Quality approved by SD BIOSENSOR / For *In vitro* diagnostic use only

STANDARD F

TB-Feron FIA (IFN-gamma)

REF F-TBF-01

STANDARD™ F TB-Feron FIA (IFN-gamma)

PLEASE READ INSTRUCTIONS CAREFULLY BEFORE YOU PERFORM THE TEST

STANDARD™

INTRODUCTION

Tuberculosis (TB) is an infectious disease, which is caused by infection with M. tuberculosis complex organisms. It spreads to new hosts through the air from patients who have respiratory tuberculosis disease. Individuals newly infected would get symptoms from tuberculosis within weeks to months. STANDARD F TB-Feron FIA (IFN-gamma) is a blood assay that can help diagnose human tuberculosis and developed based on IGRA (Interferon Gamma Releasing Assay) method. An IGRA may be used in place of a TST in all situations in which CDC recommends tuberculin skin testing as an aid in diagnosing M. tuberculosis infection. An IGRA is preferred for testing persons who have received BCG vaccine or are unlikely to return for TST reading.

INTENDED USE

STANDARD F TB-Feron FIA (IFN-gamma) is an *in vitro* diagnostic test using TB-specific recombinant protein Antigens (ESAT-6, CFP-10 and TB 7.7) to stimulate cells in heparinized whole blood. Detection of Interferon-gamma (IFN-γ) by fluorescence immunoassay (FIA) is used to identify in vitro responses to those recombinant TB Antigens that are associated with Mycobacterium tuberculosis infection. This test is intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations.

TEST PRINCIPLE

STANDARD F TB-Feron FIA (IFN-gamma) is based on immunofluorescence technology with STANDARD F Analyzer to measure the IFN-γ in samples. It is designed especially for assessment of cell mediated immunity by measurement IFN-γ after cultivating heparin treated whole blood with stimulating antigen. The IFN-γ is a cytokine which is used as a specific marker in cell-mediated immune response. When exogenous or endogenous antigens are added to the blood, antigen specific effector/memory T lymphocyte is rapidly re-stimulated to produce interferon gamma (IFN-γ). The basis of STANDARD F TB-Feron FIA (IFN-gamma) technology is the stimulation of effector T cells in whole blood with a specific antigen(s) or mitogen, and the subsequent simple quantification of the resulting interferon-gamma (IFNγ) in the plasma. STANDARD F TB-Feron FIA (IFN-gamma) uses specialized blood collection tubes, which are antigen-sensitized. Incubation of the blood occurs in the tubes for 16 to 24 hours, after which, plasma is harvested and tested for the presence of IFN-γ produced in response to the recombinant protein antigens. The test is performed in two stages. First, whole blood is collected into each of the blood collection tubes, which include a Nil tube, TB Antigen tube, and Mitogen tube. The Nil tube adjusts for background IFN-gamma level of sample. The TB Antigen tube contains TB-specific recombinant protein antigens (ESAT-6, CFP-10, and TB7.7) to assess IFN-gamma responses in T cells from individuals infected with M.tuberculosis, but generally not from uninfected or BCG vaccinated people without disease or risk for latent TB infection. And the Mitogen tube can be used with the test as a positive control. This tube may also serve as a control for correct blood handling and incubation. These three tubes should be incubated at 37°C as soon as possible, and within 16 hours of blood collection. Following 16 to 24 hours incubation period, the tubes are centrifuged to isolate the plasma. The plasma is mixed with the conjugate tablet so that IFN-γ in the specimen can interact with anti-IFN-γ conjugated with gold particles. When the mixture is loaded onto the sample port of the test panel, it migrates along the membrane of test panel by capillary action, and then IFN-γ is captured by anti-IFN-γ antibody coated test line. STANDARD F Analyzers can analyze the concentration of IFN-γ of the sample based on pre-programmed algorithms and display the test result on the screen.

