SGTi-flex

COVID-19 IgG

For *in-vitro* diagnostic use only.
For prescription use only.
For Emergency Use Authorization only.

INTENDED USE

The SGTi-flex COVID-19 IgG is a lateral flow immunoassay intended for qualitative detection of IgG antibodies to SARS-CoV-2 in human serum, venous whole blood (sodium heparin, lithium heparin, sodium citrate and tripotassium EDTA), and plasma (sodium heparin, lithium heparin, sodium citrate and tripotassium EDTA). The SGTi-flex COVID-19 IgG 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 SGTi-flex COVID-19 IgG should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, that meet requirements to perform moderate or high complexity tests.

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 SGTi-flex COVID-19 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 SGTi-flex COVID-19 IgG 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 SGTi-flex COVID-19 IgG is only for use under the Food and Drug Administration's Emergency Use Authorization.

SUMMARY AND EXPLANATION

The novel coronavirus (SARS-CoV-2) was identified in December 2019, and in February 2020, the World Health Organization (WHO) officially named the disease caused by SARS-CoV-2 as COVID-19. Belonging to the family Coronaviridae, it has a positive sense single-stranded RNA and can be transmitted between people. The coronaviruses identified for human infection include 229E, NL63 belonging to α-Coronaviruses and HKU1, OC43, SARS-CoV, MERS-CoV belonging to β-Coronaviruses.

The new coronavirus was published under the name of SARS-CoV-2, with 80% of genetic similarity to SARS-CoV by ICTV (International Committee on Taxonomy of Viruses).

COVID-19 spreads mainly through respiratory droplets, which may cause lethargy, fever, dry cough, and dyspnea in infected individuals. It may also cause severe symptoms like sepsis, MOF (Multiple Organ Failure) and ARDS (Acute Respiratory Distress Syndrome) or death. It is likely more contagious than SARS-CoV-1 which caused more than 800 deaths and 8,000 infected patients. Moreover, it has an incubation period of about 2 days to up to 14 days. Infected individuals may shed the virus and infect others even during the incubation period.

PRINCIPLE

SGTi-flex COVID-19 IgG is an immunoassay for the qualitative detection of IgG antibodies to SARS-CoV-2 in human venous whole blood, serum or plasma. The cassette contains a test strip which is located inside a plastic housing. When the sample and sample buffer are loaded onto the sample well, the specific IgG antibodies to SARS-CoV-2 flow through the membrane and move to the test line area and are captured by antibodies immobilized on the membrane, respectively.

The antigen (Recombinant SARS-CoV-2 Nucleocapsid and Spike RBD Protein) is conjugated to colloidal gold nanoparticles and the antigen-gold conjugate moves to the test line area and attaches to the specific IgG antibodies to SARS-CoV-2. This leads to the generation of a reddish colored band. The user interprets test results by eye, according to the instructions for use.

MATERIALS SUPPLIED

- Test Cassette ——— 25
- Sample Buffer ——— 1 (4.5 mL/tube)
- Instructions for Use ——— 1

MATERIALS REQUIRED BUT NOT SUPPLIED

- Micro Pipette(s)
- Single Use Disposable Pipette Tip
- Timer
- SGTi-flex COVID-19 IgG Control

STORAGE AND STABILITY

- The test kit can be stored at 2-8 ℃ for 9 months or at room temperature for 3 months. DO NOT FREEZE. The test is stable through the expiration data printed on the sealed pouch. Do not use after the expiration date.
- SGTi-flex COVID-19 IgG Test Cassette and Sample Buffer should be brought to room temperature for 30 minutes before testing.
- Do not open the pouch of Test Cassette until ready to use. After opening aluminum pouch, Test Cassette should be used immediately.
- Keep away from direct sunlight.

