-human IgG antibody used in the SARS-CoV-2 IgG assay demonstrates class-specific reactivity only to human IgG isotypes. No binding interactions were observed to human IgM, human IgA, or sheep (ovine) IgG.

Longitudinal Study

This study was performed on the ARCHITECT i2000SR System.

From the positive agreement study above, a subset of 13 subjects with 2 or more blood draws post-symptom onset were assessed longitudinally. Out of the 13 subjects, 7 presented positive results and 4 presented negative results in all the bleeds while 2 subjects showed SARS-CoV-2 IgG seroconversion as shown in the SARS-CoV-2 IgG results provided below.

Subject	Draw	Days Post-Symptom Onset	Result (Index [S/C])	Interpretation
A	1	5	0.27	Negative
	2	6	0.52	Negative
	3	7	2.12	Positive
	4	7	2.16	Positive
	5	8	4.45	Positive
B	1	9	0.41	Negative
	2	10	1.17	Negative
	3	11	2.25	Positive
	4	13	5.79	Positive

Percent Agreement

A study was performed to compare performance on the Alinity i system vs the ARCHITECT i2000SR. The results are presented in the following table.

SARS-CoV-2 IgG on Alinity i	SARS-CoV-2 IgG on ARCHITECT i2000SR	
	Positive	Negative
Positive	34 (A)	1* (B)
Negative	0 (C)	99 (D)

* Index results on the Alinity i and ARCHITECT i2000SR were 1.42 and 1.36, respectively.

PPA = A/(A + C) × 100 = 34/34 × 100 = 100.00% (95% CI: 89.72%, 100.00%)

NPA = D/(B + D) × 100 = 99/100 × 100 = 99.00% (95% CI: 94.55%, 99.97%)

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Key to Symbols

ISO 15223 Symbols	
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
REF	List Number
SN	Serial number

Other Symbols	
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
FOR USE WITH	Identifies products to be used together
INFORMATION FOR USA ONLY	Information needed for United States of America only
INVERSIONS PERFORMED	Inversions Performed
MICROPARTICLES	Microparticles
PRODUCT OF IRELAND	Product of Ireland
Rx ONLY	For use by or on the order of a physician only (applicable to USA classification only).
WARNING: SENSITIZER	Warning: May cause an allergic reaction.

Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

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