CE

INSTI®

COVID-19 Antibody Test

Single-use rapid assay for the detection of antibodies to SARS-CoV-2

INSTI® COVID-19 Antibody Test with support materials (for POC use) REF 90-1092, 90-1098

2°C 30°C **Store at 2°C to 30°C (35.6° to 86°F). For in-vitro diagnostic use only.** IVD

Read the Package Insert completely before using the product. Although the assay is designed to be simple to use, conformance with the test procedure is necessary to ensure accurate results. Scan the QR code provided on the outer packaging of the test to see how the test works.

INTENDED USE - Not for donor screening

The **INSTI COVID-19 Antibody Test** is a single use, visually read, rapid, flow-through *in vitro* qualitative immunoassay for the detection of total antibodies to SARS-CoV-2 in human whole blood, serum and plasma (EDTA, sodium heparin, sodium citrate) intended for use by Health care professionals.

The INSTI® COVID-19 Antibody Test is not intended for use in screening blood, plasma, or tissue donors. Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection.

SUMMARY

Coronaviruses (CoV) are a large family of viruses that can infect humans and animals.[1] In humans, coronaviruses cause illnesses ranging from the common cold to more severe diseases such as severe acute respiratory syndrome (SARS). SARS-CoV-2, is a new strain of coronavirus that was first identified during an outbreak in Wuhan, China in 2019 and causes Coronavirus Disease 2019 (COVID-19), a respiratory disease characterized by fever, cough, and shortness of breath.[2] In more severe cases, infection can cause pneumonia, SARS, kidney failure, and death.[3]

PRINCIPLES OF THE TEST

The **INSTI COVID-19 Antibody Test** is a manual, visually read, flow through immunoassay for the qualitative detection of **SARS-CoV-2** antibodies. The assay is packaged as a kit containing a single-use Membrane Unit, Sample Diluent (Bottle 1), Color Developer (Bottle 2), and Clarifying Solution (Bottle 3) with support materials (lancet, pipette and alcohol swab). The test consists of a synthetic filtration membrane positioned atop an absorbent material within a plastic cartridge, referred to as the Membrane Unit. The membrane has been specifically treated with SARS-CoV-2 antigens, which react with SARS-CoV-2 antibodies (test spot) and a procedural control spot capable of capturing antibodies normally present in blood and blood components. Results are visualized in as little as 60 seconds following reactions with proprietary INSTI solutions during the test procedure.

SARS-CoV-2 Antibody Detection: The INSTI COVID-19 Antibody Test utilizes recombinant proteins from SARS-CoV-2. The antigen, when used in combination with the INSTI Color Developer, will detect total antibodies specifically directed against SARS-CoV-2.

Test Complexity: The INSTI COVID-19 Antibody Test was designed to reduce protocol complexity. The INSTI COVID-19 Antibody Test requires no sample preparation, no timers for timing of process, no extra steps for multiple washes or reagents. These requirements increase the complexity of an assay and lead to procedural errors which may adversely affect sensitivity and specificity. Total test time may vary slightly depending on specimen type; but results of valid tests are always clearly readable within one minute.

SPECIMEN COLLECTION AND STORAGE

1. Only the specimens listed below were tested and found acceptable: whole blood, serum, and plasma (EDTA, sodium heparin, sodium citrate).
2. For whole blood, plasma or serum specimens, follow venipuncture blood collection procedure using lavender-top EDTA anticoagulant tubes, green-top sodium heparin and light blue-top sodium citrate for whole blood and plasma or red-top (no anticoagulant) tubes for serum. **Other anticoagulants have not been validated and may give an incorrect result.**
3. If plasma or serum is to be used, separate from the blood cells by centrifugation.
4. Serum or plasma may be stored at 2 to 8°C for up to 8 days, stored frozen at ≤ -20°C for one year.
5. Whole blood specimens collected may be stored at 2 to 8°C and should be tested within 72 hours. **Do not heat or freeze whole blood specimens.**
5. Do not dilute prior to testing.

KIT COMPONENTS AND STORAGE

2°C 30°C Store INSTI COVID-19 Antibody Test unopened at 2 to 30°C (35.6°to 86°F).

