OnSite TB IgG/IgM Combo Rapid Test- (Serum / Plasma / Whole Blood)

CE

CTK BIOTECH
SIMPLIFYING DIAGNOSTICS

REF

Catalog Number R0053C

IVD

In vitro Diagnostic

INTENDED USE

The *OnSite* TB IgG/IgM Combo Rapid Test is a lateral flow chromatographic immunoassay for the simultaneous detection and differentiation of IgM anti-*Mycobacterium tuberculosis* (*M.TB*) and IgG anti-*M.TB* in human serum, plasma or whole blood. It is intended to be used as a screening test and as an aid in the diagnosis of infection with *M. TB*. Any reactive specimen with the *OnSite* TB IgG/IgM Combo Rapid Test must be confirmed with alternative testing method(s) and clinical findings.

SUMMARY AND EXPLANATION OF THE TEST

Tuberculosis is a chronic, communicable disease caused principally by *M. TB hominis* (Koch's bacillus), occasionally *by M. TB bovis*. The lungs are the primary target, but any organ may be infected.

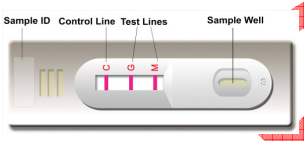
The risk of TB infection exponentially declined in the 20th century. However, the recent emergence of drug-resistant strains[1], particularly among patients with AIDS[2], has rekindled interest in TB. The incidence of infection was reported to be around 8 million cases per year with a death rate of 3 million per year. The mortality exceeded 50% in some African countries with high HIV rates[3,4].

The initial clinical suspicion and radiographic findings with subsequent laboratory confirmation by sputum examination and culture are the traditional method(s) in the diagnosis of active TB[5,6]. However, these methods either lack sensitivity or are time consuming, and are particularly not suitable for patients who are unable to produce adequate sputum, smear-negative or are suspected to have extra-pulmonary TB.

The *OnSite* TB IgG/IgM Combo Rapid Test is developed to alleviate these obstacles. The test detects IgM and IgG anti-*M.TB* in serum, plasma or whole blood in 15 minutes. An IgM positive result indicates a fresh *M.TB* infection, while an IgG positive result suggests a previous or chronic infection. Utilizing *M.TB* specific antigens[7-9], it also detects IgM anti-*M.TB* in patients vaccinated with BCG. In addition, the test can be performed by untrained or minimally skilled personnel without cumbersome laboratory equipment.

TEST PRINCIPLE

The *OnSite* TB IgG/IgM Combo Rapid Test is a lateral flow chromatographic immunoassay. The test cassette consists of: 1) a burgundy colored conjugate pad containing *M.TB* antigens conjugated with colloidal gold (*M.TB* conjugates) and rabbit IgG-gold conjugates, 2) a nitrocellulose membrane strip containing two test bands (M and G bands) and a control band (C band). The M band is pre-coated with monoclonal anti-human IgM for the detection of IgM anti- *M.TB*, the G band is pre-coated with reagents for the detection of IgG anti-*M.TB*, and the C band is pre-coated with goat anti-rabbit IgG.



When an adequate volume of test specimen is dispensed into the sample well of the cassette, the specimen migrates by capillary action across the cassette. IgM anti-*M.TB* if present in the specimen will bind to the *M.TB* conjugates. The immunocomplex is then captured on the membrane by the pre-coated anti-human IgM antibody forming a burgundy colored M line, indicating a *M.TB* IgM positive test result.

IgG anti-*M.T,B* if present in the specimen, will bind to the *M.TB* conjugates. The immunocomplex is then captured by the pre-coated reagents on the membrane forming a burgundy colored G line, indicating a *M.TB* IgG positive test result.

Absence of any test lines (M and G) suggests a negative result. The test contains an internal control (C band) which should exhibit a burgundy colored line of the immunocomplex of goat anti-rabbit IgG/rabbit IgG-gold conjugate regardless of color development on any of the T lines. Otherwise, the test result is invalid and the specimen must be retested with another device.

