TYPHOID RAPID TEST DEVICE (2-30°C)

IgG/IgM

CATALOGUE NUMBER	KIT SIZE (TESTS)
RADTYP1	20 Tests

Intended Use:
Typhoid fever Rapid Test Device is a rapid chromatographic immunoassay for the simultaneous detection and differentiation of IgG and IgM types of antibodies against Salmonella typhi (S. typhi) in human whole blood, serum or plasma. It is intended to be used as a screening test as an aid in the diagnosis of infection with S. typhi. Any reactive specimen with the Typhoid rapid test device needs to be confirmed with alternative testing method.

Summary:
Typhoid fever is caused by S. typhi, a Gram-negative bacterium. World-wide an estimated 17 million cases and 600,000 associated deaths occur annually. Patients who are infected with HIV are at significantly increased risk of clinical infection with S. typhi. Evidence of H. pylori infection also presents an increased risk of acquiring typhoid fever. 1-5% of patients become chronic carriers harbouring S. typhi in the gallbladder.
The clinical diagnosis of typhoid fever depends on the isolation of S. typhi from blood, bone marrow or a specific anatomic lesion but this is a complicated and time consuming procedure and where not feasible, the Widal test (or Weil-Felix Test) is used to aid diagnosis. However, many limitations lead to difficulties in the interpretation of the Widal test.
In contrast, the Typhoid Rapid Test Device is a simple and rapid laboratory test. The test simultaneously detects and differentiates IgG and IgM antibodies to S. typhi specific antigen in whole blood, serum or plasma thus aid in the determination of current or previous exposure the S. typhi.

Test Principle:
The Typhoid Rapid Test Device (Whole Blood/Serum/Plasma) is a qualitative membrane-based immunoassay for the detection of antibodies IgG and IgM to *Salmonella typhi* antigen in human whole blood, serum, or plasma. The IgG test line region is pre-coated with anti-human IgG for the detection of anti-S. typhi (IgG). The IgM test line region is pre-coated with anti-human IgM for detection of anti-S.typhi (IgM).
During testing sample is applied to the sample well of the test device and, if it contains anti-Typhoid antibodies, these bind with Typhoid antigen conjugate pre-coated in the sample well area. The immunocomplex thus formed migrates by capillary action. If the antibodies present in specimen are of IgG type, the immunocomplex is captured by the pre-coated antibody at the test region, forming a coloured IgG line, indicating a S. typhi IgG positive test result. If the antibodies present in the specimen are of IgM type, the immunocomplex is captured on the membrane by the pre-coated anti-human IgM antibody, forming a coloured IgM line, indicating a S. typhi IgM positive test result.
Absence of any T lines (IgM and IgG) indicates a negative result. A coloured control line (C) should always appear in case of a positive or a negative result. Its absence indicates invalid test results.

Reagents:
The test contains mouse anti-human IgM, mouse anti-human IgG and Typhoid antigen. A goat antibody is employed in the control line system.

Materials Provided:
Individual test devices sealed in pouches
Buffer
Sample Droppers
Instructions for Use sheet

Materials not provided:
Timer, Specimen collection container, centrifuge

Precautions:
- Do not smoke, drink, or eat in areas where specimens or kits reagents are handled.
- Dispose of all specimens and materials used to perform the test as biohazardous waste.
- This package insert must be read completely before performing the test.
- Bring all reagents to room temperature (15-30°C) before use.
- Do not interchange the buffer and test device of different lots.
- Do not use haemolysed blood specimen for testing.

Storage and Stability:
Store as packaged in the sealed pouch at room temperature or refrigerated (2-30°C). The kit components are stable until the expiry date printed on the sealed pouch. The test must remain in the sealed pouch until use. DO NOT FREEZE. Do not use beyond the expiry date.

