Salmonella Typhi/Paratyphi Antigen Rapid Test

(Feces)

REF

A rapid test for the qualitative detection of Salmonella Typhi and Paratyphi (type A, B and C) antigens in human fecal specimens.
For professional in vitro diagnostic use only.
Please read the package insert carefully before using.

【SPECIFICATION】
1 Test/Kit, 2 Tests/Kit, 5 Tests/Kit, 7 Tests/Kit, 10 Tests/Kit, 20 Tests/Kit, 25 Tests/Kit, 40 Tests/Kit

【INTENDED USE】
The iCARESalmonella Typhi/Paratyphi Antigen Rapid Test is a rapid, serological, lateral flow chromatographic immunoassay for the qualitative detection of *Salmonella Typhi (type A, B and C)* antigens in human fecal specimens to aid in the diagnosis of *S. Typhi* and/or *Paratyphi* bacterial infection. The test only provides preliminary analysis results but not critical diagnosis criteria. Any use or interpretation of the test must be analyzed and confirmed with alternative testing method(s) and clinical findings based on professional judgment of healthcare providers.

【SUMMARY】
Typhoid fever is a life-threatening illness caused by the bacterium Salmonella typhus, and was observed by Eberth (1880) in the mesenteric nodes and spleen of fatal cases of typhoid fever. It is common in developing countries where it affects about 12.5 million persons annually. The infection is acquired typically by ingestion. On reaching the gut, the bacilli attach themselves to the epithelial cells of the intestinal villi and penetrate the lamina and submucosa. They are then phagocytosed there by polymorphs and mesenteric lymph nodes, where they multiply and, via the thoracic duct, enter the blood stream. A transient bacteremia follows, during which the bacilli are seeded in the liver, gall bladder, spleen, bone marrow, lymph nodes, and kidneys, where further multiplication takes place. Towards the end of the incubation period, there occurs a massive bacteremia from these sites, heralding the onset of the clinical symptoms.

Serovar *Paratyphi A* is the second most prevalent cause of Typhoid. *Paratyphi* and *S. Typhi* cause a similar illness, with relapsing fever. The diagnosis of Typhoid and Paratyphoid consists of isolation of the bacilli and the demonstration of antibodies. The isolation of the bacilli is very time consuming and antibody detection is not very specific.

The iCARESalmonella Typhi/Paratyphi Antigen Rapid Test employs a combination of monoclonal antibody/colloidal gold dye conjugate and a polyclonal antibody to qualitatively detect *S. Typhi* and/or *Paratyphi* antigens in human fecal specimens

【TEST PRINCIPLE】

The iCARESalmonella Typhi/Paratyphi Antigen Rapid Test is a qualitative, lateral flow immunoassay for the detection of *S. Typhi* and *Paratyphi* (type A, B and C) antigens in human fecal specimens. The membrane is pre-coated with anti-salmonella antibodies on the test line region (T) of the strip. During testing, the tool specimen reacts with the particle coated with anti-Salmonella antibody. The mixture migrates upward on the membrane chromatographically by capillary action to react with anti-Salmonella antibodies on the membrane and generate a colored line on the test line region (T). The presence of this colored line in the test region indicates a positive result, while its absence indicates a negative result.

An internal quality control is included in the test, in the form of a colored line appearing in the control line region (C), indicating that the test is functional, and proper and sufficient volume of specimen has been applied to enable migration through the test and control line, regardless of whether there is a test line or not. If the control line (C) does not appear within the testing time, test result is invalid and the test should be repeated with a new test device.

