

Created September 2020.

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

AdviseDx SARS-CoV-2 IgM (also referred to as CoV-2 IgM or SARS-CoV-2 IgM on the reagent cartridge label)

INTENDED USE

The AdviseDx SARS-CoV-2 IgM assay is a chemiluminescent microparticle immunoassay (CMIA) intended for the qualitative detection of IgM antibodies to SARS-CoV-2 in human serum, serum separator tube, and plasma (dipotassium EDTA, tripotassium EDTA, lithium heparin, lithium heparin separator tube, sodium heparin). The AdviseDx SARS-CoV-2 IgM 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 AdviseDx SARS-CoV-2 IgM 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, that meet requirements to perform moderate or high complexity tests.

Results are for the detection of SARS CoV-2 antibodies. IgM 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 AdviseDx SARS-CoV-2 IgM assay 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 the AdviseDx SARS-CoV-2 IgM 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 IgM assay.

Samples should only be tested from individuals that are 15 days to 30 days post symptom onset. SARS-CoV-2 antibody negative samples collected 15 days or more post symptom onset should be reflexed to a test that detects and reports SARS-CoV-2 IgG.

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

SUMMARY AND EXPLANATION OF THE TEST

The AdviseDx SARS-CoV-2 IgM assay is designed to detect immunoglobulin class M (IgM) antibodies to the spike 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 swabs⁵ in as early as a few days to 2 weeks after the onset of symptoms.⁶ Specific IgM 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 IgM antibodies allows identification of people who have been recently infected and evaluation of disease courses including recovery from the illness.⁷ It is unknown if antibodies to SARS-CoV-2 confer immunity to infection. SARS-CoV-2 IgM, together with IgG 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 IgM 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 IgM antibodies to SARS-CoV-2 present in the sample bind to the SARS-CoV-2 antigen coated microparticles. The mixture is washed. Anti-human IgM 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 IgM 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

AdviseDx SARS-CoV-2 IgM Reagent Kit 06R91

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 | 06R9120 | 06R9130 |
|------------------------------|--|---------|
| 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: 0.0675% solids. Preservatives: ProClin 950 and sodium azide. | |
| CONJUGATE | Anti-human IgM (mouse, monoclonal) acridinium-labeled conjugate in MES buffer with surfactants and protein (bovine) stabilizer. Minimum concentration: 20 ng/mL. Preservatives: ProClin 300 and antimicrobial agent. | |
| ASSAY DILUENT | TRIS buffer and detergent. Preservatives: ProClin 300, sodium azide, and antimicrobial agents. | |

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 IgM 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 Federal Food, Drug, and Cosmetic 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](#), [10](#), [11](#), [12](#)

| | |
|---|--|
| The following warnings and precautions apply to: MICROPARTICLES | |
|  | |
| 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**



| | |
|----------------|--------------------------------|
| WARNING | Contains methylisothiazolones. |
|----------------|--------------------------------|

| | |
|------|--|
| H317 | May cause an allergic skin reaction. |
| H402 | Harmful to aquatic life. |
| H412 | Harmful to aquatic life with long lasting effects. |

Prevention

| | |
|------|--|
| P261 | Avoid breathing mist / vapors / spray. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P273 | Avoid release to the environment. |
| 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: **ASSAY DILUENT**



| | |
|----------------|---|
| WARNING | Contains alcohols, C11-C15-secondary, ethoxylated, methylisothiazolones and sodium azide. |
|----------------|---|

| | |
|--------|--|
| H319 | Causes serious eye irritation. |
| H317 | May cause an allergic skin reaction. |
| H402 | Harmful to aquatic life. |
| H412 | Harmful to aquatic life with long lasting effects. |
| EUH032 | Contact with acids liberates very toxic gas. |

Prevention

| | |
|------|--|
| P261 | Avoid breathing mist / vapors / spray. |
| P264 | Wash hands thoroughly after handling. |
| P272 | Contaminated work clothing should not be allowed out of the workplace. |
| P280 | Wear protective gloves / protective clothing / eye protection. |
| P273 | Avoid release to the environment. |

Response

| | |
|----------------|--|
| 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. |
| 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.