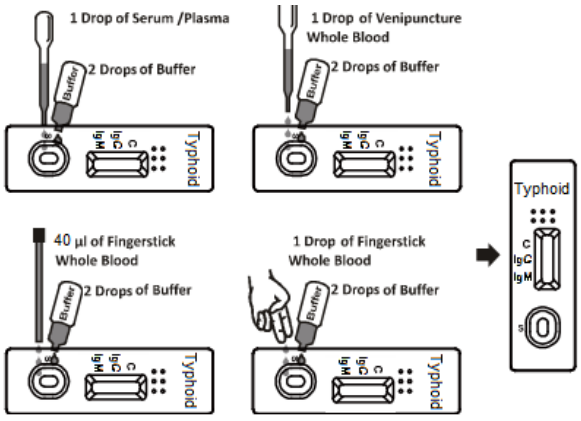
Specimen Collection and Preparation:
- Typhoid Rapid Test Device (Whole Blood/Serum/Plasma) is intended for use with human whole blood, serum or plasma specimens only.
- To collect Fingerstick Whole Blood specimens:
  - Wash the patient's hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
  - Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
  - Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
  - Add the Fingerstick Whole Blood sample to the device by using a capillary tube:
    - Touch the end of the capillary tube to the blood until filled to approximately 40µl. Avoid air bubbles.
    - Place the bulb onto the top end of the capillary tube, then squeeze the bulb to dispense the whole blood to the sample well of the test device.
- Add the Fingerstick Whole Blood specimen to the test by using hanging drops:
  - Position the patient's finger so that the drop of blood is just above the sample well of the test device.
  - Allow 1 hanging drop of Fingerstick Whole Blood to fall into the centre of the sample well on the test device, or move the patient's finger so that the hanging drop touches the centre of the sample well. Avoid touching the finger directly to the sample well.
- Separate the serum or plasma from blood as soon as possible to avoid haemolysis. Only clear, non-haemolysed specimen can be used.
- Testing should be performed immediately after the specimens have been collected. Do not leave the specimens at room temperature for prolonged periods. Serum and plasma specimens may be stored at 2-8°C for up to 3 days. For long term storage, specimens should be kept below 20°C. Whole blood collected by venepuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Do not freeze whole blood specimens. Whole blood collected by fingerstick should be tested immediately.
- Bring specimens to room temperature prior to testing. Frozen specimens must be completely thawed and mixed well prior to testing. Specimens should not be frozen and thawed repeatedly. If specimens are to be shipped they should be packed in compliance with federal regulations for transportation of etiologic agents.

Assay Procedure:

Bring tests, specimens, buffer and/or controls to room temperature (15-30°C) before use.
1. Bring the pouch to room temperature before opening it. Remove the test device from the sealed pouch and use it as soon as possible. Best results will be obtained if the assay is performed within one hour.
2. Place the device on a clean and level surface.
   For **Serum or Plasma** sample:
   - Hold the dropper vertically and transfer **1 drop of serum or plasma (approximately 40 µL)** to the sample well, then **add 2 drops of buffer** (approximately **80 µL**), and start the timer. See illustration below.

   For **Venipuncture Whole Blood** sample:
   - Hold the dropper vertically and transfer 1 **drop of whole blood** (approximately 40 µL) to the sample well, then **add 2 drops of buffer** (approximately **80 µL**), and start the timer. See illustration below.

   For **Fingerstick Whole Blood** sample:
   - Using a capillary tube: Fill the capillary tube **and transfer approximately 40 µL of fingerstick whole blood** sample to the sample well of test device, then **add 2 drops of buffer** (approximately 80 µL) and start the timer. See illustration below.
   - To use hanging drops: Allow 1 **hanging drop of fingerstick whole blood specimen** (approximately 40 µL) to fall into the sample well of test device, then **add 2 drops of buffer** (approximately 80 µL) and start the timer. See illustration below.
3. Wait for the coloured band(s) to appear. The result should be read at 15 minutes. Do not interpret the result after 20 minutes.



Interpretation of Results:
POSITIVE: * Two or three lines appear. One coloured line should always appear in the control line region (C) and another one or two apparent coloured line(s) should be in the test line region (s) (IgM and/or IgG).
IgM Positive: Along with line in Control region (C), a line appears in IgM region. It indicates a positive test result for antibodies to S. typhi (Isotype IgM)
IgG Positive: Along with line in Control region (C), a line appears in IgG region. It indicates a positive test result for antibodies to S. typhi (Isotype IgG)
*NOTE: The intensity of the colour in the test line regions (IgM and IgG) may vary depending on the concentration of Typhoid antibodies present in the specimen. Therefore, any evidence of colour in the test line region (IgM and/or IgG) should be considered positive.

NEGATIVE: One coloured line appears in the control line region (C). No line appears in the test line regions (IgM and IgG)

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test. If the problem persists, discontinue using the test kit immediately and contact your local distributor.

