Wantai SARS-CoV-2 Diagnostics

WANTAI SARS-CoV-2 Ab Rapid Test

Rapid Test for Detection of Total Antibodies to SARS-CoV-2

FOR SERUM / PLASMA / VENIPUNCTURE WHOLE BLOOD SPECIMEN

INSTRUCTIONS FOR USE

REF WJ-2710, WJ-2750

For prescription use only.
For in vitro diagnostic use only.
For use under Food and Drug Administration's Emergency Use Authorization (EUA) only.

INTENDED USE

The WANTAI SARS-CoV-2 Ab Rapid Test is a lateral flow assay for the qualitative detection of total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum, plasma (dipotassium EDTA, lithium heparin, and sodium citrate), and venous whole blood. The WANTAI SARS-CoV-2 Ab Rapid Test is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. 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. 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 positive results to the appropriate public health authorities.

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 WANTAI SARS-CoV-2 Ab Rapid Test 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 serology assay.

The WANTAI SARS-CoV-2 Ab Rapid Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

SUMMARY

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by infection with the SARS-CoV-2 virus. Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In severe cases, infection can cause pneumonia, severe acute respiratory syndrome (SARS), kidney failure and death.

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). The 2019 novel coronavirus, formerly known as 2019-nCoV and now known as SARS-CoV-2, is a new strain of coronavirus that was first identified during the recent COVID-19 pandemic.

PRINCIPLE OF THE ASSAY

The WANTAI SARS-CoV-2 Ab Rapid Test employs chromatographic lateral flow device in a cassette format. Colloidal gold conjugated recombinant antigens corresponding to SARS-CoV-2 are dry-immobilized at the end of nitrocellulose membrane strip. SARS-CoV-2 antigens are bound at the Test Zone (T) and antibodies are bound at the Control Zone (C). The antigen used in the assay is the receptor-binding domain of SARS-CoV-2 spike protein. When the specimen is added, it migrates by capillary diffusion rehydrating the gold conjugate. If present in specimen, SARS-CoV-2 antibody will bind with the gold conjugated antigens forming particles. These particles will continue to migrate along the strip until the Test Zone (T) where they are captured by the SARS-CoV-2 antigen generating a visible red line. If there is no SARS-CoV-2 antibody in specimen, no red line is formed in the Test Zone (T). The gold conjugate will continue to migrate alone until it is captured in the Control Zone (C) by the antibodies aggregating in a red line, which indicates the validity of the test.

COMPONENTS

Components	WJ-2710	WJ-2750
Test Cassette	x10	x50
Diluent Buffer	x1 vial	x5 vials

Test Cassette:
Test cassettes are packed in foil pouches with desiccant. Each foil pouch contains 1 cassette. Single use only.

Diluent Buffer (Code "0", DIL | SPE):
3ml per vial. Buffer solution containing surfactant. The Diluent Buffer can be stored at room temperature. Stable for 9 months after opening.

Wantai External Controls (Required but not Provided):

Negative Control (Code "N", CTRL | NEG):
Lyophilized, newborn calf serum buffer.

Positive Control (Code "P", CTRL | POS):
Lyophilized, monoclonal mouse anti-S-RBD antibodies in newborn calf serum buffer.

Preparation of controls: the controls should be reconstituted with distilled or deionized water to the working concentration. Add water into the ampoule according to the volume indicated on the label of the ampoule.

The reconstituted controls can be kept at 2-8°C for no longer than 7 days. For long-term storage, the reconstituted controls should be stored at below -15°C, the freeze-thaw cycles should be not more than 5 times. Before use, balance the reconstituted controls to room temperature and mix well.

Use of controls: add **80μl** of the reconstituted control to the test cassette. **DO NOT ADD DILUENT BUFFER!** One negative and one positive control should be tested for every new lot, or more frequently consistent with the good laboratory practice.

Others:
Instructions for use

Materials required but not provided:
Clock or timer, specimen collection container, centrifuge, biohazard waste container.