【MATERIALS PROVIDED】
- Test device individually foil pouched with a desiccant
- Specimen collection tube(s) with extraction buffer
- Package insert

【MATERIALS REQUIRED BUT NOT PROVIDED】
- Timer

【WARNINGS AND PRECAUTIONS】

1. For *in vitro* diagnostic use only. Do not reuse the test.
2. Do not freeze the test kit or its components.
3. These instructions must be carefully read and strictly followed by a trained healthcare professional to achieve accurate results. All users should read the instructions before performing test.
4. The test is only for the detection of *S.Typhi* and/or *Paratyphi (type A, B and C)* antigens, not for any other viruses or pathogens.
5. Inadequate or inappropriate specimen collection, storage, and transportation are likely to result in false negative test results.
6. Do not use hemolyzed blood specimens for testing, do not scoop fecal specimen as this may lead to excess fecal specimen which may block the specimen well and yield an invalid test result.
7. Do not eat, drink or smoke in the area where handling specimens or performing the test.
8. Do not use the test kit beyond its expiration date.
9. Do not mix components from different kit lots.
10. Leave test device sealed in its foil pouch until just before use. Do not use the test device if the pouch is damaged or the seal is broken.
11. To avoid contamination or inaccurate test result, do not touch the reaction area of test device when performing the test.
12. Wear appropriate personal protection equipment and gloves when performing the test, collecting and handling patient specimens.
13. Dispose of all used test devices and potentially contaminated materials in a biohazard container as if they were infectious waste and dispose according to applicable local laws and regulations.

【STORAGE AND STABILITY】

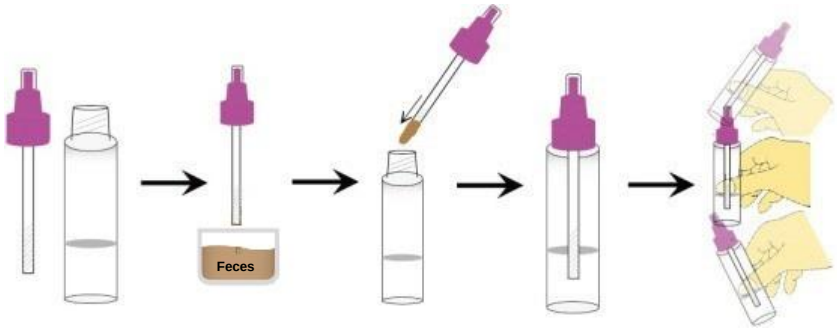
1. The test kit should be stored either at room temperature or refrigerated (2-30°C), away from direct sunlight. Do not freeze the kit or expose the kit to temperatures over 30°C.
2. The shelf life of the kit is as indicated on the outer package (24 months from date of manufacture).
3. This test kit is stable until the expiration date marked on the outer package and foil pouch. Ensure all test components are at room temperature (15-30°C) before use.
4. Perform the test immediately after taking out the test device from the foil pouch.

【SAMPLE COLLECTION AND PREPARATION】

Consider any materials of human origin as infectious and handle them using standard biosafety procedures. Follow standard laboratory procedures to collect specimens.

- **Feces**

1. Collect a random sample of feces in a clean, dry specimen collection container.
2. Label the specimen collection tube with the specimen's ID number. Unscrew the top of the specimen collection tube and then randomly stab the specimen collection stick into the fecal specimen in at least five different sites. Do not scoop the fecal specimen. Ensure that stool specimen is only in the grooves of the collection stick. Excess stool specimen may result in an invalid test result.
3. Screw on the collection stick in the tube and tighten securely to close the specimen collection tube.
4. Shake the specimen collection tube vigorously so as to extract the *S. Typhi/Paratyphi* antigens in the specimen.

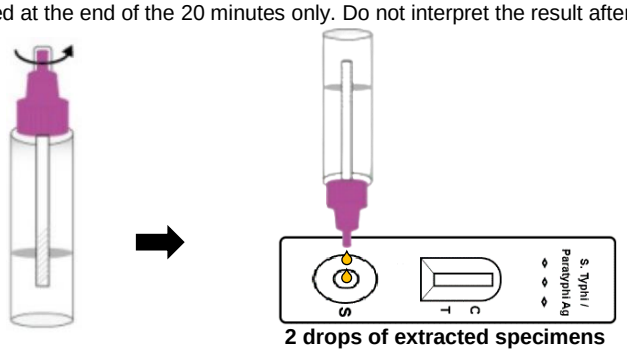


After above steps, the specimen is ready for testing, transportation or storage.

