External Control Material Options for the BioFire® Respiratory Panel 2.1 (RP2.1), the BioFire® Respiratory Panel 2.1*plus* (RP2.1*plus*), and the BioFire® Respiratory Panel 2.1-EZ (RP2.1-EZ) (EUA)

Introduction

The Clinical Laboratory Improvement Amendments (CLIA), passed in 1988, establishes quality standards for all laboratory testing to ensure the accuracy and reliability of patient test results, regardless of where the test is performed. CLIA regulations require a laboratory to have quality control (QC) procedures to monitor the accuracy and precision of the complete testing process. The Individualized Quality Control Plan (IQCP) is an optional program that is now available, allowing laboratories the option to develop a quality control plan that is unique to their testing process.

BioFire RP2.1 Panels

The U.S FDA has revoked the Emergency Use Authorization of the BioFire RP2.1 Panel (EUA) concurrent with granting the De Novo authorization. U.S. customers may continue to use their existing inventory of the EUA product, under FDA De Novo authorization labeling, until product expiration. For OUS customers, the BioFire RP2.1 Panel (EUA) will continue to be made available for a limited time.

The BioFire RP2.1 EUA and the BioFire RP2.1 De Novo are identical; assays for all analytes and the reaction conditions of the test are unchanged. All controls listed in this technical note are appropriate for EUA or De Novo panel use.

Availability of the BioFire RP2.1 EUA (REF: 423738) and RP2.1 De Novo (REF: 423742) outside of the U.S. varies by region. Please contact your local bioMérieux distributor for more information.

The U.S. FDA Emergency Use Authorization for the BioFire RP2.1-EZ remains in effect and is only available to customers within the U.S.

Quality Control or IQCP for COVID-19 Testing for CAP-Accredited Laboratories

For Emergency Use Authorization (EUA) tests authorized for use by CLIA laboratories that meet requirements to perform moderate or high complexity testing, quality control must be performed following the manufacturer's instructions, at minimum. If the manufacturer's instructions are less stringent than CLIA regulatory requirements for Analytic Systems (CFR 493.1250), the laboratory must follow the regulatory requirements or develop an Individualized Quality Control Plan (IQCP). Laboratories have the flexibility to either:

- Perform QC (internal or external) according to CLIA regulatory requirements

OR

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• Customize their control procedures and implement an IQCP which could reduce the frequency of external QC. *Written QC plans must be approved by the laboratory director prior to implementation.*

Whichever option is selected, laboratories are not permitted to establish quality control procedures that are less stringent than those specified by the manufacturer of the test system.

Please refer to the Example Individualized Quality Control Plan (IQCP) Risk Analysis for the BioFire Respiratory Panels (BFR000-8660) as a starting point for developing your individualized risk assessment plan.

All laboratories performing non-waived testing must perform external QC with each new lot and shipment of reagents.

For Laboratories implementing the FDA De Novo authorized BioFire RP2.1 (REF: 423742) that previously implemented an individualized quality control plan (IQCP) for the non-waived RP2.1 EUA (REF: 423738) - the laboratory needs to determine if there are any additional risks that were not considered and update the existing risk assessment and quality control plan if appropriate. Reference CAP accreditation checklist requirement: MIC.65220.

Note: The BioFire RP2.1 EUA and the FDA De Novo authorized BioFire RP2.1 are identical; assays for all analytes and the reaction conditions of the test are unchanged. Part numbers, labeling, and instructions for use of the EUA and De Novo differ to distinguish each product.

Note: EUA guidelines are frequently revised. Confirm that current regulatory guidelines are being followed prior to establishing your IQCP.

Note: Laboratories not subject to US regulatory jurisdiction should consult appropriate regulatory bodies for further guidance.

Purpose

This document provides a listing of external control materials that have been tested at BioFire and are compatible with BioFire RP2.1, BioFire RP2.1*plus*, and BioFire RP2.1-EZ (EUA). A list of control materials that are not compatible with BioFire RP2.1, BioFire RP2.1*plus*, or BioFire RP2.1-EZ (EUA) is included in Table 5. The information in this document is meant to be a guideline and may not be inclusive.

These materials may be used for performance verification or quality control at the discretion of the laboratory director.

Note: For each sample, follow the appropriate Instructions for Use and/or Quick Guide for pouch preparation, pouch hydration, sample loading, and sample testing.

Note: BioFire RP2.1 , BioFire RP2.1*plus*, and BioFire RP2.1-EZ (EUA) are modifications of the FDA-cleared BioFire® FilmArray® Respiratory Panel 2 (RP2) and BioFire® FilmArray® Respiratory Panel 2 *plus* (RP2*plus*); i.e. modified by the addition of assays targeting the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19.