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 IgM 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 |

| | Storage Temperature | Maximum Storage Time | Additional Storage Instructions |
|----------------|----------------------------|-----------------------------|--|
| Onboard | System Temperature | 10 days | cartridge 10 times and place in an upright position for 1 hour before use. |
| Opened | 2 to 8°C | Until expiration date | <p>Store in upright position. If cartridge does not remain upright during storage off the system, discard the cartridge.</p> <p>Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance.</p> |

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 AdviseDx SARS-CoV-2 IgM 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 | Dipotassium EDTA |
| | Tripotassium EDTA |
| | Lithium heparin |
| | Lithium heparin separator |
| | Sodium heparin |

- 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 that contain particulate matter.

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 | Special Instructions |
|----------------------|----------------------------------|-----------------------------|--|
| Serum/Plasma | Room temperature (15 to 30°C) | 2 days | Specimens may be stored on or off the clot, red blood cells, or separator gel. |
| | 2 to 8°C | 7 days | Specimens may be |

| Specimen Type | Temperature | Maximum Storage Time | Special Instructions |
|----------------------|--------------------|-----------------------------|---|
| | | | stored on or off the clot, red blood cells, or separator gel. |

If testing will be delayed longer than 7 days at 2 to 8°C storage time, remove serum or plasma from the clot, red blood cells, or separator gel and store frozen (-20°C or colder).

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

06R91 AdviseDx SARS-CoV-2 IgM Reagent Kit

Materials Required but not Provided

- AdviseDx SARS-CoV-2 IgM assay file
- 06R9101 AdviseDx SARS-CoV-2 IgM Calibrator Kit
- 06R9110 AdviseDx SARS-CoV-2 IgM Control Kit or other control material containing IgM 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 μ L
- Sample volume for each additional test from same sample cup: 25 μ L

\leq 3 hours on the reagent and sample manager:

- Sample volume for first test: 150 μ L
- Sample volume for each additional test from same sample cup: 25 μ L

$>$ 3 hours on the reagent and sample manager:

- Replace with a fresh aliquot of sample.
- Refer to the AdviseDx SARS-CoV-2 IgM calibrator package insert [REF 06R9101](#) and/or AdviseDx SARS-CoV-2 IgM control package insert [REF 06R9110](#) 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 AdviseDx SARS-CoV-2 IgM 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 10 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.

To track the 10 day calibration stability, edit the assay calibration interval from 720 hours to 240 hours in the assay settings before running the AdviseDx SARS-CoV-2 IgM assay. Refer to the Alinity ci-series Operations Manual, Section 2.

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 AdviseDx SARS-CoV-2 IgM 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.[13](#)

- 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.¹⁴

Verification of Assay Claims

To verify package insert claims, follow CLIA recommendations or internal laboratory procedures.

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

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 AdviseDx SARS-CoV-2 IgM assay is Index (S/C).

Interpretation of Results

The cutoff is 1.00 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 |
|-------------|----------------|
| < 1.00 | Negative |
| ≥ 1.00 | 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 assay 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.
- This assay must not be used for testing samples from individuals who are immunocompromised. Immunocompromised individuals who have COVID-19 may have a delayed immune response and produce levels of antibody that may not be detected as positive by this assay.
- This assay should be used for testing samples collected 15 to 30 day after symptoms onset.
- It is unknown at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
- 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 symptomatic individuals.
- Results from antibody testing should not be used to diagnose or exclude acute 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 AdviseDx SARS-CoV-2 IgM that employ mouse monoclonal antibodies.[15](#), [16](#)

- 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.[17](#)
- Rheumatoid factor (RF) in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[17](#)
- Specimens from patients who underwent hemodialysis may have autoantibodies in circulation that potentially interfere with *in vitro* immunoassays.[18](#)

CONDITIONS OF AUTHORIZATIONS FOR THE LABORATORIES

The AdviseDx SARS-CoV-2 IgM 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 AdviseDx SARS-CoV-2 IgM (“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 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.
- 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.
- Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- 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.
- 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.
- 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 or 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

