October 21, 2013

URGENT FIELD SAFETY NOTICE

QuantiFERON®-TB Gold (QFT) Test, Potential Higher than Expected Rates of Indeterminate Results Due to Low Mitogen Tube Values

We have received a number of inquiries from users of the QuantiFERON®-TB Gold (QFT) test who observed an increase in the rate of indeterminate results. The increase in indeterminate rate appears to be related to the introduction of a new lot of phytohaemagglutinin-P (PHA), the stimulating agent used in the mitogen tube. There has been a shift in the distribution of mitogen tube values, such that they are slightly lower than those observed in previous mitogen tube lots. The number of indeterminate results reported does appear to vary from customer to customer; and some users have reported a significant increase (i.e. outside the range in the QuantiFERON®-TB Gold package insert). This can frequently be associated with less precise or, in some instances, incorrect blood handling technique. The current lots of mitogen tubes may be more sensitive to handling errors and require more precision in handling than prior lots. Technique may not be the only factor and we are in the process of approving a new lot of PHA raw material that should be less susceptible to technique and handling.

The mitogen tube lots produced with the potentially sensitive lot of PHA are as follows:

QFT Cat #	Description	GBO Cat #	Mitogen Tube Lot #s
0593-0201	QFT Mitogen tube	454075	A130105N, A1302017, A130300Y, A1304015, A130500Y, A130601B
0593-0501	QFT HA Mitogen tube	454415	A1302015, A130500X

These lots of Mitogen tubes were used in packaging the following QFT kit lots :

QFT Kit Cat #	Kit Lot #s
T0593-0201	059360571, 059360591, 059360601, 059360611, 059360621, 059360631
T0593-0501	059360581
0597-0101	059771501, 059771581, 059771641
0597-0201	059771481, 059771511, 059771541, 059771551, 059771571, 059771601, 059771611, 059771621, 059771631, 059771651, 059771681, 059771691
0597-0701	059771461, 059771491, 059771521, 059771531, 059771591, 059771661, 059771671, 059771701

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Please note that QFT test results are valid. The mitogen tube in the QFT assay serves as a control, providing both information about correct blood sample handling and potential information about the immune status of the patient. A variation in the numbers of indeterminate tests has no effect on the validity of QFT test results that are either positive or negative; these values should be considered accurate. An increase in the number of indeterminate results does not pose an immediate health risk but could cause inconvenience and a delay in final diagnosis.

Where an indeterminate result is obtained, we direct physicians to review those results in light of our package insert and the 2010 CDC Guidelines for Interferon Gamma Release Assays (IGRAs) for appropriate guidance:

> *If used, the Mitogen-stimulated plasma sample serves as an IFN-gamma positive control for each specimen tested. A low response to Mitogen (<0.5 IU/mL) indicates an Indeterminate result when a blood sample also has a negative response to the TB antigens. This pattern may occur with insufficient lymphocytes, reduced lymphocyte activity due to prolonged specimen transport or incorrect filling/mixing of the Mitogen tube, or inability of the patient's lymphocytes to generate interferon gamma (IFN-gamma).*

If technical issues are suspected with the collection or handling of blood samples, repeat the entire QFT test with new blood specimens. Indeterminate tests that result from low Mitogen values would not be expected to change on repeat unless there was an error with the ELISA testing. Indeterminate results should be reported as such. Physicians may choose to redraw a specimen or perform other procedures as appropriate. (QuantiFERON®-TB Gold Package Insert. Cellestis. Doc. No.05990301J July 2012)

CDC provides the following guidance for indeterminate results;

> *Repeating an IGRA or performing a TST might be useful when the initial IGRA result is indeterminate and a reason for testing persists. A second test also might be useful when assay measurements from the initial test are unusual, such as when the Mitogen value is lower than is expected for the population being tested (e.g. the mitogen response by QFT is <0.5 IU/mL). If an IGRA is to be repeated, a new blood sample should be used. In such situations, repeat testing with another blood sample usually provides interpretable results. (Updated guidelines for using interferon gamma release assays to detect Mycobacterium tuberculosis infection – United States, 2010. Centers for Disease Control and Prevention MMWR June 25, 2010; Vol. 59. No.RR-5)*

As with any diagnostic test for TB infection, QFT is an aid to assist clinicians in their diagnosis and should be used in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations.

Please distribute this notice to all personnel within your organization who need to be aware of the potential issue including other organizations which may have received these lots or may have received indeterminate results reported from the use of them. This notice should be considered until the current supply of mitogen tubes is exhausted and new product is received and being used. The expected timeframe for availability of new product is November, 2013.

Please note that the relevant National Competent Authorities have been notified of the FSCA.

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