WARNING AND PRECAUTIONS

- Test cassettes are single use only. Do not reuse.
- For use under Emergency Use Authorization only. For IN VITRO Diagnostic use only.
- This test has not been FDA cleared or approved; the test has been authorized by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform moderate or high complexity tests.
- This test has been authorized only for the presence of IgG antibodies against SARS-CoV2, 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. § 360bbb3(b)(1), unless the authorization is terminated or revoked sooner.
- Do not use tests after the expiration date.
- Test Cassette should remain in the sealed pouch until use because it is sensitive to moisture. Use Test Cassette immediately after opening the pouch.
- Do not use the Test Cassette if it is broken or the pouch is not stored in sealed.
- Samples and Test Cassette must be at room temperature before testing.
- Please be cautious when handling the test cassette and samples because of the use of clinical samples containing potential infectious sources. Dispose of the used samples and test cassettes properly in accordance with the relevant regulations.
- Smoking and eating are prohibited at test site when handing specimens or kit reagents.
- This product was tested on serum, venous whole blood (sodium heparin, lithium heparin, sodium citrate, and tripotassium EDTA), and plasma (sodium heparin, lithium heparin, sodium citrate, and tripotassium EDTA) as anticoagulants. Using other anticoagulants may produce different results.

SAMPLE COLLECTION AND PREPARATION

SGTi-flex COVID-19 IgG can be performed with venous whole blood, plasma or serum.

1. Venous whole blood

1) The anticoagulants sodium heparin, lithium heparin, sodium citrate, and tripotassium EDTA have been tested and may be used with this assay. The correct specimen type must be used in the assay.
2) If venipuncture whole blood is not tested immediately, store at 2-8℃ for up to 5 days.

2. Serum and Plasma

1) Serum: Collect the blood specimen obtained by venipuncture into a tube without anticoagulant and allow to clot for about 30 minutes. Separate serum from the supernatant by centrifugation.
2) Plasma: Collect the blood specimen obtained by venipuncture into a tube containing anticoagulant (sodium heparin, lithium heparin, sodium citrate and tripotassium EDTA), and separate plasma from the supernatant by centrifugation.
3) Whole blood, Serum and Plasma Stability
If specimens are not tested immediately, store at 2-8℃ for up to 5 days.
For serum and plasma, the specimens should be frozen at -70℃ for longer storage. For frozen samples, avoid repeated freezing/thawing cycles. Prior to testing, bring frozen specimens to room temperature slowly and mix gently.

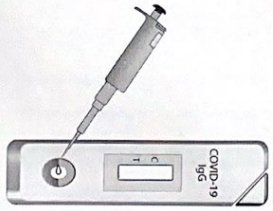
TEST PROCEDURE

Preparation before Test

1. All samples and reagents should be stored at room temperature and stabilized ~30 minutes prior to testing.
2. Test cassette is moisture sensitive so should be used **immediately** after opening.

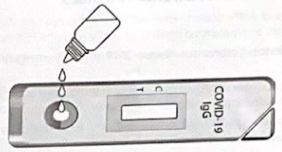
Test Procedure

1. Remove the test cassette from the foil pouch and place it on a clean and flat surface.
2. Using a pipette, add **10 µL** of the specimen (venous whole blood, plasma or serum) into the sample well on the cassette.



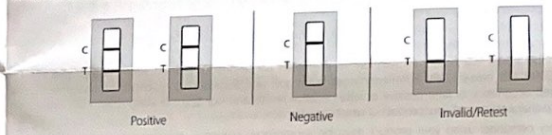
3. Add **3 drops** of sample buffer (approximately 90 µL) into the sample well on the cassette.

IVD



4. Read the result **after 10 minutes**. Results should not be read after 30 minutes, as the result after 30 minutes is invalid.

