OnSite CE

REF R0160C IVD In vitro Diagnostic

INTENDED USE

The Typhoid IgG/IgM Rapid Test is a lateral flow immunoassay for the qualitative detection and differentiation of anti-*Salmonella typhi* (*S. typhi*) and *paratyphi* IgG and IgM in human serum or plasma. It is intended to be used by professionals as a screening test and provides a preliminary test result to 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.

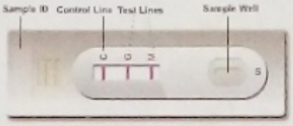
SUMMARY AND EXPLANATION OF THE TEST

Typhoid fever and paratyphi fever are bacterial infections caused by *Salmonella typhi and paratyphi A, B, and C respectively*, which are transmitted through the ingestion of tainted food and water. Worldwide an estimated 17 million cases and 600,000 associated deaths occur annually[1]. Patients who are infected with HIV are at 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 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, Filix-Widal test is used to facilitate diagnosis. However, many limitations lead to difficulties in the interpretation of the Widal test[2,4].

In contrast, the Typhoid IgG/IgM Rapid Test is a simple, fast laboratory test that simultaneously detects and differentiates IgG and IgM antibodies to *S. typhi* and *paratyphi* antigen[5] thus aiding in the determination of current or previous exposure to *S. typhi* and *paratyphi*. IgM positive or IgM /IgG both positive suggest current infection, while IgG positive suggests late stage of infection, previous infection, or latent infection.

TEST PRINCIPLE



The Typhoid IgG/IgM 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, 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 patient 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 patient 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 the color development on any of the test 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 (REF SB-R0160, 5 mL/bottle)
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

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°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 hemolyzed 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 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.

ASSAY PROCEDURE

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

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: Fill the plastic dropper with the specimen.

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

Then immediately add 1 drop (about 35-50 µL) of sample diluent into the center of the sample well with the bottle positioned vertically.

1 drop of serum/plasma 1 drop of sample diluent

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 minute window should be considered invalid and must be repeated. Discard used devices after interpreting the result following local requirements governing the disposal of devices.***

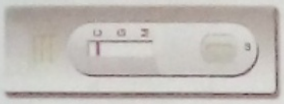
QUALITY CONTROL

1. **Internal Control:** This test contains a built-in control feature, the C line. The C line develops after adding specimen and sample diluent. Otherwise, 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 testing of specimens.
   b. A new lot of test kit 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

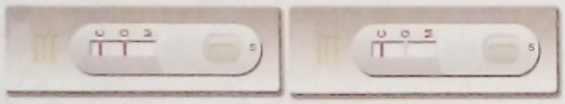
1. **NEGATIVE OR NON-REACTIVE RESULT:** If only the C line is present, the absence of any color in the both test lines (M and G) indicates that no anti-*S. typhi* or *paratyphi* antibody is detected in the specimen. The result is negative or non-reactive.



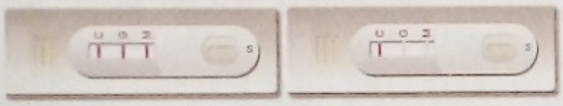
2. **POSITIVE OR REACTIVE RESULT:**

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

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

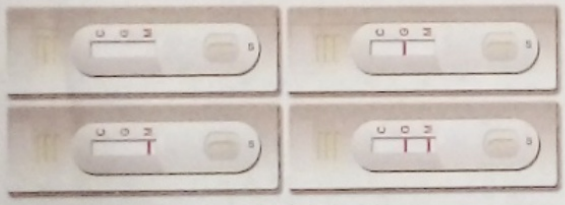


2.3 In addition to the presence of C line, both M and G lines develop, the test indicates for the presence of anti-*S. typhi* or *paratyphi* IgG and IgM in the specimen. The result is both IgG and IgM positive or reactive.



Samples with positive or reactive results should be confirmed with alternative testing method(s) and clinical findings before a diagnosis decision 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

Clinical Performance for IgM Test

A total of 334 specimens were collected from susceptible subjects and tested by the Typhoid IgG/IgM Rapid Test and by a commercial *S. typhi* IgM EIA. Comparison for all subjects is shown in the following table:

	Typhoid IgG/IgM Rapid Test		
IgM EIA	**Positive**	**Negative**	**Total**
Positive	31	3	34
Negative	2	298	300
Total	33	301	334

Relative Sensitivity: 91%, Relative Specificity: 99.3%, Overall Agreement: 98.5%

2. **Clinical Performance for IgG Test**

A total of 314 specimens were collected from susceptible subjects and tested by the Typhoid IgG/IgM Rapid Test and by a commercial *S. typhi* IgG EIA kit. Comparison for all subjects is shown in the following table:

	Typhoid IgG/IgM Rapid Test		
IgG EIA	**Positive**	**Negative**	**Total**
Positive	13	1	14
Negative	2	298	300
Total	15	299	314

Relative Sensitivity: 92.9%, Relative Specificity: 99.3%, Overall Agreement: 99.0%

3. **Performance Comparison with Blood Culture**

Nine (9) *S. paratyphi* A positive and eleven (11) *S. typhi* positive specimens confirmed with the blood culture were tested with the Typhoid IgG/IgM Rapid Test. The Typhoid IgG/IgM Rapid Test correctly indentified 9 *S. paratyphi* A and 10 *S. typhi* specimens. The agreement was 95%.

LIMITATIONS OF TEST

1. The Assay Procedure and the Test Result Interpretation must be followed closely when testing the presence of antibodies to *S. typhi* or *paratyphi* in serum or plasma from individual subjects. Failure to follow the procedure may give inaccurate results.
2. The Typhoid IgG/IgM Rapid Test is limited to the qualitative detection of antibodies to *S. typhi* or *paratyphi* in human serum or plasma. The intensity of the test line does not have 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 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 limit of the assay, or the antibodies that are detected are not present during the stage of disease in which a sample is collected.
5. Infection may progress rapidly. If the symptom persists, while the result from Typhoid IgG/IgM Rapid Test is negative or non-reactive result, it is recommended to test with an alternative test method, such as bacterial culture method.
6. Some specimens containing unusually high titer of heterophile antibodies or rheumatoid factor may affect expected results.
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
	Store between 2-30°C	EC REP	Authorized Representative	2	Do not reuse
	Manufacturer		Date of manufacture		

Mfd. by: M/s. CTK Biotech, Inc,
13855 Stowe Dr, Poway, California 92064,
United States having factory premises at M/s.
Beijing Genesee Biotech, Inc., 36, Yanqi Donger
Road, Huairou Yanqi Industrial Development
Zone 101407 Beijing, China

EC REP MDSS GmbH
Schiffgraben 41
30175 Hannover, Germany

PI-R0160C-ATH Rev. HP1.0
Date released: 2019-09-05
English version

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