[Kit contents]

① Test device ② Conjugate tablet ③ Instructions for use

[Materials required but not provided]

- Heparin blood collection tubes
- Calibrated micropipets (10µl to 1000µl) with disposable tips
- Incubator capable of maintaining temperature at 37±1°C/96.8~100.4°F
- Waste discard container with suitable fresh disinfectant
- Personal Protective Equipment(PPE)

KIT STORAGE AND STABILITY

[STNADARD F TB-Feron Tubes 100, 200]

1. Store TB-Feron Tubes 100, 200, 300 at 2~25°C.
2. This test kit is stable through the expiration date printed in the package and in the label of each tube.

[STANDARD F TB-Feron FIA (IFN-gamma)]

1. Store the kit at room temperature, 2-30°C / 36-86°F, out of direct sunlight. Kit materials are stable until the expiration date printed on the outer box. Do not freeze the kit.

WARNINGS AND PRECAUTIONS

1. Do not re-use the test kit.
2. Do not use the test kit if the pouch is damaged or the seal isb roken.
3. Do not smoke, drink or eat while handling specimen.
4. Use the STANDARD F TB-Feron FIA (IFN-gamma) at 15-32°C / 59-90°F and 10-90%RH.
5. Wear personal protective equipment, such as gloves and lab coats when handling kit reagents. Wash hands thoroughly when afterwards.
6. Clean up spills thoroughly using an appropriate disinfectant.
7. Handle all specimens as if they contain infectious agents.
8. Observe established precautions against microbiological hazards throughout testing procedures.
9. Dispose of all specimens and materials used to perform the test as bio-hazard waste. Laboratory chemical and bio-hazard wastes must be handled and discarded in accordance with all local, state, and national regulations.
10. Silica gel in foil pouch is to absorb moisture and keep humidity from affecting products. If the moisture indicating silica gel beads change from yellow to green, the test device in the pouch should be discarded.
11. Immediately use the test device after taking out of aluminum foil pouch.
12. As the detection reagent is a fluorescent compound, no visible results will form on the test device.
13. The bar code of the test device is used by analyzer to identify the type of test being run and to identify the individual test device so as to prevent to a second read of the test device by the same analyzer.
14. Once a test device has been successfully scanned by analyzer, do not attempt to scan the test device again in the same analyzer.
15. Improper specimen collection, handling or transport may yield inaccurate results.
16. Do not write on the bar code or damage the bar code of the test device.

SPECIMEN COLLECTION AND PREPARATION

(Blood incubation and harvesting)

1. STANDARD F TB-Feron FIA (IFN-gamma) should use the following tubes.
   1) Mitogen tubes (purple cap)
   2) TB Antigen tubes (red cap)
   3) Nil tubes (gray cap)
2. Take out the TB-Feron Tubes at room temperature (15-25°C/59-77°F) for 15~30 minutes before using, and inject the blood without cold air.
3. Collect blood from the patient and inject respectively 1ml into each TB-Feron Tube (Nil tube, TB Antigen tube, and Mitogen tube).
   1) Insert a needle into the tube for 2~3 seconds after the injection is completed in order to collect the correct volume.
   2) The black line on the side of the tube indicates 1.0ml.
   3) When using Butterfly needle, Purge tube must be used.
   4) If the tubes are not filled to the black line due to vacuum, open the cap and fill it up with additional blood up to the black line.
4. As soon as the tube is filled with blood, shake it 10 times gently or use a Roller-rocker to allow the entire surface of the tube to be immersed in blood so that it can mix well with the antigen on the tube wall.
   - DO NOT SHAKE THE TUBE EXCESSIVELY to prevent blood cells from breaking. Since it is an experiment that requires living lymphocytes, it should be mixed to the extent that cell damage does not occur. Also, Excessive shaking may cause gel disruption and could lead to inaccurate results.
5. Incubate the well-mixed blood tubes at 37°C for 16 to 24 hours. When incubating, the tubes should be inserted into a rack vertically.
   * When it is difficult to incubate right after blood collection, it should be stored at room temperature (15-25°C/59-77°F). The tubes must be incubated within 16 hours after collection.