Note: The BioFire RP2.1*plus* is not FDA-cleared and is only available for sale to customers located outside of the US.

External Quality Control Materials

Table 1. Control Materials Compatible with BioFire RP2.1, BioFire RP2.1*plus*, and BioFire RP2.1-EZ

Vendor	Product Name	Part Number
Maine Molecular Quality Controls, Inc	BioFire RP2.1/RP2.1*plus* Control Panel M441	M441*
Microbiologics	Respiratory Control Panel (22 Targets)	8247¥
ZeptoMetrix Corporation	NATtrol™ Respiratory Panel 2.1 (RP2.1) Controls	NATRPC2.1-BIO

* For in vitro Diagnostic Use; an FDA Cleared Class II Assayed control
¥ For in vitro Diagnostic Use; an FDA Cleared Class I Unassayed control

Use of external quality control materials listed in Table 1 will generate detections for all analytes on the BioFire RP2.1, RP2.1*plus,* and RP2.1-EZ (EUA).

Table 2. Control Materials Compatible with BioFire RP2, BioFire RP2*plus* and all non-SARS-CoV -2 analytes on BioFire RP2.1, BioFire RP2.1*plus*, and BioFire RP2.1-EZ (EUA)

Vendor	Product Name	Part Number
Exact Diagnostics	RP Positive Run Control/ RP Negative Run Control	RPPOS§/ RPNEG
Maine Molecular Quality Controls, Inc	FilmArray® RP2/RP2plus Control Panel	M315*§
Microbiologics	Respiratory (21 Targets) Control Panel	8217¥
ZeptoMetrix Corporation	NATtrol™ Respiratory Panel 2 (RP2) Controls	NATRPC2-BIO

* For in vitro Diagnostic Use; an FDA Cleared Class II Assayed control
¥ For in vitro Diagnostic Use; an FDA Cleared Class I Unassayed control
§Control contains MERS-CoV2 synthetic/ recombinant material

Note: Control materials listed in Table 2 provide detections for all analytes on the BioFire RP2/RP2*plus* (all non-SARS-CoV-2 analytes on the BioFire RP2.1/RP2.1*plus*/RP2.1-EZ*),* but targets may be split between tubes allowing for positive and negative detections with each test run.

Materials in Table 2 provide detections for all analytes on the BioFire RP2/RP2*plus*, and therefore also provide detections for all non-SARS-CoV-2 analytes on the BioFire RP2.1/ RP2.1*plus/* BioFire RP2.1-EZ (EUA) when tested as directed by the manufacturer.

Table 3. Control Materials Compatible with SARS-CoV-2 Targets on BioFire RP2.1, BioFire RP2.1*plus*, and BioFire RP2.1-EZ (EUA)

Vendor	Product Name	Part Number	Target concentration for BioFire RP2.1/RP2.1*plus*/ RP2.1-EZ Testing*
AlphaTec/Microbix	REDx SARS-CoV02 Positive Control (liquid)	RED-19-01	No dilution required
ATCC	Heat-inactivated SARS-CoV-2	ATCC® VR-1986HK™	1:10,000
ATCC	Genomic RNA from Severe acute respiratory syndrome-related coronavirus 2	ATCC® VR-1986D	1:1,000
ATCC	Heat-killed SARS-CoV-2, strain 2019nCoV/USA-WA1/2020 at 20,000 copies/mL	ATCC® MP-32™	No dilution required
BEI	Genomic RNA from SARS-Related Coronavirus 2, Isolate USA-WA1/2020	NR-52285	1:10,000
LGC SeraCare	AccuPlex™ SARS-CoV-2 Reference Material Kit v2	0505-0133	No dilution required
LGC SeraCare	AccuPlex™ SARS-CoV-2 Reference Material Kit - Full Genome	0505-0159	No dilution required
Microbiologics	SARS-CoV-2 Process Control Pellet	HE0062S¥	Rehydrate as directed
Microbiologics	SARS-CoV-2 Process Control Swab	HE0063S¥	Rehydrate in water only
ThermoFisher	AcroMetrix SARS-CoV-2 Control	94517	No dilution required
ZeptoMetrix	NATtrol™ SARS-Related Coronavirus 2 (SARS-CoV-2) External Run Control	NATSARS(COV2)-ERC	No dilution required

* The indicated dilution ensures robust detection with various lots, concentrations, etc.
¥ For in vitro Diagnostic Use; an FDA Cleared Class I Unassayed control

Many control materials listed in Table 3 are provided at high concentrations. Testing a dilution of the control material will maximize the material, as well as reduce risk of environmental contamination. Consult the vendor for further instructions on diluting the material.