Components	90-1092	90-1098
Membrane	x 1 unit	x 50 unit
Sample Diluent	x 1 vial	x 50 vials
Colour Developer	x 1 vial	x 50 vials
Clarifying Solution	x 1 vial	x 50 vials
Lancets	x 1	x 50
Alcohol Swabs	x 1	x 50
Pipettes	x 1	x 50

Each test contains the following materials:

1. **Membrane Unit**, individually packaged, prepared with control (antibody capture) and test (SARS-CoV-2 antigen) reaction spots. For single use only in the INSTI procedure.
2. **Sample Diluent** Bottle 1 containing 1.5 mL of a proprietary Tris-Glycine buffered solution containing cell lysis reagents.
3. **Color Developer** Bottle 2 containing 1.5 mL of a blue-colored Borate buffered proprietary indicator solution designed to detect antibodies in the control spot and specific SARS-CoV-2 antibodies in the test spot.
4. **Clarifying Solution** Bottle 3 containing 1.5 mL of a proprietary Tris-Glycine buffered clarifying solution designed to remove background staining from the Membrane Unit prior to reading the result.

SUPPORT MATERIALS

The following materials are required when testing fingerstick whole blood and are included with each kit:

1. Single-use Pipette, 50 µL
2. Single-use Alcohol Swab
3. Single-use Lancet INSTICE CE0050 Becton, Dickinson and Company Limited located at Pottery road, Dun Laoghaire, Co. Dublin, Ireland.

MATERIALS REQUIRED BUT NOT PROVIDED

- Personal protective equipment such as gloves, lab coat, or gown
- Biohazard waste containers
- Absorbent cotton balls for fingerstick or venipuncture wound closure or bandage

For venipuncture blood collection and testing:

- Venipuncture apparatus if collecting blood samples
- Appropriate blood collection tubes
- Appropriate shipping containers
- Precision pipette capable of delivering 50 µL of sample

MATERIALS AVAILABLE AS AN ACCESSORY BUT NOT PROVIDED IN THE KIT

INSTI® COVID-19 Test Controls
See INSTI COVID-19 Test Controls Package Insert before use.

WARNINGS

1. **Do not mix reagents from different lots**.
2. Do not use reagents or kits beyond the stated expiration date on the outer packaging.
3. Order of bottle use must be strictly followed as per the Package Insert. Any deviation may result in false or invalid results.
4. Do not use the Membrane Unit if the foil pouch has been previously opened or if the packaging integrity has been compromised. Once the Membrane Unit has been opened, it must be used immediately.
5. Avoid microbial contamination and exercise care in handling the kit components.
6. ⚠ Sodium Azide is present at concentrations from 0.02% to 0.1% in all assay reagents and is harmful if inhaled, swallowed, or exposed to skin. Sodium Azide may react with lead or copper plumbing to form highly explosive metal azides. If products containing Sodium Azide are discarded into a drain, flush with large amounts of water to prevent azide build-up. Check with local regulatory agencies to determine at what concentration Sodium Azide may cause a product to be regulated as hazardous waste.
7. Failure to use the recommended reagent and specimen volumes may result in leakage and/or overflow of liquids from the Membrane Unit.
8. If the kit is refrigerated, ensure it is brought to room temperature before performing the test. Use the INSTI COVID-19 Test Controls to ensure proper kit performance.

SAFETY PRECAUTIONS

1. Wear disposable gloves while handling kit reagents or specimens. Change gloves and wash hands thoroughly after performing each test.
2. Avoid contact with skin and eyes. If contact occurs, wash affected areas with water.
3. Dispose of all specimens and materials used to perform the test in a biohazard waste container. The preferred method of disposal is sterilization by autoclaving for a minimum of one hour at 121°C. Disposable materials may be incinerated. Liquid waste may be mixed with sodium hypochlorite (bleach) in volumes such that the final mixture contains 1.0% sodium hypochlorite (using a freshly prepared solution containing 10% household bleach). Allow at least 60 minutes for decontamination to be completed. Do not autoclave solutions that contain bleach.
4. Spills should be cleaned up and decontaminated in accordance with the user facility's established procedures for handling biohazardous spills.
5. For additional information on biosafety, refer to "Universal Precautions for prevention of transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other bloodborne pathogens"[4] and in accordance with Local, State Federal or European Regulations. Follow standards biosafety guidelines for handling and disposal of potentially infective material.

INSTRUCTIONS FOR USE

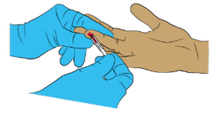
Workplace Preparations

- Gather the material you will need.
- Allow the INSTI COVID-19 Assay to come to operating temperature before use.
- Refer to the *Quality Control* section in this Package Insert to determine when the Test Controls should be run.

Specimen Collection and Test Procedure
Sampling Fingerstick Blood:

1. Massage the finger to allow the blood to move to the surface (fingertip will become pink). Use heating pad if available to warm the hand. Hand must be positioned at waist level or lower.
2. Wipe the fingertip with the alcohol swab. Allow the finger to air dry.
3. Twist and remove the protective insert from the lancet. Press the finger firmly at the point just below where the lancet will be applied. With the other hand, place the lancet on the side of the fingertip and press hard until it clicks.

