



Technical Bulletin

Updated Interpretive Comments for QuantiFERON-TB Gold Plus

TO: Medical Staff and Clients

FROM: Dr. Wesley Kim, MD Dr. Chris Whelen, PhD Dr. Amy Woron, PhD Dr. Ana Ortega-Lopez, MD
Medical Director Scientific Affairs Advisor VP & Technical Director Medical Director
DLS and QMC West Microbiology & Molecular Microbiology & Molec. QMC PB, NH and Molokai

DATE: June 30, 2023

SUBJECT: Updated Interpretive Comments for QuantiFERON-TB Gold Plus

Beginning July 1, 2023 DLS will be updating its interpretive comments for QuantiFERON-TB Gold Plus results. The main change will be to discontinue the comment concerning high test background signal in results that are currently interpreted as positive or negative. Samples with significantly high background signal, resulting in an indeterminate result per the manufacturer, will still be called indeterminate.

High Background Signal Comment (to be discontinued)

When DLS began running this test many years ago, we observed background values in our population that were higher than reported in the manufacturer's literature. While significantly high background signal can interfere with interpretation and trigger an indeterminate result, the majority of the values we were seeing were NOT high enough to trigger this indeterminate result. However, a comment was still added to all results with increased background signal, in case additional evaluation was deemed clinically necessary. After monitoring and reviewing this data for several years now, it is clear that the normal variation in background signal within our population is greater than that reported in the manufacturer's study population, and does not necessarily represent a problem with the methodology. Importantly, this variation in background signal does not significantly impact the result of the test, positive or negative, and as such is no longer necessary from an interpretive standpoint. If the background signal is significantly elevated, this will still result in an indeterminate reading.

The following comments will still be used by DLS:

Low Mitogen comment

This comment is utilized to alert the clinician to the observation that the lymphocytes in the patient's sample are not being readily stimulated by mitogen. The lack of mitogen stimulation implies that the patient's lymphocytes may also not be stimulated appropriately by the TB-specific antigens used in the test method. This could result in lower than expected interferon results and an incorrect interpretation. This scenario can be seen in patients who are immunocompromised secondary to other disease states, or immunosuppressed due to pharmacotherapy. However in some cases, it is unclear as to the reason for the lack of lymphocyte stimulation. In these cases, repeat collection and retesting may be considered.

Equivocal result

Although the manufacturer has a finite cut off value for positive and negative interpretation, there is well documented uncertainty around the cut off (<https://dlslab.com/documents/bulletins/2022/tech-alert-false-pos-qft-6-2-2022.pdf>). We established a "gray zone" around the cutoff in response to this uncertainty. Any result that falls in this zone will be interpreted as equivocal, where essentially, we cannot determine with certainty, the true positive or negative status of that sample. It is important to understand that even outside this equivocal zone, all results should be interpreted and correlated with the clinical findings. If the result does not fit the clinical picture, consideration should be given to repeat the test or use a different methodology.

Indeterminate result

Indeterminate results are uncommon and occur when one or more test parameters have not been met, such as a significantly high background signal in the patient's sample. It could relate to the immune status of the individual or the testing process. In this case, the likelihood of *M. tuberculosis* infection cannot be determined, and additional or alternative testing may have to be considered. Please note that "Equivocal" is related to the uncertainty around the cut off and is different from "Indeterminate" which implies something is actually wrong with test parameters related to the patient's sample itself. However, in both circumstances, **repeat testing may help to resolve** the issue.

QuantiFERON®-TB Gold Plus (QFT®-Plus) ELISA Package Insert 04/2019

Please refer any questions to Jantzen Lim at 589-5265, Dr. Amy Woron at 441-5436, or DLS Client Services at 589-5101.

Diagnostic Laboratory Services Inc.

99-859 Iwaiwa Street – Aiea, HI 96701

(808) 589-5100 – www.dlslab.com