SPECIMEN COLLECTION

1. Human serum, plasma or venous whole blood specimens are used for this test. Plasma or whole blood specimens containing K2EDTA, sodium citrate or lithium heparin can be used for this test.
2. Specimens containing suspended fibrin or aggregates and severe hemolysis (hemoglobin content greater than 400mg/L) cannot be detected, but jaundice (bilirubin content less than 1.71mmol/L) and hyperlipemia (triglyceride content less than 170mmol/L) can be detected.
3. Serum and plasma specimens can be refrigerated at 2-8°C for one week; In case of long-term storage, it shall be frozen below -15°C for no more than three weeks, and repeated freezing and thawing shall not exceed 3 times. Specimens should be balanced to room temperature, mix the specimen before testing.
4. It is recommended to test the whole blood specimen immediately after blood collection. Do not use the specimen after long-term storage.

STORAGE AND STABILITY

The WANTAI SARS-CoV-2 Ab Rapid Test can be stored at room temperature (2-30°C, do not freeze!) for 9 months from the date of manufacture.

PRECAUTIONS AND SAFETY

The WANTAI SARS-CoV-2 Ab Rapid Test is
For prescription use only.
For in vitro diagnostic use only.
For Emergency Use Authorization Only.

1. 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.
2. This test has been authorized only for the presence of total antibodies against SARS-CoV-2, not for any other viruses or pathogens.
3. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb3(b)(1), unless the authorization is terminated or revoked sooner.
4. This reagent is only used for in vitro testing, and the operation should be carried out in strict accordance with the instructions. Make sure that the test is not expired (EXP Date indicated on the kit box). The test cassette cannot be reused.
5. Do not use the specimens that have been placed for too long, bacteria and peculiar smell, so as to avoid

non-specific reactions caused by contamination of specimens and bacteria.

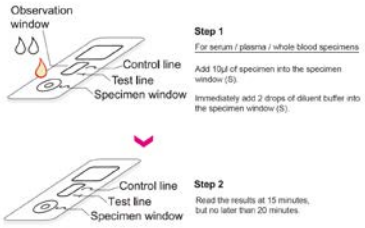
6. Use of this test kit with sample types other than those specifically approved for use with this device may result in inaccurate test results.
7. Bring all reagents to room temperature (15-30°C) before use.
8. Do not use the components of any other type of test kit as a substitute for the components in this kit.
9. Due to the different antibody levels of the positive samples, the test line (T) may show the different color intensity. During the indicated reading time, regardless of color intensity, even very weak color, should be judged as reactive.
10. All the waste and specimens should be treated in case of transmitting disease and must be properly disinfected (autoclaving is preferred) before disposal. The desiccant in aluminum foil pouch cannot be taken internally.
11. Use routine laboratory precautions. Do not eat, drink or smoke in the area where samples and kit reagents are handled. Avoid any contact between hands, eyes or mouth during sample collection and testing.
12. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when handling patient samples. Wash hands thoroughly after handling specimens and kit reagents.
13. At room temperature, the test cassette should be used within 30 minutes after it is taken out of the package to avoid prolonged exposure to humid air (humidity > 60%), which may affect the test result. If the kit is stored at 2-8°C, the reagent should be balanced to room temperature (30 minutes) before the experiment, then open the aluminum foil pouch for use.
14. During the test, the test cassette should be laid flat on the table, so as not to cause the lateral flow speed of specimen to be faster (or slower) and affect the test result.
15. Always interpret the results under good light conditions to avoid misreading of the test results. The result read after 20 minutes is invalid.

ASSAY PROCEDURE

Place the cassette on flat surface. Before opening, allow the test cassette to reach room temperature. Use it immediately (within 30 minutes) after opening.

1. **For venous whole blood / serum / plasma specimens:**
   Add **10µl** of specimen into the specimen window (S). Immediately add **two drops** of diluent buffer into the specimen window.
2. Read the results at 15 minutes after specimen and buffer loading, but no later than 20 minutes.

Procedure Diagram

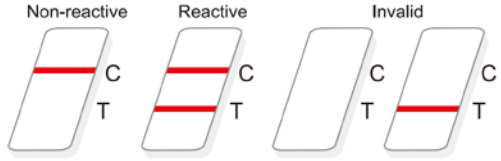


RESULTS

Quality Control: One red line should appear next to the Control Zone (C) indicating the validity of the test.
Invalid test run: If no red line appears next to the Control Zone (C), the test is invalid - discard the test and repeat with new specimen and new cassette.

Reactive Results: One red line appears next to the Test Zone (T) and another line next to the Control Zone (C) which indicates that antibodies to SARS-CoV-2 have been detected through using this test.