4. As the blood droplet forms, hold the pipette horizontally and touch the tip of the pipette to the blood sample. Capillary action automatically draws the sample to the fill line and stops. If very little blood trickles out of the puncture, gently apply intermittent pressure below the puncture site to obtain the required blood volume. If blood is inadequate, perform a second skin puncture using a new lancet.



⚠ **CAUTION!** Filling is automatic: Never squeeze the tube while sampling.

5. Transfer the blood held in the pipette to the Sample Diluent vial (Bottle 1). Align the tip of the pipette with the Sample Diluent vial and squeeze the bulb to dispense the sample. **NOTE:** If the sample will not expel, hold the pipette vertically and slide a finger over (without pressing) the vent hole, then squeeze the bulb. Recap the vial and mix by inversion. Follow General Procedure after Sampling, below.

Sampling Venipuncture Whole Blood, serum, plasma and Test Controls:

1. Bring specimens to room temperature and mix each specimen thoroughly prior to use. **Do not heat or repeatedly freeze/thaw specimens.**
2. Using a pipette, add 50 µL of whole blood, serum, plasma, or kit controls (see NOTE below) to the Sample Diluent vial. Recap the vial and mix by inversion. ⚠ Adding an excessive amount of specimen may cause the device to overflow or leak.

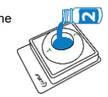
NOTE: In POC settings, for INSTI Test Controls, it is important to use a 50 µL pipette to add the control material to the Sample Diluent vial. Do not use the disposable single-use pipette provided for finger stick blood collection.

General Procedure after Sampling:

1. Tear open the Membrane Unit pouch and remove the Membrane Unit without touching the center well. Place the device on a level surface. For sample identification purposes the tab of the Membrane Unit may be labeled with the patient's name or number.

NOTE: At this point, it is important that the following steps be performed immediately and in sequence.

2. Mix the Sample Diluent-specimen mixture by inverting several times and pour the entire contents to the center of the Membrane Unit well. (**NOTE:** Do this immediately after the specimen has been added to the Sample Diluent vial). The sample should be absorbed through the membrane in less than 30 seconds; however, absorption times will vary slightly depending upon sample type.



3. Resuspend the Color Developer by slowly inverting to mix the solution thoroughly until the reagent is evenly suspended and add the entire contents to the center of the Membrane Unit well. The colored solution should flow through completely in about 20 seconds.

4. Open the Clarifying Solution and add the entire contents to the center of the Membrane Unit well. This will lighten the background color and facilitate reading. Results can be read immediately. **Do not read the results if more than 20 minutes has elapsed following the addition of Clarifying Solution.**

QUALITY CONTROL

Kit Controls:
The INSTI COVID-19 Antibody Test has a built-in antibody capture procedural control that demonstrates assay validity and adequate sample addition. A blue color on the control dot indicates that the proper specimen was added and that the assay procedure was performed correctly. The control dot will appear on all valid tests. (Refer to Interpretation of Results, below.)

INSTI COVID-19 Test Controls are available separately for use only with the INSTI COVID-19 Antibody Test. The controls are used to verify test performance and interpretation of results. Kit controls should be run under the following circumstances:

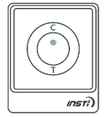
- for new INSTI operator verification prior to performing testing on patient specimens
- when switching to a new lot number of INSTI test kits
- whenever a new shipment of kits is received
- when temperature during storage of the kit falls outside of 2° to 30°C
- when the temperature of the test area falls outside of 15° to 30°C
- at regular intervals as determined by the user facility.

Refer to the INSTI COVID-19 Test Controls Package Insert for additional information on the use of these reagents. It is the responsibility of each laboratory using the INSTI COVID-19 Antibody Test to establish an adequate quality assurance program to ensure the performance under their specific locations and conditions of use.

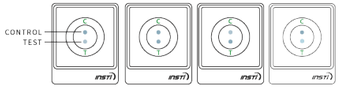
INTERPRETATION OF RESULTS

- **Do not read the results if more than 20 minutes have elapsed following the addition of Clarifying Solution.**
- **If using the control samples provided by bioLytical, all Positive Controls must be reactive with INSTI and all Negative Controls must be non-reactive with INSTI. Controls that produce incorrect or invalid results must be re-tested with INSTI. If results are still incorrect or invalid, inform bioLytical immediately.**

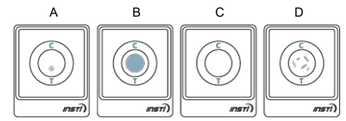
NON-REACTIVE ► One blue dot that is clearly discernable above any background tint should appear on the membrane. This is the procedural Control Dot and shows that the test has been performed correctly. The control dot is located towards the top of the read frame furthest from the plastic tab on the Membrane Unit. No reaction should be visible at the test spot located below the control. A non-reactive result indicates that SARS-CoV-2 antibodies were not detected in the specimen.



