Interim Guidelines for Laboratory Verification of Performance of the BioFire® Global Fever Panel

TECHNICAL NOTE

Note

The ZeptoMetrix NATrol™ Control Material for the BioFire® Global Fever (GF) Panel is currently under development. This interim verification guidance utilizes the BIOFIRE® SHIELD™ Control Kit for the BioFire Global Fever Panel.

Purpose

The Clinical Laboratory Improvement Amendments (CLIA) establishes quality standards for all laboratory testing to ensure the accuracy and reliability of patient test results, regardless of where the test is performed. The CLIA regulations include a requirement for verifying the performance specifications of unmodified tests cleared or approved by the FDA.

This document provides an example of a verification procedure to assist your laboratory in developing a protocol for the verification of BioFire Global Fever (GF) Panel performance on BioFire® FilmArray® 2.0 and FilmArray® Torch Systems. The verification scheme described below utilizes the BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel. The verification scheme has been designed to provide positive and negative tests for each pathogen detected by the BioFire GF Panel and may be easily modified or expanded to meet specific criteria. Day-to-day variation is evaluated by testing each control type on two separate days. To evaluate operator-to-operator variability, multiple laboratory technicians may test the same controls.

Alternatively, under the direction of the Laboratory Director, patient samples or contrived samples using commercially available, quantified organism stocks may be used to evaluate the performance of the BioFire GF Panel. The general outline of the procedure described below may be followed; however, some modifications may be required. If using a commercially acquired organism stock BioFire Defense recommends contriving the sample at a concentration of 3-10× the limit of detection (LoD) as indicated in the *BioFire Global Fever Panel Instructions for Use*.

The Laboratory Director is ultimately responsible for ensuring that verification procedures meet the appropriate standards for CLIA and any other applicable laboratory accrediting agencies.

Refer to the *BioFire Global Fever Panel Instructions for Use* for detailed information regarding the BioFire Global Fever Panel.

Intended Use

The BioFire Global Fever (GF) Panel is a multiplexed nucleic acid test intended for use with BioFire FilmArray Systems for the simultaneous qualitative detection and identification of multiple viral, bacterial, and protozoan nucleic

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acids in EDTA whole blood collected from individuals with signs and/or symptoms of acute febrile illness, or recent acute febrile illness and known or suspected exposure to the following target pathogens: *Leptospira* spp., chikungunya virus, dengue virus (serotypes 1, 2, 3 and 4), and *Plasmodium* spp. (including species differentiation of *Plasmodium falciparum* and *Plasmodium vivax/ovale*).

The complete intended use statement and additional information about the use of the FilmArray System can be found in the *BioFire Global Fever Panel Instructions for Use*.

Performance Verification: Materials

Table 1 lists materials required to perform the described verification procedure.

Table 1. Materials for Verification Procedure

Material	Part Number
BioFire Global Fever Panel Kit (6 tests)	DFA2-ASY-0004
BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel (6 positive controls and 6 negative controls)	DFA2-ASY-0006

Performance Verification: Overview

This protocol is an example of a verification procedure to assist your laboratory in developing a protocol for the verification of BioFire GF Panel performance on BioFire FilmArray Systems.

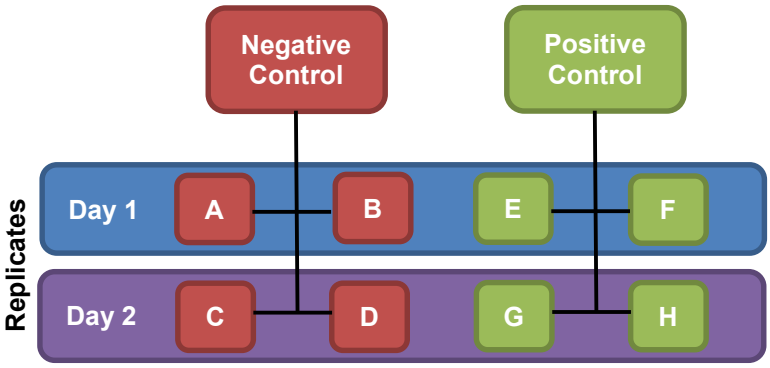
A BioFire FilmArray System is defined as all BioFire FilmArray Instruments or Modules that are connected to and controlled by a single computer system. If the Laboratory Director chooses not to perform the verification protocol on each individual instrument, it is advised that test replicates be evenly distributed among the instruments or modules.