It is recommended to test the specimen immediately after extraction. If test is not performed immediately, the extracted specimen may be stored at 2-8°C for up to 3 days. For longer storage, the extracted specimen may be frozen at ≤-20°C. Avoid multiple freeze-thaw cycles (maximum 3 times).

【TEST PROCEDURES】

1. Before testing, open the package and equilibrate the test device, specimens and/or controls to room temperature(15-30°C). Once the specimen is thawed, mix well prior to performing the test.
2. Take out the test device from sealed foil pouch and place on a dry, clean and level surface. Be sure to label the device with specimen's ID number.
3. Add specimen to test device: Shake the specimen collection tube vigorously to ensure a homogenous liquid suspension. Hold the specimen collection tube vertically. Unscrew the cap. Add 2 drops (approximately 70-90 µL) of the extracted specimen into the specimen well(S) of the test device. Do not overload samples. See illustrations below.
4. Start the timer immediately.
5. Wait for the colored line to appear. Read test results at 15-20 minutes. Positive results may be visible in as short as 1 minute. Negative results must be confirmed at the end of the 20 minutes only. Do not interpret the result after 20 minutes.



2 drops of extracted specimens

【INTERPRETATION OF TEST RESULTS】

(Please refer to the illustrations below)

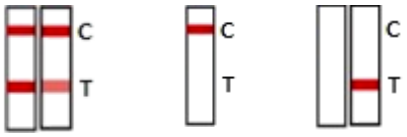
POSITIVE: Two lines appear. One colored line should be in the control line region (C) and another apparent colored line should be in the test line region (T).

NOTE: The intensity of the color in the test line region (T) will vary depending on the concentration of *S. Typhi/Paratyphi (type A, B and C)* antigens present in the specimen. Therefore, the presence of any test line (T), no matter how faint, within the designated observation time, indicates a positive result.

NEGATIVE: One colored line appears in the control line region (C). No line appears in the test line region (T).

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 device. If the problem persists, stop using the test kit immediately and contact your local distributor.

【QUALITY CONTROL】



Positive **Negative** **Invalid**

1. **Internal Control:** An internal quality control is included in the test, in the form of a colored line appearing in the control line region (C), indicating that the test is functional, and proper and sufficient volume of specimen has been applied to enable migration through the test and control line, regardless of whether there is a test line or not. If the control line (C) does not appear within the testing time, test result is invalid and the test should be repeated with a new test device.
2. **External Control:** Control standards are not supplied with this kit; however, it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance.

【LIMITATIONS】

1. The test is only used for the qualitative detection of *S.Typhi* and/or Paratyphi antigens in human fecal specimens by healthcare professionals. The intensity of the test line does not have a linear correlation with the antigen titers in the specimen.
2. The test does not indicate the titer of *S.Typhi* and/or *Paratyphi* antigens in the specimen, and should not be used as the sole criteria for the diagnosis of infection with *S.Typhi* or *Paratyphi*.
3. A negative test result may occur if the quantity of *S.Typhi* and/or *Paratyphi* antigens in a specimen is below the detection limit of the test, or if the antigen that are detected are not present during the stage of disease in which a sample is collected.
4. A negative or non-reactive result indicates the *S.Typhi* and/or *Paratyphi* antigen is not present in the specimen. However, a negative or non-reactive result at any time does not preclude the possibility of exposure to or infection with *S.Typhi* or *Paratyphi*.
5. The test cannot confirm and determine the *Paratyphi* serotype(s) present in a specimen.
6. Infection may develop rapidly. If symptoms are suspicious or persist while test result from the iCARESalmonella Typhi/Paratyphi Antigen Rapid Test is negative or non-reactive, additional testing using alternative clinical method is recommended, such as PCR or Blood Culture.
7. Test results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

【PERFORMANCE CHARACTERISTICS】

1. Clinical Performance

The iCARESalmonella Typhi/Paratyphi Antigen Rapid Test has been evaluated with a reference commercial RT-PCR assay using clinical fecal samples obtained from symptomatic, culture positive patients (1st week), respectively. Test results are presented in the tables below.