REACTIVE ► Two blue dots (visible in the control and test area) indicate that the specimen contains SARS-CoV-2 antibodies. One dot may be darker than the other, the presence of any visible blue dot in the test spot should be considered as reactive, even if faint. A sample giving this pattern is considered a **preliminary reactive**.



INVALID ► The test is invalid if any of the following occurs:
A. The test dot appeared without the control dot
B. Uniform tint across the membrane
C. There is no dot on the membrane
D. Only blue specks appear on the membrane



NOTE: An invalid test result means that the test was run incorrectly or insufficient specimen was added. Invalid test results cannot be interpreted. Repeat the test with a fresh specimen using a new Membrane Unit, kit components and support materials. Contact bioLytical's Technical Support if you are unable to produce a valid result upon repeat testing.

LIMITATIONS OF THE TEST

- In some instances, samples may exhibit longer than normal flow times (from the time the Sample Diluent specimen mixture is poured in the membrane well to the time the Clarifying Solution has fully flowed through the membrane). This is due to variable factors such as cellular components, especially with whole blood.
- The INSTI COVID-19 Antibody Test must be used in accordance with the instructions in this package insert to obtain accurate results.
- The clinical significance of the test results of the kit needs to be analyzed in combination with other test indicators and clinical manifestations
- 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 adaptive immune response.
- Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions.
- A negative result may be obtained if the specimen is inadequate or antibody concentration is below the sensitivity/detection limit of the test. Therefore, it is recommended that all negative test results undergo confirmatory testing using other method and/or qualified assays.

PERFORMANCE CHARACTERISTICS

Precision
Precision was determined using INSTI® COVID-19 Antibody Test reagents, samples and Controls. Testing was performed in a blinded and randomized manner by three operators, with three lots of the test over the course of five days. A total of 900 tests were performed and the following results obtained:

Sample	Replicates	Total Reactive	Total Non-Reactive
Negative Plasma (C_0)	225	0	225
Negative Whole Blood (C_0)	225	0	225
Weak Positive Plasma (C_{95})	225	225	0
Weak Positive Whole Blood (C_{95})	225	225	0

Clinical Agreement
Positive and Negative Percent Agreement to PCR was evaluated using plasma and serum samples. In this study, a blind coded and randomized panel of 166 SARS-CoV-2 PCR positive and 260 SARS-CoV-2 negative samples obtained prior to October 2019 were tested on one lot of INSTI® COVID-19 Antibody Test.

The overall Positive Percent Agreement (PPA) was determined to be 98.2% and the Negative Percent Agreement (NPA) was determined to be 99.6%.

Analysis of the PPA results is provided below:

	INSTI® COVID-19 Antibody Test Results (PPA)		
Number of Samples Tested*	Reactive Results	Non Reactive Results	Overall PPA, % (95% CI)
166	163	3	98.2% (94.8 – 99.4%)

Further analysis of the PPA results with consideration of the "days from symptom onset" for positive samples confirmed by PCR is provided below.

Days post PCR confirmation	N*	Reactive	Non-Reactive	Sensitivity % (95% CI)
0-7 days	0	N/A	N/A	N/A
8-14 days	6	6	0	100.0% (61.0 – 100.0%)
≥15 days	156	153	3	98.1% (94.5 – 99.3%)
Days post PCR confirmation not available	4	4	0	100% (51.0 – 100.0%)

*SARS-CoV-2 PCR positive plasma/serum sample (confirmed by PCR).

Analysis of the NPA results is provided below:

	INSTI® COVID-19 Antibody Test Results (NPA)		
Number of Samples Tested*	Reactive Results	Non-Reactive Results	Overall NPA% (95% CI)
260	1	259	99.6% (97.9-99.9%)

*Collected prior to October 2019

The clinical agreement in SARS-CoV-2 PCR negative symptomatic donor specimens was also evaluated using plasma/serum. In this study, a blind-coded panel of 190 SARS-CoV-2 PCR negative symptomatic and 5 SARS-CoV-2 PCR positive samples were tested on INSTI COVID-19 Antibody Test.

True Negative Rate and Positive Rate were determined using a Serological Comparator Algorithm in which two internationally-approved serological assays were used to determine the SARS-CoV-2 antibody status of each sample. The comparison between the INSTI COVID-19 Antibody Test and the Comparator Algorithm result for the presence of SARS-CoV-2 antibodies is provided below.

