OnSite® Typhoid IgG/IgM Combo Rapid Test

REF R0161C CE

Instructions for Use

INTENDED USE

The *OnSite* Typhoid IgG/IgM Combo Rapid Test is a lateral flow immunoassay for the detection and differentiation of IgG and IgM antibodies to *Salmonella typhi* (*S. typhi*) and *paratyphi* in human serum, plasma or whole blood. It is intended to be used by professionals as an aid in the diagnosis of infection with *S. typhi* and *paratyphi*.

Any use or interpretation of this preliminary test result must also rely on other clinical findings and the professional judgment of health care providers. Alternative test method(s) should be considered to confirm the test result obtained by this device.

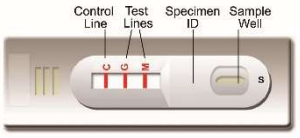
SUMMARY AND EXPLANATION OF THE TEST

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 cannot 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 colored conjugate pad containing recombinant H antigen and O antigen conjugated with colloidal gold (HO conjugates) and a control antibody conjugated with colloidal gold, 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 anti-*S. typhi* and *paratyphi* IgM, the G line is pre-coated with reagents for the detection of anti-*S. typhi* and *paratyphi* IgG, and the C line is pre-coated with a control line antibody.

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 colored M line, indicating an anti-*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 colored G line, indicating an anti-*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 colored line of the immunocomplex of the control antibodies 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 (REF SB-R0161, 5 mL/bottle)
4. Instructions 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. Read these Instructions for Use completely before performing the test. Failure to follow the instructions could lead to 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°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 hemolyzed 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 15 minutes after a specimen is applied to the sample well or sample pad of the device. Any results interpreted outside of the 15 minutes window should be considered invalid and must be repeated.
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 2-30°C. If stored at 2-8°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 to temperature above 30°C.

SPECIMEN COLLECTION AND HANDLING

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

Plasma/Serum

Step 1: Collect blood specimen into collection tube containing EDTA, citrate or heparin for plasma or collection tube containing no anticoagulants for serum by venipuncture.
Step 2: To make plasma specimen, centrifuge collected specimens and carefully withdraw the plasma into a new pre-labeled tube.
Step 3: To make serum specimen, allow blood to clot, then centrifuge collected specimens and carefully withdraw the serum into a new pre-labeled tube.

Test specimens as soon as possible after collecting. Store specimens at 2-8°C, if not tested immediately. The specimens can be stored at 2-8°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 with result interpretation.

Whole Blood

Step 1: Drops of whole blood can be obtained by either fingertip puncture or venipuncture. Collect blood specimen into a collection tube containing EDTA, citrate or heparin. Do not use hemolyzed blood for testing.

Whole blood specimens should be stored in refrigeration (2-8°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.

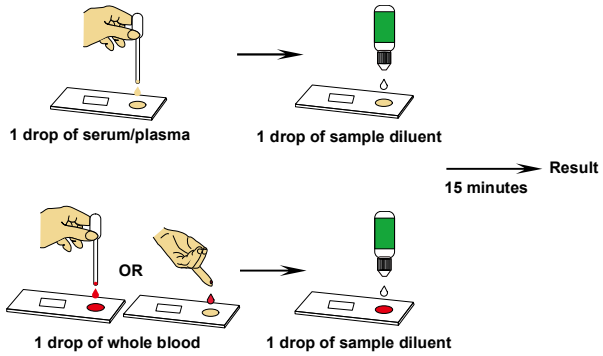
Step 2: When ready to test, open the pouch at the notch and remove the device. Place the test device on a clean, flat surface.

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 center of sample well with the bottle positioned vertically.



Step 5: Set up timer.

Step 6: Results should be read at 15 minutes. Positive results may be visible in as short as 1 minute. Negative results must be confirmed at the end of the 15 minutes only. ***Any results interpreted outside of the 15 minutes window should be considered invalid and must be repeated. Discard used devices after interpreting the result following local requirements governing the disposal of devices.***

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. 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 2-30°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 color in both test lines (M and G) indicates that no anti-*S. typhi* or *paratyphi* antibody is detected. The result is non-reactive or negative.

2. POSITIVE RESULT:

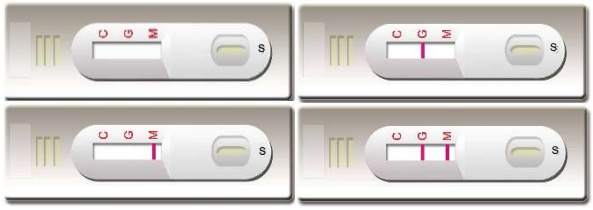
2.1 In addition to the presence of the C line, if only the M line develops, the test indicates the presence of anti-*S. typhi* or *paratyphi* IgM. The result is IgM reactive or positive.

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

2.3 In addition to the presence of the C line, if both the M and the G lines develop, the test indicates the presence of anti-*S. typhi* or *paratyphi* IgG and IgM. The result is both IgG and IgM reactive or positive.

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 develops, the assay is invalid regardless of any 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 specimens were collected from susceptible subjects and 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% (95% CI: 76.3-98.1%),
Relative Specificity: 99.0% (95% CI: 96.4-99.9%),
Overall Agreement: 97.9% (95% CI: 95.1-99.3%).

2. Clinical Performance for IgG Test

A total of 214 specimens were collected from susceptible subjects and 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% (95% CI: 66.1-99.8%),
Relative Specificity: 99.0% (95% CI: 96.4-99.9%),
Overall Agreement: 98.6% (95% CI: 96.0-99.7%).

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 negative or non-reactive result for an individual subject indicates absence of detectable anti-*S. typhi* or *paratyphi* antibodies. However, a negative or non-reactive test result does not preclude the possibility of exposure to *S. typhi* or *paratyphi*.
4. A negative or non-reactive 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. Infection may progress rapidly. If the symptoms persist while the result from *OnSite* Typhoid IgG/IgM Combo Rapid Test is negative or non-reactive, it is recommended to 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

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2. Gotuzzo E, Frisancho O, Sanchez J, et al. 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 Commune. 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
2°C 30°C	Store between 2-30°C	EC REP	Authorized Representative		Do not reuse
	Manufacturer		Date of manufacture		

CTK Biotech, Inc.
13855 Stowe Drive
Poway, CA 92064, 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. E2.1
Date released: 2020-11-12
English version

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