A study was performed based on guidance from CLSI EP05-A3.¹⁹ Testing was conducted using 1 lot of the AdviseDx SARS-CoV-2 IgM Reagent Kit, 1 lot of the AdviseDx SARS-CoV-2 IgM Calibrator Kit, and 1 lot of the AdviseDx SARS-CoV-2 IgM Control Kit and 1 Alinity i instrument. Two controls and 2 human plasma panels were assayed in replicates of 3, at 2 separate times per day, on 10 different days, for a total of 60 replicates for each test sample.

| Sample | n | Mean (Index [S/C]) | Repeatability (Within-Run) | | Within-Laboratory ^a | |
|------------------|----|-----------------------|-------------------------------|------------------|--------------------------------|------------------|
| | | | SD | %CV | SD | %CV |
| Negative Control | 60 | 0.02 | 0.000 | N/A ^b | 0.000 | N/A ^b |
| Positive Control | 60 | 2.86 | 0.055 | 1.9 | 0.081 | 2.8 |
| Negative Panel | 60 | 0.76 | 0.021 | N/A ^b | 0.036 | N/A ^b |
| Positive Panel | 60 | 1.98 | 0.024 | 1.2 | 0.053 | 2.7 |

^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 AdviseDx SARS-CoV-2 IgM assay was evaluated for potentially cross-reacting antibodies. A total of 143 specimens from 30 different categories were tested. One hundred forty-two (142) specimens were negative and 1 specimen was positive by the AdviseDx SARS-CoV-2 IgM assay. The data are summarized in the following table.

| Category^a | n | Positive | Negative |
|---|----------|-----------------|-----------------|
| Anti-Hepatitis A Virus (HAV) | 5 | 0 | 5 |
| Anti-Hepatitis C Virus (HCV) | 5 | 0 | 5 |
| Anti-Hepatitis D Virus (HDV) | 5 | 0 | 5 |
| Anti-Herpes Simplex Virus (HSV) | 5 | 0 | 5 |
| Anti-Human T-Lymphotropic Virus (HTLV) Type 1 | 5 | 0 | 5 |
| Anti-HTLV Type 2 | 5 | 0 | 5 |
| Anti-Respiratory Syncytial Virus (RSV) | 5 | 0 | 5 |
| Anti-Varicella Zoster Virus | 5 | 0 | 5 |
| Antinuclear Antibody (ANA) | 5 | 0 | 5 |
| Cytomegalovirus (CMV) Immunoglobulin Class G | 5 | 0 | 5 |
| CMV 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 |
| <i>Escherichia coli</i> (<i>E. coli</i>) Antibody | 5 | 0 | 5 |
| Enterovirus IgG | 5 | 0 | 5 |
| Enterovirus IgM | 5 | 0 | 5 |
| HAMA | 5 | 0 | 5 |
| Hepatitis B Core (HBc) IgM | 4 | 0 | 4 |
| Heterophilic Antibody Positive | 5 | 0 | 5 |
| Monoclonal Hyper IgG | 5 | 0 | 5 |

| Category^a | n | Positive | Negative |
|-----------------------------|------------|-----------------|-----------------|
| Mycoplasma IgM | 5 | 0 | 5 |
| Parainfluenza IgG | 5 | 0 | 5 |
| Parainfluenza IgM | 2 | 0 | 2 |
| Polyclonal Hyper IgG | 3 | 0 | 3 |
| Rheumatoid Factor | 5 | 1 ^b | 4 |
| Rubella IgG | 5 | 0 | 5 |
| Rubella IgM | 5 | 0 | 5 |
| Toxoplasmosis IgG | 5 | 0 | 5 |
| Toxoplasmosis IgM | 4 | 0 | 4 |
| Total | 143 | 1 | 142 |

^a Samples containing antibodies against the four coronavirus (common cold) strains 229E, NL63, OC43, HKU1, were not evaluated in the study.

