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

CE

CTK Biotech, Inc.
The New Wave of Diagnosis

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.

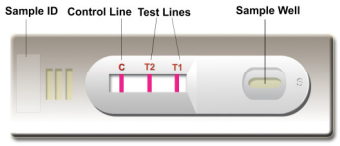
The risk of TB infection has exponentially declined in the 20th century. However, the recent emergence of drug-resistant strains[1], particularly among patients with AIDS[2], has rekindled interest in TB. The incidence of infection was reported around 8 million cases per year with a death rate of 3 million 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, in particularly are not suitable for patients who are unable to produce adequate sputum, smear-negative, or 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, plasm, or whole blood in 15 minutes . An IgM positive result indicates for a fresh *M.TB* infection, while an IgG positive response 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 minimal 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 colloid gold (*M.TB* conjugates) and rabbit IgG-gold conjugates, 2) a nitrocellulose membrane strip containing two test bands (T1 and T2 bands) and a control band (C band). The T1 band is pre-coated with monoclonal anti-human IgM for the detection of IgM anti- *M.TB*, the T2 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 T1 band, indicating a *M.TB* IgM positive test result.

IgG anti- *M.TB*, 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 T2 band, indicating a *M.TB* IgG positive test result.

Absence of any T bands (T1 and T2) suggests a negative result. The test contains an internal control (C band) which should exhibit a burgundy colored band of the immunocomplex of goat anti rabbit IgG/rabbit IgG-gold conjugate regardless of the color development on any of the T bands. Otherwise, the test result is invalid and the specimen must be retested with another device.

REAGENTS AND MATERIALS PROVIDED

1. Each kit contains 30 test devices, each sealed in a foil pouch with three items inside:
   a. One cassette device.
   b. One plastic dropper.
   c. One desiccant.
2. Sample diluent (1 bottle, 5 mL)
3. One package insert (instruction for use).

MATERIALS REQUIRED AND AVAILABLE FOR PURCHASE

1. Positive Control (1 vial, red cap, 1 mL, Cat # R0053-P)
2. Negative Control (1 vial, green cap, 1 mL, Cat # R0053-N)

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℃-30℃) 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 biohazardous waste.
11. Handle the Negative and Positive Control 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. Read result after 15 minutes may give erroneous results.
13. Do not perform the test in a room with strong air flow, ie. 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℃ -30℃. The positive and negative controls should be kept at 2℃ -8℃**.** If stored at 2℃ -8℃, 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℃.

SPECIMEN COLLECTION AND HANDLING

Consider any materials of human origin as infectious and handle them using standard biosafety 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℃-8℃ if not tested immediately.

Store specimens at 2℃-8℃ up to 5 days. The specimens should be frozen at -20℃ 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℃ -8℃) 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 specimen's ID number.

Step 4: **For whole blood test**
Apply 1 drop of whole blood (about 40-50 µL) into the sample well.

Then add 1 drop (about 35-50 µL) of Sample Diluent immediately.

1 drop of whole blood **1 drop of sample diluent**

For serum or plasma test
Fill the pipette dropper with the specimen.

Holding the dropper vertically, dispense 1 drop (about 30-45 µL) of specimen into the sample well making sure that there are no air bubbles.

Then add 1 drop (about 35-50 µL) of Sample Diluent immediately.

1 drop of specimen **1 drop of sample diluent** **15 minutes**

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

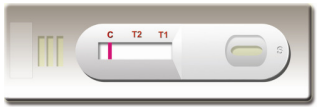
Using individual *OnSite* TB IgG/IgM Rapid Test cassettes as described in the Assay Procedure above, run 1 Positive Control and 1 Negative Control (provided upon request) under the following circumstances to monitor test performance:

1. A new operator uses the kit, prior to performing testing of specimens.
2. A new test kit is used.
3. A new shipment of kits is used.
4. The temperature used during storage of the kit falls outside of 2℃-30℃.
5. The temperature of the test area falls outside of 15℃-30℃.

Expected results are as follows:

Negative Control

Only the C band shows color development, the two T bands (T1 and T2) show no color development.



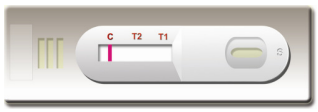
Positive Control

The C band and two T bands (T1 and T2) show color development.

The appearance of any burgundy color in the T bands, regardless of intensity, must be considered as presence of the band.

INTERPRETATION OF ASSAY RESULT

1. NEGATIVE RESULT: If only the C band is present, the absence of any burgundy color in the both T bands (T1 and T2) indicates that no anti- *M.TB* antibodies are detected. The result is negative.



2. POSITIVE RESULT:

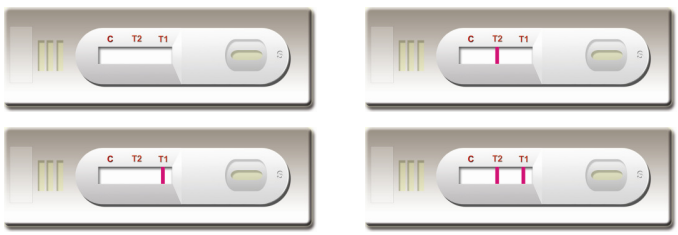
2.1 In addition to the presence of C band, if only T1 band is developed, indicates for the presence of IgM anti- *M.TB*. The result is positive.

2.2 In addition to the presence of C band, if only T2 band is developed, the test indicates for the presence of IgG anti- *M.TB*. The result is positive.

2.3 In addition to the presence of C band, both T1 and T2 bands are developed, indicates for 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 band is developed, the assay is invalid regardless of any burgundy color in the T bands 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 for all subjects is showed 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 for all subjects is showed 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 Assay Result Interpretation must be followed closely when testing 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 band does not have 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 condition such as HIV infection may reduce the test sensitivity. If HIV co-infection is highly suspected, the *OnSite* TB Plus (R0055C) Rapid Test is highly recommended.
8. Some specimens containing unusually high titer 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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PI-R0053C Rev. A Effective date: June 01-2006
English version

For Export Only, Not For Re-sale In the USA

Index of CE Symbol

	Attention, see instructions for use
IVD	For *in vitro* diagnostic use only
REF	Catalog #
LOT	Lot Number
	Use by
	Tests per kit
2°C 30°C	Store between 2-30℃
	Do not reuse
	Manufacturer
	Date of manufacture