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

CE

CTK BIOTECH SIMPLIFYING DIAGNOSTICS

REF

Catalog Number R0161C

IVD

In vitro Diagnostic

INTENDED USE

The *OnSite* Typhoid IgG/IgM Combo Rapid Test is a lateral flow immunoassay for the detection and differentiation of IgG and IgM anti-*Salmonella typhi* (*S. typhi*) and *paratyphi* in human serum, plasma or whole blood. This device is intended to be used by professionals as a screening test and as an aid in the diagnosis of infection with *S. typhi* and *paratyphi.* Any reactive specimen with the *OnSite* Typhoid IgG/IgM Combo Rapid Test must be confirmed with alternative testing method(s).

SUMMARY AND EXPLANATION OF THE TEST

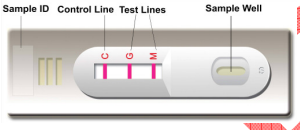
Typhoid fever and Paratyphoid fever are bacterial infections caused by *Salmonella typhi and paratyphi* types A, B, and C, respectively, which are transmitted through the ingestion of tainted food and water. World-wide, an estimated 17 million cases and 600,000 associated deaths occur annually[1]. Patients who are infected with HIV are at a significantly increased risk of clinical infection. 1-5% of patients become chronic carriers harboring *S. typhi* in the gallbladder.

The clinical diagnosis of infections depends on the isolation of *S. typhi and paratyphi* from blood, bone marrow or a specific anatomic lesion. In facilities that can not afford to perform this complicated and time-consuming procedure, the Felix-Widal test is used to facilitate diagnosis. However, many limitations lead to difficulties in the interpretation of the Widal test[3,4].

In contrast, the *OnSite* Typhoid IgG/IgM Combo Rapid Test is a simple and rapid, laboratory test. The test simultaneously detects and differentiates IgG and IgM antibodies to *S. typhi* and *paratyphi* in serum, plasma or whole blood specimens thus aiding in the determination of current or previous exposure to *S. typhi* and *paratyphi.*

TEST PRINCIPLE

The *OnSite* Typhoid IgG/IgM Combo Rapid Test is a lateral flow chromatographic immunoassay. The test cassette consists of: 1) a burgundy colored conjugate pad containing recombinant H antigen and O antigen conjugated with colloidal gold (HO conjugates) and rabbit IgG-gold conjugates, 2) a nitrocellulose membrane strip containing two test lines (G and M lines) and a control line (C line). The M line is pre-coated with monoclonal anti-human IgM for the detection of IgM anti-*S. typhi* and *paratyphi,* the G line is pre-coated with reagents for the detection of IgG anti-*S. typhi* and *paratyphi* , and the C line 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 test specimen migrates by capillary action across the test cassette. IgM antibodies, if present in the specimen, will bind to the HO 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 *S. typhi* or *paratyphi* IgM positive test result.

IgG antibodies if present in the specimen will bind to the HO conjugates. The immunocomplex is then captured by the pre-coated reagents on the membrane forming a burgundy colored G line, indicating an *S. typhi* or *paratyphi* IgG positive test result.

Absence of any test lines (M and G) suggests a negative result. The test contains an internal control (C line) which should exhibit a burgundy colored line goat anti-rabbit IgG/rabbit IgG-gold conjugate immunocomplex regardless of color development on any of the test lines. If the C line does not develop, 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 components from any other type of test kit as a substitute for the components in this kit.
6. Do not use hemolized blood specimens 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 test results should be read within 15 minutes after a specimen is applied to the sample well or sample pad 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 devices 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

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

Serum

Step 1: Collect blood specimen into a red top collection tube (containing no anticoagulants in Vacutainer®) by veinpuncture.
Step 2: Allow the blood to clot.
Step 3: Separate the serum by centrifugation.
Step 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 for up to 5 days. 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 hemolized blood for testing.

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

ASSAY PROCEDURE

Step 1: Bring the specimen and the test components to room temperature if refrigerated or frozen. Once the specimen is thawed, mix well prior to performing assay.

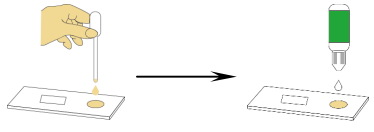
Step 2: When ready to test, open the pouch at the notch and remove the device. Place the test device on a clean, flat surface.

Step 3: Label device with the specimen's ID number.

Step 4: Fill the plastic dropper with the specimen.

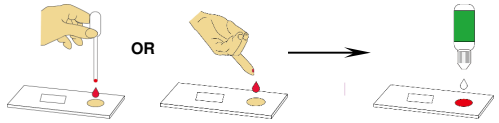
Holding the dropper vertically, dispense 1 drop (about 30-45 µL) of serum/plasma or 1 drop of whole blood (about 40-50 µL) into the sample well making sure that there are no air bubbles.