INTERPRETATION OF RESULTS



1. Positive
Test line (T) and Control line (C) appear in the result window: Positive for IgG antibody to SARS-CoV-2

2. Negative
If only Control line (C) appears in the result window: Negative for IgG antibody to SARS-CoV-2

3. Invalid/Retesting
If control line fails to appear, the result is invalid and retest with a new test cassette.

QUALITY CONTROL

A procedural control is included in the test. A colored line appearing in the control line region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Control Materials are available for purchase from Sugentech Inc. (Cat no: COVC0001E) and are not supplied with this kit. However, external positive and negative controls should be tested to ensure the proper performance of the assay, particularly under the following circumstances:

- A new operator uses the kit;
- A new lot of test kits is used;
- A new shipment of kits is used;
- To investigate the cause of repeated invalid results;
- The temperature used during storage of the kit falls outside of 2-30℃.

LIMITATIONS OF THE SYSTEM

For use under an Emergency Use Authorization Only

1. This test is only to be used in CLIA certified laboratories that meet requirements to perform moderate or high complexity tests, and not in point-of-care or at-home testing settings.
2. The test is for qualitative detection of anti-SARS-CoV-2 IgG antibody in human whole blood, serum or plasma and does not indicate the quantity of the antibodies. The intensity of the test line does not necessarily correlate to SARS-CoV-2 antibody titer in the specimen.
3. Performance has only been established with the specimen types listed in the Intended Use. Other specimen types have not been evaluated and should not be used with this assay. This test should not be used to test fingerstick whole blood.
4. The test results should be interpreted between 10 and 30 minutes after addition of buffer. The test results should not be interpreted after 30 minutes.
5. The test is for in vitro diagnostic use only.
6. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. The sensitivity of the SGTi-flex COVID-19 IgG early after infection is unknown. False positive results for IgG antibodies may occur due to cross-reactivity from pre-existing antibodies or other possible causes.
7. A negative result can occur if the quantity of antibodies for the SARS-CoV-2 virus present in the specimen is below the detection limit of the assay, or if the virus has undergone minor amino acid mutation(s) in the epitope recognized by the antibody used in the test.
8. Testing with a molecular diagnostic should be performed to evaluate symptomatic patients for acute SARS-CoV-2 infection, particularly in those who have been in contact with the virus.
9. Results from antibody testing should not be used to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
10. 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. Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

11. It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to reinfection.
12. Not for the screening of donated blood.
13. The test may have lower sensitivity for IgG detection in symptomatic individuals prior to 8 days since symptom onset.
14. Testing must be performed immediately after opening the pouch.

CONDITIONS OF AUTHORIZATION FOR LABORATORIES

The SGTi-flex COVID-19 IgG Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Recipients, and authorized labeling are available on the FDA website:

https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas

Authorized laboratories using the SGTi-flex COVID-19 IgG Letter of Authorization ("your product" in the conditions below), must adhere to the Conditions of Authorization indicated in the Letter of Authorization as listed below:

1. Authorized laboratories* using your product will include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
2. Authorized laboratories using your product will use your product as outlined in the Instructions for Use. Deviations from the authorized procedures, including the authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
3. Authorized laboratories that receive your product will notify the relevant public health authorities of their intent to run your product prior to initiating testing.
4. 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.
5. 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 Sugentech Inc. (email: info@sugentech.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of your product of which they become aware.
6. All laboratory personnel using your product must be appropriately trained in immunoassay techniques and use appropriate laboratory and personal protective equipment when handling this kit and use this 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.
7. Sugentech Inc., 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, that meet requirements to perform moderate or high complexity tests" as "authorized laboratories."

PERFORMANCE CHARACTERISTICS

1. Cross-Reactivity

SGTi-flex COVID-19 IgG was evaluated with a total of 38 other viruses, bacteria or autoantibodies (151 samples total). The results show that the SGTi-flex COVID-19 IgG has no cross-reactivity with samples containing antibodies to other viruses, bacteria as well as autoantibodies.