		Serological Comparator Algorithm Result as the reference method	
		Positive (n)	Negative (n)
INSTI COVID-19 Test Results	Reactive (n)	44	2
	Non-Reactive (n)	2	121
Total		46	123
		Positive Rate (%) [95%CI]	True Negative Rate (%) [95%CI]
		95.6% [85.5-98.8%]	98.4% [94.3-99.6%]

Interfering Substances
The effect of the following pharmaceutical compounds and endogenous substances on assay performance was tested. Interference was tested up to the listed concentration and no impact on results was observed.

Pharmaceutical Compounds	Maximum concentration tested*
Oseltamivir phosphate	0.399 µg/mL
Azithromycin	11.1 µg/mL
Meropenem	0.339 mg/mL
Tobramycin	33.0 µg/mL
Acetylsalicylic acid	30.0 µg/mL
Paracetamol	0.156 mg/mL
Ibuprofen	0.219 mg/mL
Enalapril	0.819 µg/mL
Nifedipine	0.588 µg/mL
Metformin	12.0 µg/mL
Glimepiride	1.64 µg/mL
Ribavirin	5.40 µg/mL
Hydroxychloroquine sulfate	0.84 mg/mL
Ritonavir	53.0 µg/mL
Lopinavir	2.0 µg/mL
Endogenous Substances	**Maximum concentration tested***
Hemoglobin	10 mg/mL
Bilirubin, conjugated	0.4 mg/mL
Bilirubin, unconjugated	0.4 mg/mL
Cholesterol	4.0 mg/mL
Total Protein	60 mg/mL
Intralipid	20.5 mg/mL
IgG	6 mg/mL

Analytical Specificity
Out of 72 potentially cross-reactive samples, no samples showed reactivity in the INSTI COVID-19 Antibody Test, resulting in an overall specificity in this cohort of 100%. The following are conditions tested.

Indication	Number of Unique Samples	Non-Reactive	Reactive
Human coronavirus 229E*	10	10	0
Human coronavirus OC43*	9	9	0
Human coronavirus HKU1*	6	6	0
Human coronavirus NL63*	6	6	0
Influenza Vaccination	5	5	0
Influenza A**	12	12	0
Influenza B**	13	13	0
*H. influenzae***	17	17	0
Respiratory Syncytial Virus (RSV)[2]**	15	15	0
Parainfluenza 1-4**	18	18	0
Adenovirus**	8	8	0
Enterovirus**	7	7	0
*M. pneumoniae***	17	17	0
*Legionella***	5	5	0
*B. pertussis***	8	8	0
*C. pneumoniae***	13	13	0
Acute bacterial pneumonia**	18	18	0
Anti-nuclear Antibody	7	7	0
Rheumatoid Factor	5	5	0
Pregnancy (1st Trimester)	5	5	0
Pregnancy (2nd Trimester)	5	5	0
Pregnancy (3rd Trimester)	5	5	0
Multiparous Women	6	6	0

*Represents 10 unique samples overall, some samples were co-infected with multiple species of the coronavirus.
**Represents 24 unique samples overall, some samples were co-infected

BIBLIOGRAPHY

1. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015;1282:1-23. doi:10.1007/978-1-4939-2438-7_1
2. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html
3. Wadman M, Couzin-Frankel J, Kaiser J, Maticic C. How does coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes. doi:10.1126/science.abc3208
4. Centers for Disease Control and Prevention (CDC) Universal Precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in health-care settings. MMWR 1988; 37(24):377-388.

TECHNICAL INFORMATION
For further information or assistance, contact the Technical Services at 1-604-644-4677.

Reference herein to any specific third party by name, trade name, trade-mark, manufacturer or otherwise does not constitute or imply an endorsement or recommendation of this Kit by such third party, or of the products or services of such third party by bioLytical or that such products or services are necessarily best suited for the intended purpose.

Store at 2°C to 30°C

Caution

Harmful if swallowed

In Vitro diagnostic medical device

Consult Package Insert

Do not reuse

CE Mark

Solution bottles 1,2,3

Lancet

Pipette

Sterilization using irradiation

Lot number

Catalogue Number

Manufacturer

Use By Date

Contains sufficient for <n> tests

Membrane Unit

Alcohol swab

bioLytical Laboratories, Inc.
406 – 13251 Delf Place
Richmond, BC, Canada V6V 2A2
Phone: +1 604-204-6784
Fax: +1 604-244-8399
www.biolytical.com

EC REP

Qarad EC-REP BV
Pas 257
2440 Geel
Belgium

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