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



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

Results
15 minutes



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 soon as 1 minute.

Do not read results 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 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 test kits is used.
   d. The temperature used during storage of the kits fall outside of 2°C - 30°C.
   e. The temperature of the test area falls outside of 15°C - 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 test lines (M and G) indicates that no anti-*S. typhi* or *paratyphi* antibody is detected. The result is nonreactive.

2. POSITIVE RESULT:

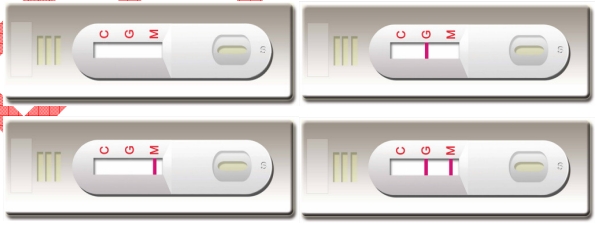
2.1 In addition to the presence of the C line, if only the M line is developed, the test indicates the presence of anti- *S. typhi* or *paratyphi* IgM. The result is reactive.

2.2 In addition to the presence of the C line, if only the G line is developed, the test indicates the presence of anti-*S. typhi* or *paratyphi* IgG. The result is reactive.

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 anti-*S. typhi* or *paratyphi* IgG and IgM. The result is also reactive.

Samples with reactive results should be confirmed with alternative testing method(s) and clinical findings before a diagnostic 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 234 samples from susceptible subjects were tested by the *OnSite* Typhoid IgG/IgM Combo Rapid Test and by a commercial *S. typhi* IgM EIA. Comparison for all subjects is shown in the following table:

	OnSite Typhoid IgG/IgM Combo Rapid Test		
IgM EIA	**Positive**	**Negative**	**Total**
Positive	31	3	34
Negative	2	198	200
Total	33	201	234

Relative Sensitivity: 91.2% , Relative Specificity: 99.0%, Overall Agreement: 97.9%

2. **Clinical Performance For IgG Test**

A total of 214 samples from susceptible subjects were tested by the *OnSite* Typhoid IgG/IgM Combo Rapid Test and by a commercial *S. typhi* IgG EIA kit. Comparison for all subjects is shown in the following table:

	OnSite Typhoid IgG/IgM Combo Rapid Test		
IgG EIA	**Positive**	**Negative**	**Total**
Positive	13	1	14
Negative	2	198	200
Total	15	199	214

Relative Sensitivity: 92.9% , Relative Specificity: 99.0 %, Overall Agreement: 98.5%

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 *S. typhi* or *paratyphi* in serum, plasma or whole blood from individual subjects. Failure to follow the procedure may give inaccurate results.
2. The *OnSite* Typhoid IgG/IgM Combo Rapid Test is limited to the qualitative detection of antibodies to *S. typhi* or *paratyphi* in human serum, plasma or whole blood. The intensity of the test line does not have a linear correlation with the antibody titer in the specimen.
3. A nonreactive result for an individual subject indicates absence of detectable anti-*S. typhi* or *paratyphi* antibodies. However, a nonreactive test result does not preclude the possibility of exposure to *S. typhi* or *paratyphi*.
4. A nonreactive result can occur if the quantity of anti-*S. typhi* or *paratyphi* 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.
5. Some specimens containing unusually high titers of heterophile antibodies or rheumatoid factor may affect expected results.
6. If the symptoms persist while the result from *OnSite* Typhoid IgG/IgM Combo Rapid Test is nonreactive, it is recommended to re-sample the patient a few days later or test with an alternative test method such as ELISA.
7. The results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

REFERENCES

1. Ivanoff BN, Levine MM, Lambert PH. Vaccination against typhoid fever: present status. Bulletin of the World Health Organization 1994; 72: 957-71.
2. Gotuzzo E, Frisancho O, Sanchez J, Liendo G, Carillo C, Black RE, Morris JG. Association between the acquired immunodeficiency syndrome and infection with Salmonella typhi or Salmonella paratyphi in an endemic typhoid area. Archives of Internal Medicine 1991; 151: 381-2.
3. Clegg A, Passey M, Omena MK, et al. Re-evaluation of the Widal agglutination test in response to the changing pattern of typhoid fever in the highlands of Papua New Guinea. Acta Tropica 1994;57:255-63.
4. Pang T. False positive Widal test in nontyphoid Salmonella infection. Southeast Asian Journal of Tropical Medicine and Public Health 1989; 20: 163-4.
5. Ismail A, Hai OK, Kader ZA. Demonstration of an antigenic protein specific for Salmonella typhi. Biochem Biophys Res Commun. 1991;181(1):301-5.

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
30°C 2°C	Store between 2-30°C	EC REP	Authorized Representative		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

PI-R0161C Rev. E

Effective date: 2013-06-04
English version