The described protocol can be followed to test a total of eight controls, providing four positive control 'Pass' results and four negative control 'Pass' results on a single instrument. The estimated total time for completion is two days for a FilmArray 2.0 System configured with a single module. An overview of the testing scheme is shown in Figure 1. An overview of the expected results is shown in Table 2. The testing scheme may be modified to run more samples per day based on the number of instruments in the FilmArray® System and should be determined by individual laboratory requirements.

Table 2. Overview of Expected Results

Required Control Material	Number of Tests	Days of Testing	Expected Positive Control 'Pass' Results	Expected Negative Control 'Pass' Results
BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel	8	2	4	4

Figure 1. Single Module Verification Workflow



Protocol

The protocol uses the BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel. Positive controls included in the BIOFIRE SHIELD Control Kit contain freeze-dried synthetic DNA designed to be amplified by the BioFire Global Fever Panel. The amplified products produce melting temperatures distinct from amplified products from true pathogens, which mitigates the risk of potential contamination. The Positive and Negative External Control pouch protocols are required when performing testing with the BIOFIRE SHIELD Control Kit. Note that these protocols are only compatible with the BIOFIRE SHIELD Control Kit. Do not use these protocols to run other types of controls or patient specimens.

Day 1

1. Obtain two Positive External Control Injection Vials, two Negative External Control Injection Vials, and four BioFire Global Fever Panel pouches.

   NOTE: *The replicates for each day should be run by the same operator to evaluate run-to-run variation or different operators to evaluate operator-to-operator variation.*

   NOTE: *To minimize the risk of cross-contamination set up only one pouch at a time.*

2. Follow the instructions on the *BIOFIRE SHIELD Control Kit Quick Guide for the BioFire Global Fever Panel* to prepare and run two Negative External Controls on the BioFire Global Fever Panel (replicates A and B in Figure 1).
3. Follow the instructions on the *BIOFIRE SHIELD Control Kit Quick Guide for the BioFire Global Fever Panel* to prepare and run two Positive External Controls on the BioFire Global Fever Panel (replicates E and F in Figure 1).

Day 2

To evaluate day-to-day variation, test the remaining Negative External Controls (replicates C and D in Figure 1) and Positive External Controls (replicates G and H in Figure 1) by repeating Steps 1-3 of Day 1.

Result Interpretation

The GF Panel External Control Report will automatically be displayed upon completion of each run and can be printed or saved as a PDF file. The report will indicate whether the control 'Passed', or 'Failed'.

When running a Positive External Control, a 'Passed' result indicates that all assays for pathogens on the BioFire GF Panel returned positive results. When running a Negative External Control, a 'Passed' result indicates that no pathogen or control amplification was detected. If the result is 'Failed', the operator will be instructed to retest the External Control once, either immediately (Positive External Control) or after decontaminating the workspace (Negative External Control).

Refer to the *BIOFIRE SHIELD Control Kit Quick Guide for the BioFire Global Fever Panel* or the *BIOFIRE SHIELD Control Kit for the BioFire Global Fever Panel Instructions for Use* for additional information on how to interpret the report.

Expanding the Protocol

The protocol described above can be expanded to include more replicates per day, more replicates per operator, and/or more instruments per FilmArray System.

Verification of Replaced, Repaired or New Instruments

If it becomes necessary to verify the performance of a loaner or repaired instrument, the above protocol may serve as a guideline, but the Laboratory Director should determine the appropriate number of replicates to test. Two positive replicates and two negative replicates following the Day 1 testing plan may be sufficient.

Technical Support Contact Information

BioFire Defense is dedicated to providing the best customer support available. If you have any questions or concerns about this process, please contact the BioFire Technical Support team for assistance.

General Information
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