Measuring the other side of immunity

Cellestis Incorporated
28358 Constellation Road
Unit 698
Valencia, CA 91355
USA

23 April 2013

Official response from Cellestis concerning the voluntary recall of QuantiFERON®-TB Gold blood collection tubes; Lot #A1210004

Dear Valued Customer;

On 11 April 2013, Cellestis officially notified our distributor Japan BCG Laboratory to issue a product recall of QuantiFERON-TB Gold (QFT) blood collection tubes in Japan. The product recall relates specifically to the following QuantiFERON-TB Gold blood collection tubes:

Product Number (GBO Cat #)	Product Description	Lot number
0591-0601 (454477)	QFT TB Gold NIL Tubes	A1210008
0592-0601 (454476)	QFT TB Gold TB Tubes	A1210004
0593-0601 (454477)	QFT Gold Mitogen Tubes	A1210006

The recall was issued as a precautionary measure in response to several product complaints received by Japan BCG Laboratory from customers who reported a higher than expected rate of QFT positive results. Cellestis and Japan BCG Laboratory immediately initiated an investigation into the situation. Testing performed confirmed that Lot #A1210004 demonstrated an increase in positive QFT responses among otherwise QFT negative samples. Our investigation identified that this abnormality was likely the result of the contamination of the QFT TB Antigen blood collection tube (Lot #A1210004) with a low level of endotoxin. Although the level of endotoxin detected in Lot #A1210004 was sufficiently low to pass our quality control release criteria, comparison with other non-affected QFT TB-antigen blood collection tube lots revealed that the endotoxin level was higher.

Most importantly, the nature of the contamination resulted in an increase in QFT positive responses only; **negative results generated using the affected tubes are valid and would be considered reliable**.

Cellestis has subsequently implemented corrective actions to prevent a repeat occurrence of this situation. These include reducing our Quality Control criteria for the lower acceptable limit of endotoxin in our blood collection tubes, and increasing the number of quality control samples tested. We believe that these actions will reduce the possibility of endotoxin contamination in all future lots of tubes.

If unexpected positive results were obtained using the affected TB antigen tube lot, physicians should question the QFT result in light of all clinical information and a decision to retest using a different lot of QFT blood collection tubes should be based on the following:

- Probability of true infection and risk of disease progression
- Whether the result from retesting will change the decision on the clinical management of the patient. (If no change in the clinical management of the patient is likely to occur, then retesting should be discouraged to avoid confusion associated with discordant results).
- Status of treatment for latent TB infection. (Particular care should be taken if retesting a patient already started on TB treatment. Treatment can result in lower interferon gamma responses and the impact of treatment is likely stronger with the duration of therapy. Hence, a negative QFT result after treatment has begun may result from treatment itself).

If unexpected *grey zone* results were obtained using the effected TB antigen tube lot, these results should be questioned in consideration of risk of infection and likely exposure to tuberculosis. The need for re-testing in this situation will be dependent on the population being tested and the risk of tuberculosis exposure.

In all TB testing situations, we kindly remind our customers to follow the guidance provided by the Japanese Society of Tuberculosis and that provided in the QFT package insert.

Unfortunately, this recall has resulted in the depletion of stocks of QFT blood collection tubes in Japan. Japan BCG Laboratory is currently unable to provide replacement tubes. Cellestis is making every effort to re-supply our customers and expects to have a new lot of QFT tubes available as early as next month. We thank you for your continued patience.

In the absence of QFT blood collection tubes, customers may have questions on how to proceed with TB testing.

When using QFT for surveillance or serial screening of health care workers, we would like to offer the following guidance. Testing for latent TB infection (LTBI) status can be delayed until a new lot of QFT blood collection tubes are available. Temporarily switching from QFT to another TB test could lead to changes in results due to the differences of each test's sensitivity and specificity. Even a small change in specificity or sensitivity could lead to unresolvable differences in test results making a clinical interpretation difficult. We refer to the advice provided in the U.S. CDC 2005 Guidelines for Preventing Transmission of Mycobacterium tuberculosis in Health-Care Settings, which do not recommend changing testing reagents. For example, when referring to tuberculin products, CDC states: "TB screening programs should use one antigen consistently and should realize that changes in products might make serial changes in TST results difficult to interpret" (CDC MMWR Dec 30, 2005, Vol. 54, No. RR-17, page 51). This recommendation is even more relevant to differences between the tuberculin skin test and the two commercially available IGRAs because of the large differences in sensitivity and specificity. For health care worker screening, alternatives such as symptom review, risk factor assessment and selective chest x-ray screening may be considered to accomplish active case finding among those individuals at low risk of infection.

For contact investigations and other at risk situations, we recommend that customers seek guidance from their local health authority.

Cellestis sincerely regrets any inconvenience caused by this recall. Please accept our apology and thank you for continued patronage.

Yours sincerely,

Mark Boyle
Vice President
TB Management Program Lead

Kevin Liddle
Director
Quality and Regulatory Affairs