Non-reactive Results: No red line appears next to the Test Zone (T) and one line appears next to the control zone (C) which indicates that no antibodies to SARS-CoV-2 have been detected with this test. However, this does not exclude the possibility from infection with SARS-CoV-2.



The reactive result obtained with the WANTAI SARS-CoV-2 Ab Rapid Test should not be used to diagnose or exclude acute SARS-CoV-2 infection. Any reactive results must be interpreted in conjunction with the patient clinical history and another laboratory testing results. Follow-up and supplementary testing of all reactive specimens with other tests is required to confirm any reactive result.

CONDITIONS OF AUTHORIZATION FOR THE LABORATORY

The WANTAI SARS-CoV-2 Ab Rapid Test 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 WANTAI SARS-CoV-2 Ab Rapid Test ("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 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
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 Beijing Wantai Biological Pharmacy Enterprise Co., Ltd (wtexport@ystwt.com) 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.
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 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
7. 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 DATA

1. Clinical validation study of the WANTAI SARS-CoV-2 Ab Rapid Test was conducted at three sites in China in 2020. Serum and plasma specimens were evaluated from 403 subjects. Out of the 403 samples, 132 subjects were COVID-19 cases confirmed positive by an RT-PCR assay while 271 subjects were confirmed PCR negative. All patients who were confirmed positive exhibited clinical signs or symptoms of COVID-19.

The WANTAI SARS-CoV-2 Ab Rapid Test evaluation centers

Clinical institution	PCR Positive (Cases)	PCR Negative (Cases)	Total
Site 1	12	0	12
Site 2	39	195	234
Site 3	81	76	157
Total	132	271	403

Of the 132 positive samples, 125 were reactive on the WANTAI SARS-CoV-2 Ab Rapid Test, and of the 271 negative samples, 268 were non-reactive. The kit demonstrated the overall Positive Percent Agreement (PPA) of 94.70% (125/132) and the Negative Percent Agreement (NPA) of 98.89% (268/271), as indicated in the table below.

Summary of clinical evaluation results

Cases		PCR Comparator SARS-CoV-2 results		Total
		Positive	Negative	
WANTAI SARS-CoV-2 Ab Rapid Test results	Positive	125	3	128
	Negative	7	268	275
Total		132	271	403

Summary of clinical performance

Performance	Results	95% CI

PPA	94.70%	89.46%-97.41%
NPA	98.89%	96.80%-99.62%

It was observed that the detection rate of the kit was closely related to the time of disease onset, the kit showed higher positive detection rate in specimens from patients who had symptoms for longer periods of time. Therefore, the interpretation of the test results should consider the specimen's collection time. The WANTAI SARS-CoV-2 Ab Rapid Test was evaluated with 415 samples collected over the course of time from 132 PCR-positive subjects. For performance calculation, only the results of the first bleed from each patient are considered, the performance of the test is as follows:

Positive percent agreement (PPA) according to days from onset of symptoms

Days from onset of symptoms	Total PCR positive specimens	Number Wantai reactive result	PPA	95% CI
≤ 7	62	38	61.29%	48.85%-72.42%
8 - 14	58	45	77.59%	65.34%-86.41%
≥ 15	12	11	91.67%	64.61%-98.51%
Total	132			

The table below represents the study design and results of serial bleeds by days from onset of symptoms.

Detection rate in serially collected specimens

Days from onset of symptoms	1st serial results		2nd serial results		3rd serial results		4th serial results		5th serial results	
	No. tests	No. +	No. tests	No. +	No. tests	No. +	No. tests	No. +	No. tests	No. +
0 - 7	62	38	15	10	3	3	0	0	0	0
8 - 14	58	45	67	58	35	31	8	8	0	0
≥ 15	12	11	34	34	51	49	46	45	24	24
Total	132		116		89		54		24	

2. Independent Clinical Agreement Validation Study: The WANTAI SARS-CoV-2 Ab Rapid Test was tested on 06/16/2020 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 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 WANTAI SARS-CoV-2 Ab Rapid Test. 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 one lot of the WANTAI SARS-CoV-2 Ab Rapid Test. Confidence intervals for sensitivity and specificity were calculated per a score method described in CLSI EP12-A2 (2008).