^b 1 out of 5 samples with antibodies to Rheumatoid Factor had a positive result with the AdviseDx SARS-CoV-2 IgM assay.

Potentially Interfering Medical Conditions

The AdviseDx SARS-CoV-2 IgM assay was evaluated for potential cross-reactivity from individuals with potentially interfering medical conditions. A total of 65 specimens from 13 different categories were tested. Sixty-four (64) specimens were negative and 1 specimen was positive by the AdviseDx SARS-CoV-2 IgM assay. The data are summarized in the following table.

| Category | n | Positive | Negative |
|------------------------------------|----------|-----------------|-----------------|
| Adenovirus | 5 | 0 | 5 |
| Autoimmune Hepatitis | 5 | 0 | 5 |
| Hemodialysis | 5 | 1 ^a | 4 |
| Hepatitis B Virus (HBV) | 5 | 0 | 5 |
| Human Immunodeficiency Virus (HIV) | 5 | 0 | 5 |
| Influenza A | 5 | 0 | 5 |
| Influenza A/B | 5 | 0 | 5 |
| Influenza B | 5 | 0 | 5 |

| Category | n | Positive | Negative |
|-------------------------------|----|----------|----------|
| 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 | 1 | 64 |

^a1 out of 5 samples from hemodialysis patients had a positive result with the AdviseDx SARS-CoV-2 IgM assay.

Interference

This study was performed on the ARCHITECT i2000SR System.

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.²⁰ Each substance was tested at 2 levels of the analyte (approximately 0.80 Index [S/C] and 2.20 Index [S/C]). The observed interference was within ± 0.10 Index (S/C) or $\pm 10.0\%$ at the following concentrations; 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 Substances

A study was performed based on guidance from CLSI EP07, 3rd ed.²⁰ Each substance was tested at 2 levels of the analyte (approximately 0.80 Index [S/C] and 2.20 Index [S/C]). The observed interference was within ± 0.10 Index (S/C) or $\pm 10.0\%$ at the following concentrations; therefore, the study showed no interference from these substances.

| Potentially Interfering Substance | Interferent Level |
|-----------------------------------|-------------------|
| Acetaminophen | 15.6 mg/dL |

| Potentially Interfering Substance | Interferent Level |
|--|--------------------------|
| Alprazolam | 0.0258 mg/dL |
| Ascorbic Acid | 5.25 mg/dL |
| Azithromycin | 1.11 mg/dL |
| Biotin | 4250 ng/mL |
| Captopril | 0.264 mg/dL |
| Fluoxetine | 14.2 mg/dL |
| Guaifenesin | 0.450 mg/dL |
| Hydroxychloroquine | 388.8 ng/mL |
| Ibuprofen | 21.9 mg/dL |
| Remdesivir | 27 μ mol/L |

Clinical Performance

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

All specimens tested were assayed in replicates of one using one lot of the AdviseDx SARS-CoV-2 IgM Reagent Kit, one lot of the AdviseDx SARS-CoV-2 IgM Calibrator Kit, and one lot of the AdviseDx SARS-CoV-2 IgM Control Kit on one Alinity i instrument.

To estimate the positive percent agreement (PPA)- between the AdviseDx SARS-CoV-2 IgM assay and the polymerase chain reaction (PCR) comparator, 355 retrospective frozen serum and plasma specimens, collected at different times, were purchased from medical institutions, from a total of 111 subjects whose respiratory samples tested positive for SARS-CoV-2 by a US FDA authorized PCR method and who also presented with COVID-19 symptoms. Specimens from a total of 8 immunocompromised subjects were not included in the data analysis. Specimens from 2 subjects that were collected greater than 30 days post-symptom onset were not included in the data analysis. Specimens from the remaining 101 immunocompetent study subjects were included in the data analysis. The PPA and the 95% confidence interval (CI) were calculated using the initial sample collected in each of the 3 designated time frames after symptom onset (i.e. ≤ 7 days, 8-14 days, and 15-30 days), per subject. The performance summary data is illustrated in the table below.