1.1 Clinical performance compared to reference RT-PCR Assay: *S. Typhi*

iCARESalmonella Typhi/Paratyphi Antigen Rapid Test	RT-PCR		
	Positive	**Negative**	**Total**
Positive	100	1	101
Negative	2	199	201
Total	102	200	302

Sensitivity (Positive Percent Agreement): 98.03% = 100/102 (95% CI: 93.13%~99.46%)
Specificity (Negative Percent Agreement): 99.50% = 199/200 (95% CI: 97.22%~99.91%)
Accuracy (Overall Percent Agreement): 99.00% = (100+199)/302 (95% CI: 97.12%~99.66%)

1.2 Clinical performance compared to reference RT-PCR Assay: *Paratyphi*

iCARESalmonella Typhi/Paratyphi Antigen Rapid Test	RT-PCR		
	Positive	**Negative**	**Total**
Positive	49	1	50
Negative	1	219	220
Total	50	220	270

Sensitivity (Positive Percent Agreement): 98.00% = 49/50 (95% CI: 89.50%~99.65%)
Specificity (Negative Percent Agreement): 99.54% = 219/220 (95% CI: 97.47%~99.92%)
Accuracy (Overall Percent Agreement): 99.25% = (49+219)/270 (95% CI: 97.34%~99.80%)

2. Cross-Reactivity:

The cross reactivity of the iCARESalmonella Typhi/Paratyphi Antigen Rapid Test was evaluated by testing fecal specimens from patients with other gastrointestinal infectious diseases. Test results are presented in the table below.

Fecal Specimens	Sample Number	S.Typhi Antigen Reactivity	Paratyphi Antigen Reactivity

Typhoid fever	10	Positive	Negative
Paratyphoid	10	Negative	Positive
Rotavirus	15	Negative	Negative
Adenovirus	15	Negative	Negative
H. Pylori	15	Negative	Negative
Cholera (spiked)	5	Negative	Negative

【REFERENCES】

1. Ivanoff B. Typhoid fever, global situation and WHO recommendations. Southeast Asia J. Trop. Med. Public Health, 1995, 26: supp2 1-6.
2. Parry CM, Hien TT Dougan G et al., Typhoid fever, N. Eng. J. Med. 2002, 347:1770-82.
3. Ashish P. Maskey et al. Salmonella enterica Serovar Paratyphi A and S. enterica Serovar Typhi Cause Indistinguashable Clinical Syndromes in Kathmandu, Nepal. CID 2006:42 (1 May).
4. Fangtham, Dr. Monthida; Wilde, Dr. Henry; Emergence of Salmonella paratyphi A as a Major Cause of Enteric Fever: Need for Early Detection, Preventative Measures, and Effective Vaccines. Journal of Travel Medicine Vol15, Issue5, 2008 344-350.
5. Wu, Weiyuan et al. Genetic Diversity of Salmonella enteric Serovar Typhi and Paratyphi in Shenzhen, China from 2002 through 2007. BMC Microbiology 2010, 10:32.
6. Baker, Stephen; Favorov, Michael,' Dougan, Gordon. Searching for the elusive typhoid diagnostic. BMC Microbiology 2010, 10:45

【INDEX OF SYMBOLS】

	Consult instruction for use	IVD	For *in vitro* diagnostic use only	REF	Catalog number		Temperature limit
LOT	Lot number		Use by		Do not reuse		Contains sufficient for <X> tests
	Keep dry		Manufacturer		Date of manufacture		Keep away from sunlight
	Do not use if package is damaged						

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