NOTE

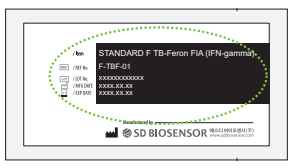
- If it is difficult to inject blood into each TB-Feron Tube, collect blood in the blood collection tube containing heparin. Collect a least 3.5ml of blood in a heparin tube and shake it gently up and down blood to dissolve the heparin. It prevents blood from clotting. After blood collection, it should be stored at room temperature (15-25°C/59-77°F). Within 16 hours after collection, dispense 1ml into each TB-Feron Tube with pipette, mix well and start incubating. When dispensing blood with pipette after opening the cap of the TB-Feron Tubes, sterile tips must be used so that blood could be dispensed in an aseptic.

6. After incubation of the tubes at 37°C, collect plasma by centrifuging tubes for 15 minutes at RCF 2200 to 2300g.
   - When collecting plasma, DO NOT pipetting or plasma mixing in the tube and spearing the gel with pipette tip.

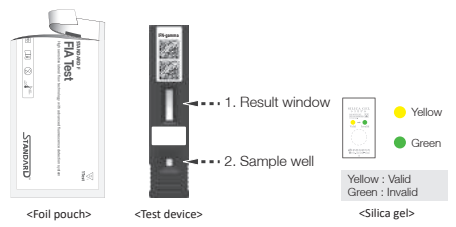
TEST PROCEDURE

[Preparation]

1. Allow test device and collected sample to room temperature (15-30°C/59-86°F) prior to testing.
2. Carefully read the instructions for using the STANDARD F TB-Feron FIA (IFN-gamma).
3. Check the expiry date at the back of the foil pouch. Use another lot, if expiry date has passed.



4. Open the foil pouch, and check the test device and the silica gel pack in the foil pouch.



<Foil pouch> <Test device> <Silica gel>

CAUTION

- Do not write on the bar code or damage the bar code of the test device.

[Test Procedure]

- **Using a STANDARD F2400 Analyzer**

1. Prepare a STANDARD F Analyzer and select the 'Standard Test' mode according to the analyzer's manual. Go to the 'Workplace' in the main screen. And select the 'Run Test'.
2. Input patient ID and/or operator ID on the analyzer.
3. Take the test device out of the foil pouch.
4. Insert the test device to the test slot of the analyzer. When inserting the test device to the analyzer, the analyzer will read the barcode data, and check the test device is valid.

5. Prepare a Nil sample according to the sample preparation method, and inject it into the sample spot of the test device.

Nil tube (Gray cap)	TB antigen tube (Red cap)	Mitogen tube (Purple cap)
		
This is used to adjust for background noise INF-γ as negative control.	This is used to assess INF-γ response to specific TB antigens.	This can be useful as positive control to check patient's immune status.

6. On the screen, you can see "Nill Tube" and insert the device for inspection.
7. Collect 100µl of plasma sample from Nil tube using a pipette, and mix the sample and a conjugate tablet.
8. Apply the sample mixture into the sample well of the test device and immediately press the **'TEST START'** button.

<F2400>

9. The analyzer will automatically display the test result within 15 minutes.

Repeat the following steps in the order Nil sample, TB Antigen sample and Mitogen sample.

INTERPRETATION OF TEST RESULT

1. Results of the STANDARD F should be judged according to the following criteria.

NOTE

- Diagnosing or excluding tuberculosis disease, and assessing the probability of LTBI, requires a combination of epidemiological, historical, medical, and diagnostic findings that should be taken into account when interpreting STANDARD F TB-Feron FIA (IFN-gamma) results.