Positive Percent Agreement by Days Post-Symptom Onset

| Days Post-Symptom Onset | n | Positive | Negative | PPA (95% CI) |
|-------------------------|----|----------|----------|-----------------------|
| ≤ 7 | 54 | 22 | 32 | 40.74% (28.68, 54.03) |
| 8 - 14 | 77 | 62 | 15 | 80.52% (70.31, 87.82) |
| 15 - 30 | 40 | 38 | 2 | 95.00% (83.50, 98.62) |

To estimate the negative percent agreement (NPA), frozen serum and plasma specimens from 2985 unique study subjects were tested using the AdviseDx SARS-CoV-2 IgM assay. All specimens were collected prior to September 2019 (pre-COVID-19 outbreak) and were therefore assumed to be negative. The NPA and the 95% CI were calculated. The performance summary data are illustrated in the table below.

Negative Percent Agreement

| n | AdviseDx SARS-CoV-2 IgM Results | | NPA (95% CI) |
|------|---------------------------------|----------|-----------------------|
| | Positive | Negative | |
| 2985 | 13 | 2972 | 99.56% (99.26, 99.75) |

Longitudinal Study

From the positive agreement study above, a subset of 72 subjects with 2 or more blood draws post-symptom onset were assessed longitudinally. Out of the 72 subjects, 42 presented positive results in all bleeds, while 30 subjects showed SARS-CoV-2 IgM seroconversion. Representative AdviseDx SARS-CoV-2 IgM seroconversion results are provided below. Seroconversion was detected by the AdviseDx SARS-CoV-2 IgM assay at 10 days and 7 days post-symptom onset for subjects A and B, respectively.

| Subject | Draw | Days Post-Symptom Onset | Result (Index) | Interpretation |
|---------|------|-------------------------|----------------|----------------|
| A | 1 | 1 | 0.02 | Negative |
| | 2 | 4 | 0.03 | Negative |
| | 3 | 7 | 0.82 | Negative |
| | 4 | 10 | 17.28 | Positive |
| | 5 | 15 | 28.02 | Positive |

| Subject | Draw | Days Post-Symptom Onset | Result (Index) | Interpretation |
|----------------|-------------|--------------------------------|-----------------------|-----------------------|
| | 6 | 19 | 27.24 | Positive |
| B | 1 | 0 | 0.03 | Negative |
| | 2 | 4 | 0.11 | Negative |
| | 3 | 7 | 3.78 | Positive |
| | 4 | 14 | 23.27 | Positive |
| | 5 | 20 | 19.12 | Positive |

Method Comparison Between ARCHITECT i2000SR and Alinity i Analyzers

A study was performed to compare performance of the AdviseDx SARS-CoV-2 IgM assay on the Alinity i system vs the ARCHITECT i2000SR. The results of the study demonstrate equivalent performance between these instrument platforms.

Class Specificity

The anti-human IgM antibody used in the AdviseDx SARS-CoV-2 IgM assay demonstrates class-specific reactivity only to human SARS-CoV-2 IgM. No binding interactions were observed to human SARS-CoV-2 IgG.

A Class Specificity study was conducted to determine the impact of dithiothreitol (DTT) treatment on the detection of IgM and/or IgG positive samples by the Abbott AdviseDx SARS-CoV-2 IgM assay. DTT dissolves IgM antibody disulfide bonds and eliminates activity of the antibody. Upon treatment with DTT, five SARS-CoV-2 patient samples (initially positive for both IgG and IgM) were negative for IgM when tested with the Abbott AdviseDx SARS-CoV-2 IgM assay and remained positive for IgG when tested with the Abbott SARS-CoV-2 IgG assay. This establishes the specificity of the Abbott AdviseDx SARS-CoV-2 IgM kit to the IgM class of antibodies.

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Key to Symbols

ISO 15223 Symbols

| | |
|--|---|
|  | Consult instructions for use |
|  | Manufacturer |
|  | Sufficient for |
|  | Temperature limitation |
|  | Use by/Expiration date |
| IVD | <i>In Vitro</i> 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 |

Other Symbols

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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