# T-SPOT.®TB

## THE T-SPOT.*TB* BORDERLINE RESULT

The vast majority of T-SPOT.*TB* test results are either Positive or Negative; however, a small percentage of test results can be Borderline (equivocal), where the higher of (Panel A minus nil control) and (Panel B minus nil control) is 5, 6 or 7 spots.[1]

### Why does the T-SPOT.*TB* test have a Borderline category?

- Interferon-Gamma Release Assays (IGRAs) including the T-SPOT.*TB* test, are designed to measure an adaptive immune response to TB and are therefore subject to biologic variability[2]

- To address test variation and uncertainty of results near a dichotomous cut point, the T-SPOT.*TB* test has a Borderline category, which is intended to minimize false-positive and false-negative results around the test cutoff[2] (See Figure 1)

- King et al. reported that the use of the FDA-approved Borderline category for the T-SPOT.*TB* test resulted in substantially lower observed conversion and reversion rates than without its use, suggesting that the Borderline category is useful in decreasing the number of discrepant results[2]

- According to the Centers of Disease Control and Prevention (CDC), "Incorporation of a borderline category for the T-SPOT [.*TB*] test as approved by FDA increases test accuracy by classifying results near the cut point (at which small variations might affect the interpretation) as neither positive nor negative"[3]

### What should I do with a Borderline T-SPOT.*TB* test result?

- When a Borderline result is obtained, retesting by collecting another sample is recommended[1]
   - In a large multi-center study by King et al., the majority of Borderline results, 79.8%, resolved as clearly Positive or Negative upon retesting[2]
   - This study also demonstrated that 23% of Borderline results were Positive on retesting, concluding that the Borderline category is clinically relevant and useful in maintaining test sensitivity[2]

- Upon retesting, if the test result remains Borderline, other diagnostic tests and/or epidemiologic information should be used to help determine the TB infection status of the patient[1]

### How long should I wait to retest a patient after receiving an initial Borderline test result?

- There is no set guideline established for the time interval between an initial Borderline test result and a retest

- The ordering provider, having access to the patient's medical history, is best equipped to determine the appropriate time interval between tests
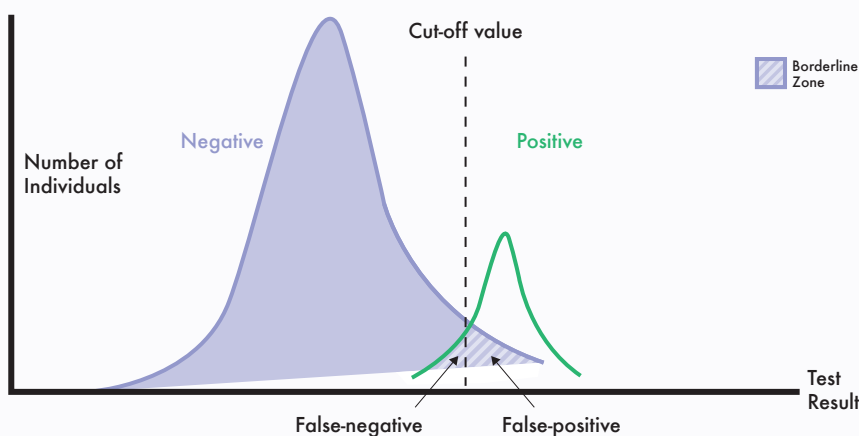


Most quantitative tests do not perfectly discriminate between subjects with and without a given disease.[4] To address test variation and uncertainty of results near a dichotomous cut point, the T-SPOT.*TB* test has a Borderline category, which is intended to minimize false-positive and false-negative results around the test cut-off.

Figure 1. Hypothetical graph of test results from true-positive and true-negative subjects

# THE T-SPOT.*TB* INVALID RESULT

A small percentage of all T-SPOT.*TB* results will not be considered clinically interpretable and will be reported as Invalid.

## What is an Invalid T-SPOT.*TB* result?

- A T-SPOT.*TB* result is considered Invalid if the positive and/or nil (negative) control does not perform as expected:[1]

    o The nil control is designed to control for non-specific T-cell reactivity.[1] A nil control spot count in excess of 10 spots should be considered as 'Invalid'

    o The positive control serves as an indicator of patient cell functionality.[2] If the positive control spot count is < 20 spots, the result should be considered Invalid, unless either Panel A or Panel B are Positive or Borderline

- Invalid results are uncommon (<1%[5]) and may be related to the immune status of the individual being tested. They may also be related to a number of technical factors, potentially resulting in high background, low mitogen, and high nil results, including:[1,2]

    o Inappropriate blood storage conditions

    o Delay in sample transport

    o Patient specific conditions

    o Laboratory error

## What should I do with a Invalid T-SPOT.*TB* test result?

- Invalid results are not clinically interpretable and retesting by collecting another sample is recommended[2]

- Upon retesting, if the test result remains Invalid, other diagnostic tests and/or epidemiologic information should be used to help determine the TB infection status of the patient[2]

## How does a T-SPOT.*TB* Invalid result differ from a T-SPOT.*TB* Borderline result?

- Invalid results cannot be interpreted due to the failure of the test's positive and/or nil (negative) control[1]

- A Borderline result is a valid test where the spot count is too close to the established test cut-off to classify the result as Positive or Negative

**REFERENCES:**

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5. Rego K, Pereira K, MacDougall J, Cruikshank W. Utility of the T-SPOT®.*TB* test's borderline category to increase test resolution for results around the cut-off point. Tuberculosis. 2018;108:178-185.doi:10.1016/j.tube.2017.12.005.

# T-SPOT®.*TB*

## Oxford Immunotec