Quality Controls:
- An Internal procedural control is included in the test. A coloured band appearing in the control region (C) is considered a correct internal procedural control, confirming sufficient specimen volume and correct procedural technique.
- Good laboratory practice recommends the use of quality control materials to ensure proper kit performance.

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Limitations of the assay:

1. The assay procedure and the test result interpretation must be followed closely when performing the assay. Failure to follow the procedure may give inaccurate results.
2. The Typhoid Rapid Test Device is for qualitative detection of antibodies to S. typhi in human whole blood, serum or plasma. The intensity of the test band has no linear correlation with the antibody titer in the specimen.
3. A negative result only indicates absence of anti-S. typhi antibodies above detectable levels. A negative test result does not preclude the possibility of exposure to S. typhi as a negative result can occur if the quantity of anti-S typhi antibodies present in the specimen is below the detection limit of the assay, or the antibodies that are detected dare not present during the stage of disease in which a sample is collected.
4. Specimens containing unusually high titer of heterophile antibodies or rheumatoid factor may affect expected results.
5. The results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

Expected Values:

The Typhoid Rapid Test Device (Whole Blood/Serum/Plasma) has been compared with a leading commercial Typhoid ELISA test. The correlation between these two systems is over 99%.

Performance Characteristics:

Sensitivity and Specificity

A clinical evaluation was conducted comparing the results obtained using the Typhoid Rapid Test Device to Typhoid IgG/IgM ELISA testing. The study included 314 IgG specimens and 334 IgM specimens, and about the IgG specimen both assays identified 298 negative and 13 positive results, about the IgM specimen both assays identified 298 negative and 31 positive results.

IgM Results

Method		S. typhi EIA (IgM)		Total Results
Typhoid Rapid Test Device for IgM	Results	Positive	Negative	
	Positive	31	3	34
	Negative	2	298	300
Total Results		33	301	334

Sensitivity: 93.9% (95% CI*:79.8% - 99.2%)
Specificity: 99.0% (95% CI*:97.1% - 99.8%)
Accuracy: 98.5% (95% CI*:96.5% - 99.5%) *Confidence Intervals

IgG Results

Method		S. typhi EIA (IgM)		Total Results
Typhoid Rapid Test Device for IgG	Results	Positive	Negative	
	Positive	13	1	14
	Negative	2	298	300
Total Results		15	299	314

Sensitivity: 86.7% (95% CI*:59.5% - 89.3%)
Specificity: 99.6% (95% CI*:98.2% - 99.9%)
Accuracy: 99.0% (95% CI*:97.2% - 99.8%) *Confidence Intervals

Precision

Intra-Assay

Within-run precision has been determined by using 10 replicates of three specimens: a negative, a low positive, and a high positive. The negative, low positive and high positive values were correctly identified > 99% of the time.

Inter-Assay

Between-run precision has been determined by 10 independent assays on the same three specimens a negative, a low positive, and a high positive. Three different lots of the Typhoid Rapid Test Device (Whole Blood/Serum/Plasma) have been tested over a 3-day period using negative, low positive, and high positive specimens. The specimens were correctly identified > 99% of the time.

Cross reactivity

The Typhoid Rapid Test Device has been tested for HBsAg, HBsAb, HbeAg, HBeAb, HBcAb, HCV, HIV, Syphilis, H.pylori, CMV, Rubella and Toxo positive specimens. The results showed no cross-reactivity.

Interfering Substances

The following potentially interfering substances were added to Typhoid negative and positive specimens:

Acetaminophen	20mg/dl
Acetylsalicylic Acid	20mg/dl
Ascorbic Acid	2g/dl
Bilirubin	1g/dl
Caffeine	20mg/dl
Gentisic Acid	2g/dl
Albumin	10500mg/dl
Oxalic Acid	600mg/dl

None of the substances at the concentration tested interfered in the assay.

References:

1. Ivanoff B, Levine MM, Lambert PH (1994). Vaccination against typhoid fever: present status. Bull World Hlth Org 72: 957-71.
2. Gotuzzo E, Frisancho O, Sanchez J, Liendo G, Carillo C, Black RE, Morris JG. 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 I non-typhoid 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.

REF	Catalog number		Temperature limitation
	Consult instructions for use	LOT	Batch code
IVD	*In vitro* diagnostic medical device		Use by
	Manufacturer		Do not reuse

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