REAGENTS AND MATERIALS PROVIDED

1. Individually sealed foil pouches containing:
   a. One cassette device
   b. One desiccant
2. Plastic droppers
3. Sample diluent (1 bottle, 5 mL)
4. One package insert (instruction for use)

MATERIALS MAY BE REQUIRED AND NOT PROVIDED

1. Positive Control
2. Negative Control

MATERIALS REQUIRED BUT NOT PROVIDED

1. Clock or Timer
2. Lancing device for whole blood test

WARNINGS AND PRECAUTIONS

For *in Vitro* Diagnostic Use

1. This package insert must be read completely before performing the test. Failure to follow the insert gives inaccurate test results.
2. Do not open the sealed pouch unless ready to conduct the assay.
3. Do not use expired devices.
4. Bring all reagents to room temperature (15°C-30°C) before use.
5. Do not use the components in any other type of test kit as a substitute for the components in this kit.
6. Do not use hemolized blood specimen for testing.
7. Wear protective clothing and disposable gloves while handling the kit reagents and clinical specimens. Wash hands thoroughly after performing the test.
8. Users of this test should follow the US CDC Universal Precautions for prevention of transmission of HIV, HBV and other blood-borne pathogens.
9. Do not smoke, drink, or eat in areas where specimens or kit reagents are being handled.
10. Dispose of all specimens and materials used to perform the test as bio-hazardous waste.
11. Handle the negative and positive controls in the same manner as patient specimens.
12. The testing results should be read within 15 minutes after a specimen is applied to the sample well of the device. Reading the results after 15 minutes may give erroneous results.
13. Do not perform the test in a room with strong air flow, i.e. an electric fan or strong air-conditioning.

REAGENT PREPARATION AND STORAGE INSTRUCTIONS

All reagents are ready to use as supplied. Store unused test device unopened at 2°C -30°C**.** If stored at 2°C -8°C, ensure that the test device is brought to room temperature before opening. The test device is stable through the expiration date printed on the sealed pouch. Do not freeze the kit or expose the kit over 30°C.

SPECIMEN COLLECTION AND HANDLING

Consider any materials of human origin as infectious and handle them using standard bio-safety procedures.

Plasma

1. Collect blood specimen into a lavender, blue or green top collection tube (containing EDTA, citrate or heparin, respectively in Vacutainer®) by veinpuncture.
2. Separate the plasma by centrifugation.
3. Carefully withdraw the plasma into new pre-labeled tube.

Serum

1. Collect blood specimen into a red top collection tube (containing no anticoagulants in Vacutainer®) by veinpuncture.
2. Allow the blood to clot.
3. Separate the serum by centrifugation.
4. Carefully withdraw the serum into a new pre-labeled tube.

Test specimens as soon as possible after collecting. Store specimens at 2°C-8°C if not tested immediately.

Store specimens at 2°C-8°C for up to 5 days. The specimens should be frozen at -20°C for longer storage.

Avoid multiple freeze-thaw cycles. Prior to testing, bring frozen specimens to room temperature slowly and mix gently. Specimens containing visible particulate matter should be clarified by centrifugation before testing. Do not use samples demonstrating gross lipemia, gross hemolysis or turbidity in order to avoid interference on result interpretation.

Blood

Drops of whole blood can be obtained by either finger tip puncture or veinpuncture. Do not use any hemolized blood for testing.

Whole blood specimens should be stored in refrigeration (2°Ċ -8°Ċ) if not tested immediately. The specimens must be tested within 24 hours of collection.

ASSAY PROCEDURE

Step 1: Bring the specimen and test components to room temperature if refrigerated or frozen. Mix the specimen well, prior to assay, once thawed.

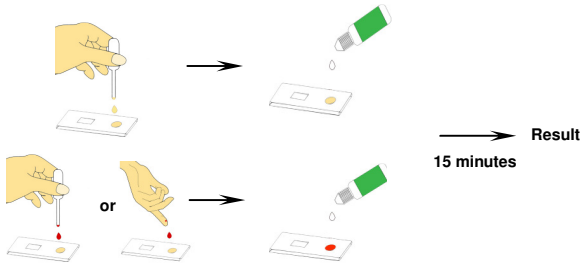
Step 2: When ready to test, open the pouch at the notch and remove device. Place the test device on a clean, flat surface.

Step 3: Be sure to label the device with the specimen's ID number.

Step 4: Fill the plastic dropper with the specimen.

Holding the dropper vertically, dispense 1 drop (about 30-45 µL) of serum/plasma or 1 drop of whole blood (about 40-50 µL) into the sample well making sure that there are no air bubbles.

Immediately add 1 drop (about 35-50 µL) of Sample Diluent to the sample well.



1 drop of specimen **1 drop of sample diluent**

Step 5: Set up timer.

Step 6: Results can be read in 15 minutes. Positive results can be visible in as short as 1 minute.

Don't read result after 15 minutes. To avoid confusion, discard the test device after interpreting the result.

QUALITY CONTROL

1. **Internal Control:** This test contains a built-in control feature, the C line. The C line develops after adding the specimen and the sample diluent. If the C line does not develop, review the whole procedure and repeat the test with a new device.