Table 1. When Nil, TB Antigen and Mitogen tubes are used

Nil [IU/mL]	TB Antigen - Nil [IU/mL]	Mitogen - Nil [IU/mL][1]	STANDARD F Result	Report/Interpretation
≤ 8.0	< 0.35	≥ 0.5	Negative	M. tuberculosis infection NOT likely
	≥ 0.35 and < 25% of Nil value	≥ 0.5	Negative	
	≥ 0.35 and ≥ 25% of Nil value	Any	Positive[1]	M. tuberculosis infection likely
	< 0.35	< 0.5	Indeterminate	Results are indeterminate for TB Antigen responsiveness
	≥ 0.35 and < 25% of Nil value	< 0.5	Indeterminate	
> 8.0	Any	Any	Indeterminate	

[1] When M.tuberculosis infection is not suspected, initial positive results can be confirmed by re-testing the original plasma samples. If the repeated test results of the replicates are positive, they should be considerd as positive.

Table 2. When Only Nil and TB Antigen are used

Nil [IU/mL]	TB Antigen - Nil [IU/mL]	STANDARD F Result	Report/Interpretation
≤ 8.0	< 0.35	Negative	M. tuberculosis infection NOT likely
	≥ 0.35 and < 25% of Nil value	Negative	
	≥ 0.35 and ≥ 25% of Nil value	Positive	M. tuberculosis infection likely
> 8.0	Any	Indeterminate	Results are indeterminate for TB Antigen responsiveness

If you want to test using only Nil and TB Antigen samples, please contact SD Biosensor or distributors so that you can be provided technical assistance.

SD BIOSENSOR

QUALITY CONTROL

[STANDARD F Analyzers calibration check]

The calibration set test of STANDARD F Analyzers should be conducted according to the analyzer's manual.

When to use calibration set

1. Before using the analyzer for the first time
2. When you drop the analyzer
3. Whenever you do not agree with your result
4. When you want to check the performance of an analyzer and test device

How to use calibration set

Calibration set test is a required function that ensures optimal performance by checking the internal analyzer optics and functions.

1. Select the 'Calibration' menu.
2. The specific calibration set is included with the analyzer.
3. Insert the CAL-1 first, and then insert the CAL-2 for UV-LED testing and the CAL-3 for RGB-LED testing in order.

EXTERNAL QUALITY CONTROL

Quality control testing should be run to check the performance of STANDARD F TB-Feron FIA(IFN-gamma) and STANDARD F Analyzers. STANDARD F TB-Feron FIA(IFN-gamma) Control manufactured by SD BIOSENSOR should be used for quality control testing. Control test should be conducted in accordance with the instructions of STANDARD F TB-Feron FIA(IFN-gamma) Control.

Control test should be run:

- once for each new lot.
- once for each untrained operator.
- as required by test procedures in instructions for use of STANDARD F TB-Feron FIA(IFN-gamma) Control and in accordance with local, state and federal regulations or accreditation requirements.

LIMITATION OF TEST

1. The test procedure, precautions and interpretation of results sections for this test kit must be followed closely when testing.
2. Testing could be performed on patients with clinical symptoms on when exposure is suspected.
3. Unreliable or indeterminate results may occur due to:
   1) Excessive levels of circulating IFN-γ or presence of heterophile antibodies.
   2) The TB-Feron tubes must be incubated within 16 hours after blood collecting.
4. Test results must be considered with other clinical data available to the physician.
5. For more accuracy of immune status, additional follow-up testing using other laboratory methods is recommended

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Product Disclaimer

Whilst every precaution has been taken to ensure the diagnostic ability and accuracy of this product, the product is used outside of the control of the SD BIOSENSOR and distributor and the result may accordingly be affected by environmental factors and/or user error. A person who is the subject of the diagnosis should consult a doctor for further confirmation of the result.

Warning

The SD BIOSENSOR and distributors of this product shall not be liable for any losses, liability, claims, costs or damages whether direct or indirect of consequential arising out of or related to an incorrect diagnosis, whether positive or negative, in the use of this product.

CE IVD

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IVD *In vitro* Diagnostics
Consult Instructions for Use
Contains Sufficient for <n> Tests
Caution
To indicate the temperature limitations in which the transport package has to be kept and handled.
Note
Do not re-use.
Use by
LOT Batch code
Manufacturer
Date of manufacture
CE Fulfill the requirements of Directive 98/79/EC on *in vitro* diagnostic medical devices