Table 1. Cross-reactive substances

No	Analytical reactive substances	Number of Samples	No	Analytical reactive substances	Number of Samples
1	Coronavirus 229E IgG	5	20	Mycoplasma IgM	1
2	Coronavirus NL63 IgG	5	21	Mycoplasma IgG	1
3	Adenovirus type 1 IgM	5	22	Rotavirus IgM	5
4	Adenovirus type 1 IgG	5	23	Rotavirus IgG	5
5	Parainfluenza virus IgM	5	24	Epstein-Barr Virus (EBV) VCA IgM	1
6	Parainfluenza virus IgG	5	25	Epstein-Barr Virus (EBV) VCA IgG	1
7	Influenza A virus (H1N1+H3N2) IgM	5	26	Cytomegalovirus IgM	1
8	Influenza A virus (H1N1+H3N2) IgG	5	27	Cytomegalovirus IgG	1
9	Influenza B virus (Yamagata+Victoria) IgM	5	28	Varicella Zoster Virus (VZV) IgM/IgG	5
10	Influenza B virus (Yamagata+Victoria) IgG	5	29	Mumps IgM	5
11	Enterovirus group A IgM	5	30	Mumps IgG	5
12	Enterovirus group A IgG	5	31	Measles IgM	5
13	Respiratory syncytial virus IgM	5	32	Measles IgG	5
14	Respiratory syncytial virus IgG	5	33	anti-HIV-1 Virus Type 1	5
15	Rhinovirus group A IgM	5	34	anti-HBs positive	5
16	Rhinovirus group A IgG	5	35	anti-HCV	3
17	Chlamydia IgM	1	36	ds-DNA	5
18	Chlamydia IgG	1	37	Autoimmune Control	3
19	Haemophilus Influenzae IgG	5	38	Rheumatoid Arthritis	2

2. Clinical Agreement Study

A. Sugentech, Inc. Clinical Agreement Study

Comparison studies between the test device (SGTi-flex COVID-19 IgG) and an EUA authorized PCR-based test were conducted by lab professionals, using total 419 specimens. The sensitivity and specificity (positive and negative percent agreements) were 92.43% and 99.15%, respectively.

Table 2. Clinical Performance analysis

		Reference method		
		Positive	Negative	Total
Test device	Positive	171	2	173
	Negative	14	232	246
	Total	185	234	419

(1) Sensitivity (Positive percent agreement): 92.43% (171/185, 95% CI: 87.70%~95.44%)

(2) Specificity (Negative percent agreement): 99.15% (232/234, 95% CI: 96.94%~99.77%)

When estimating the sensitivity of IgG over time from symptom onset for all positive samples, the proportion of IgG positive patients reached 98.6% approximately 15 days after symptom onset.

Table 3. The sensitivity estimates for IgG over time

Days after symptom onset (days)	IgG Positive
0~7	41.2 % (7/17) (95% CI: 21.61~63.99 %)
8~14	91.7 % (22/24) (95% CI: 74.15~97.68 %)
≥15	98.6 % (142/144) (95% CI: 95.08~99.62 %)

B. Independent Clinical Agreement Validation Study

The SGTi-flex COVID-19 IgG was tested on August 19, 2020 at the Frederick National Laboratory for Cancer Research (FNLCR) sponsored by the National Cancer Institute (NCI). The test was validated against a panel of previously frozen samples consisting of 30 SARS-CoV-2 antibody-positive serum samples and 80 antibody-negative serum and anticoagulant citrate dextrose (ACD) plasma samples. Each of the 30 antibody-positive samples were confirmed with a nucleic acid amplification test (NAAT) and both IgM and IgG antibodies were confirmed to be present in all 30 samples. The presence of antibodies in the samples was confirmed by several orthogonal methods prior to testing with the SGTi-flex COVID-19 IgG. The presence of IgM and IgG antibodies specifically was confirmed by one or more comparator methods. Antibody-positive samples were selected at different antibody titers.