2. **External Control:** Good Laboratory Practice recommends using external controls, positive and negative, to assure the proper performance of the assay, particularly under the following circumstances:
   a. New operator uses the kit, prior to performing the testing of specimens.
   b. A new lot of test kits is used.
   c. A new shipment of kits is used.
   d. The temperature used during storage of the kit falls outside of 2-30°C.
   e. The temperature of the test area falls outside of 15-30°C.
   f. To verify a higher than expected frequency of positive or negative results.
   g. To investigate the cause of repeated invalid results.

INTERPRETATION OF ASSAY RESULT

1. NEGATIVE RESULT: If only the C line is present, the absence of any burgundy color in both the test lines (M and G) indicates that no anti-*M.TB* antibodies are detected. The result is negative.

2. POSITIVE RESULT:

2.1 In addition to the presence of the C line, if only the M line is developed, the test indicates the presence of IgM anti- *M.TB*. The result is positive.

2.2 In addition to the presence of the C line, if only the G line is developed, the test indicates the presence of IgG anti-*M.TB*. The result is positive.

2.3 In addition to the presence of the C line, if both the M and the G lines are developed, the test indicates the presence of IgG and IgM anti-*M.TB*. The result is also positive.

Samples with positive results should be confirmed with alternative testing method(s) and clinical findings before a positive determination is made.

3. INVALID: If no C line is developed, the assay is invalid regardless of any burgundy color in the test lines as indicated below. Repeat the assay with a new device.

PERFORMANCE CHARACTERISTICS

1. **Clinical Performance For IgM Test**

A total of 200 specimens from non-TB patients and 35 specimens from patients under anti-TB treatment were tested by the *OnSite* TB IgG/IgM Combo Rapid Test and a commercial TB IgM ELISA kit. Comparison of the results for all subjects is shown in the following table.

	OnSite TB IgG/IgM Combo Rapid Test		
IgM ELISA Test	**Positive**	**Negative**	**Total**
Positive	30	5	35
Negative	7	193	200
Total	37	198	235

Relative Sensitivity: 85.7%, Relative Specificity: 96.5%, Overall Agreement: 94.9%

2. **Clinical Performance For IgG Test**

A total of 200 specimens from the non-TB patients and 35 specimens from the patients under anti-TB treatment were tested by the *OnSite* TB IgG/IgM Combo Rapid Test and a commercial TB IgG ELISA kit. Comparison of the results for all subjects is shown in the following table.

	OnSite TB IgG/IgM Combo Rapid Test		
IgG ELISA Test	**Positive**	**Negative**	**Total**
Positive	31	4	35
Negative	7	193	200
Total	38	197	235

Relative Sensitivity: 88.6%, Relative Specificity: 96.5%, Overall Agreement: 95.3%

LIMITATIONS OF TEST

1. The Assay Procedure and the Interpretation of Assay Result sections must be followed closely when testing for the presence of antibodies to *M.TB* in serum or plasma from individual subjects. Failure to follow the procedure may give inaccurate results.
2. The *OnSite* TB IgG/IgM Rapid Test is limited to the qualitative detection of IgG and IgM anti-*M.TB* in human serum or plasma. The intensity of the test line does not have a linear correlation with the antibody titer in the specimen.
3. The test also recognizes antibodies to *M. bovis* and *M. africanum*.
4. An IgG positive response may be detected in BCG vaccinated personnel.
5. A negative result for an individual subject indicates absence of detectable antibodies to *M.TB*. However, a negative test result does not preclude the possibility of exposure to or infection with *M.TB*.
6. A negative result can occur if the quantity of the antibodies to *M.TB* 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.
7. Immunocompromised conditions such as HIV infection may reduce the test sensitivity.
8. Some specimens containing unusually high titers of heterophile antibodies or rheumatoid factor may affect expected results.
9. The results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

REFERENCES

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Index of CE Symbols

	Consult instructions for use	IVD	For *in vitro* diagnostic use only		Use by
REF	Catalog #	LOT	Lot Number	Σ N	Tests per kit
2°C 30°C	Store between 2-30°C	EC REP	Authorized Representative	2	Do not reuse
	Manufacturer		Date of manufacture		

CTK Biotech, Inc.
10110 Mesa Rim Road
San Diego, CA 92121, USA
Tel: 858-457-8698
Fax: 858-535-1739,
E-mail: info@ctkbiotech.com

EC REP **MDSS GmbH**
Schiffgraben 41, 30175 Hannover, Germany
Tel.: (+49)-511-6262 8630

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English version

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