   For evaluation of cross-reactivity with HIV+, it was evaluated 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). Study results and summary statistics are presented in the following tables:

Summary results of the independent evaluation

WANTAI SARS-CoV-2 Ab Rapid Test	Comparator Method			Total
	Positive (IgM/IgG)+	Negative (IgM/IgG)-	Negative HIV+	
Positive	30	1	0	31
Negative	0	69	10	79
Total	30	70	10	110

Summary statistics of the independent evaluation

Measure	Estimate	Confidence Interval
Sensitivity/PPA	100% (30/30)	88.7%-100%
Specificity/NPA	98.8% (79/80)	93.3%-99.8%
Combined PPV for prevalence = 5.0%	80.8%	40.9%-96.0%
Combined NPV for prevalence = 5.0%	100%	99.4%-100%
Cross-reactivity with HIV+	0.00% (0/10), not detected	

Limitations of the study:

- Samples were not randomly selected, and sensitivity and specificity estimates may not be indicative of the real-world performance of the device.
- These results are based on serum and plasma samples only and may not be indicative of performance with other sample types, such as whole blood, including finger stick blood.
- Information about anticoagulants used is not known.
- 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. To evaluate the potential cross-reactivity of the WANTAI SARS-CoV-2 Ab Rapid Test to antibodies to other viruses that may be present in the population the following viruses and autoimmune conditions were assessed. No false positive results were observed with the WANTAI SARS-CoV-2 Ab Rapid Test.

Specimen	No.	Lot #1		Lot #2		Lot #3		Specificity
		+	-	+	-	+	-	
Flu A	8	0	8	0	8	0	8	100%
Flu B	6	0	6	0	6	0	6	100%
HCV	6	0	6	0	6	0	6	100%
HBV	6	0	6	0	6	0	6	100%
ANA	5	0	5	0	5	0	5	100%
RSV	8	0	8	0	8	0	8	100%
Rhinovirus	6	0	6	0	6	0	6	100%

Specimen	No.	+	-	Specificity
alpha COV 229E	5	0	5	100%
alpha COV NL63	5	0	5	100%
beta COV OC43	7	0	7	100%
beta COV HKU1	4	0	4	100%

LIMITATIONS

1. Use of the WANTAI SARS-CoV-2 Ab Rapid Test is limited to laboratory personnel who have been trained. Not for home use.
2. The test is limited to the qualitative detection of antibodies specific for the SARS-CoV-2 virus. The intensity of the test line does not necessarily correlate to SARS-CoV-2 antibody titer in the specimen. This test cannot be used as a quantitative test.
3. SARS-CoV-2 antibodies may be below detectable levels in patients who have been exhibiting symptoms for less than 15 days.
4. Reactive results must be confirmed with another available method and interpreted in conjunction with the patient's clinical information.
5. Do not use the WANTAI SARS-CoV-2 Ab Rapid Test with fingerstick samples.
6. Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection or to inform infection status.
7. It is not known at this time if the presence of antibodies to SARS-CoV-2 confers immunity to re-infection.
8. 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.
9. 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 WANTAI SARS-CoV-2 Ab Rapid Test early after infection is unknown. False positive may occur due to cross-reactivity from pre-existing antibodies or other possible causes. Samples with positive results should be confirmed with alternative testing method(s) and clinical findings before a diagnostic determination is made. A negative result can occur if the quantity of the anti-SARS-CoV-2 antibodies present in the specimen is below the detection limits of the assay, or the antibodies that are detected are not present during the stage of disease in which a sample is collected.
10. This test is only used for the detection of human serum, plasma or venous whole blood specimens. This test should not be used for screening of donated blood.
11. This test has not been validated for cross-reactivity with anti-Haemophilus influenzae positive samples.
12. The kit should be used within 30 minutes after the aluminum foil bag is opened.
13. Testing should not be performed when ambient temperature is higher than 30ºC or the relative humidity is higher than 70%.

REFERENCES

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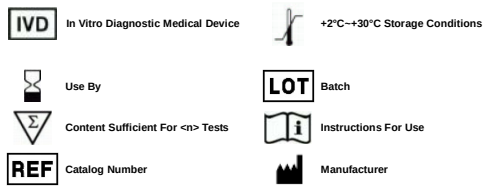
SYMBOLS



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