All antibody-negative samples were collected prior to 2020 and include i) seventy (70) samples selected without regard to clinical status, "Negatives" and ii) ten (10) samples selected from banked serum from HIV+ patients, "HIV+". Testing was performed by one operator using 1 lot of SGTi-flex COVID-19 IgG. Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008).

For the evaluation of cross-reactivity with HIV+, it was determined whether an increased false positive rate among antibody-negative samples with HIV was statistically higher than the false positive rate among antibody-negative samples without HIV (for this, a confidence interval for the difference in false positive rates was calculated per a score method described by Altman). The results and data analysis are shown in the tables below.

Summary Results

	Comparator Method			Collected pre-2020		
	Antibody Positive			Antibody Negative		
SGTi-flex COVID-19 IgG	IgM+, IgG+	IgM+, IgG-	IgM-, IgG+	Neg.	HIV	Total
IgG+	29					29
IgG-	1			70	10	81
Total	30			70	10	110

Summary Statistics

Measure	Estimate	Confidence Interval
IgG Sensitivity	96.7% (29/30)	(83.3%; 99.4%)
IgG Specificity	100% (80/80)	(95.4%; 100%)
PPV for prevalence = 5.0%	100%	(48.9%; 72.9%)
NPV for prevalence = 5.0%	99.8%	(99.1%; 100%)
Cross-reactivity with HIV+	0.0% (0/10), not detected	

Important limitations:

1. Samples were not randomly selected, and sensitivity and specificity estimates may not be indicative of the real-world performance of the device.
2. These results are based on serum and ACD plasma samples only and may not be indicative of performance with other sample types, such as whole blood, including finger stick blood.
3. The number of samples in the panel is a minimally viable sample size that still provides reasonable estimates and confidence intervals for test performance, and the samples used may not be representative of the antibody profile observed in patient populations.

3. Antibody Class Specificity

SGTi-flex COVID-19 IgG showed 100% agreement with expected result before and after competitive treatment with capture IgG and IgM antibodies to establish antibody class specificity.

4. Matrix Equivalency

Matrix equivalency studies with the test device (SGTi-flex COVID-19 IgG) in the claimed matrices were conducted by lab professionals. Five (5) matched sets of samples from individual donors, comprised of serum, plasma (sodium heparin, lithium heparin, sodium citrate and tripotassium EDTA), and whole blood (sodium heparin, lithium heparin, sodium citrate and tripotassium EDTA) were evaluated. A negative, low positive, and moderate positive sample was evaluated using each matrix. Results of the study demonstrate that performance is equivalent for all matrices tested.

REFERENCES

1. WHO, Coronavirus disease 2019 (COVID-19) Situation report
2. Emerging Infectious Diseases (www.cdc.gov/eid) Vol. 13, No. 10, (Oct, 2007), Duration of Antibody Response after Severe Acute Respiratory Syndrome, Li-Pin Wu, et, al.
3. Scientific Report, 9, 1390 (Feb, 2019) Development and Evaluation of a Multiplexed Immunoassay for Simultaneous Detection of Serum IgG Antibodies to Six Human coronaviruses Suvang U. Trivedi. et, al.
4. J.virol. Methods. 2008, 152(1-2): 77-84, A rapid point of care immunoswab assay for SARS-CoV detection
5. Clinical and Diagnostics laboratory immunology, 2004, vol.11(4) : 792-794, kinetics of Severe acute respiratory syndrome(SARS) coronavirus specific antibodies in 271 Laboratory- confirmed cases of SARS

EXPLANATION OF SYMBOLS USED ON PACKAGE

IVD	*In vitro* diagnostic medical device	Σ 25	Contains sufficient for 25 tests
	Do not reuse		Consult instructions for use.
2°C 30°C	Store between 2°C and 30°C		Caution, consult accompanying documents
LOT	Batch code		Use by
REF	Catalogue number		Manufacturer

INQUIRIES AND GENERAL INFORMATION

Please visit website www.sugentech.com or

Contact Sugentech via email: info@sugentech.com

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