Table 4. Control Materials Partially Compatible with the SARS-CoV-2 Targets on BioFire RP2.1/RP2.1*plus*/ RP2.1-EZ (EUA)

Vendor	Product Name	Part Number	BioFire RP2.1 / RP2.1*plus*/RP2.1-EZ Panel Target	
			SARS-CoV-2-1 S (Spike)	SARS-CoV-2-2 M (Membrane)
ATCC	Quantitative Synthetic SARS-CoV-2 RNA: ORF, E, N	ATCC® VR-3276SD™	Not Detected	X

Vendor	Product Name	Part Number	BioFire RP2.1 / RP2.1*plus*/RP2.1-EZ Panel Target	
			SARS-CoV-2-1 S (Spike)	SARS-CoV-2-2 M (Membrane)
ATCC	Quantitative Synthetic SARS-CoV-2 RNA: Spike 3'	ATCC® VR-3278SD™	X	Not Detected
Exact Diagnostics	SARS-CoV-2 Standard	COV019	X	Not Detected
Microbiologics	SARS-CoV-2 Synthetic RNA (N/E/RdRp/S Gene Targets)	HE0061S	X	Not Detected
LGC SeraCare	AccuPlex™ SARS-CoV-2 Reference Material Kit	0505-0126	Not Detected	X*

* The M-gene is included in the "E region" of this product.

Controls from Table 4 only target one assay on the BioFire RP2.1/RP2.1*plus*/RP2.1-EZ (EUA). For QC purposes it may be necessary to demonstrate that both assays are detected; consult your laboratory director for further guidance.

Note: Pooling of multiple control materials has not been tested at BioFire and may lead to erroneous results.

Table 5. Control Materials Not Compatible with the SARS-CoV-2 Target on BioFire RP2.1/RP2.1*plus*/RP2.1-EZ (EUA)

Vendor	Product Name	Part Number
ATCC	Quantitative Synthetic SARS-CoV-2 RNA: Spike 5'	ATCC® VR-3277SD™
Microbiologics	SARS-CoV-2 Synthetic RNA (N Gene Targets)	HE0060S
ThermoFisher	AcroMetrix™ Coronavirus 2019 (COVID-19) RNA Control	954519
ZeptoMetrix	SARS-CoV-2 (recombinant) Stock	0831042
ZeptoMetrix	SARS-CoV-2 (E/ORF1ab recombinant) Stock	0831043

The external control materials in Table 5 are not compatible with the SARS-CoV-2 assay targets on the BioFire RP2.1/RP2.1*plus*/RP2.1-EZ (EUA) and should not be used for quality control purposes. Materials listed in Table 5 may be incompatible due to incompatible gene target regions or low concentration levels.

Quality Control Interpretations

BioFire RP2.1, BioFire RP2.1*plus*, and BioFire RP2.1-EZ (EUA) (all targets)

Note: The BioFire RP2.1 EUA and the FDA De Novo authorized BioFire RP2.1 are identical; assays for all analytes and the reaction conditions of the test are unchanged. Part number and labeling of the EUA and De Novo products differ to distinguish each product.

In order to report all analytes on the BioFire RP2.1/RP2.1*plus*/ RP2.1-EZ (EUA), follow one of the testing strategies below.

1. Use a control material listed in Table 1 in order to obtain all positive detections in a single test run.

2. Alternatively- use a combination of control materials listed in Table 2, 3 and 4. Control materials listed in Table 2 provide detections for the BioFire RP2/RP2*plus*/ RP2.1-EZ (all non-SARS-CoV-2 analytes on the BioFire RP2.1/RP2.1*plus*/ RP2.1-EZ) when tested as directed by the manufacturer. The SARS-CoV-2 detection will require running an additional test with a control material listed in Table 3 or 4.
   Many materials from Table 3 will require dilution prior testing.

Note: Table 4 control materials are only compatible with one of the two SARS-CoV-2 targets on the BioFire RP2.1/RP2.1*plus*/RP2.1-EZ. Consult your laboratory director for further guidance.

Note: Pooling of different control materials is not recommended and may lead to erroneous results.

SARS-CoV-2 only

For reporting only Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on the BioFire RP2.1 , BioFire RP2.1*plus*, or BioFire RP2.1-EZ follow one of the testing strategies below.

1. Test a control material listed in Table 1 in order to report SARS-CoV-2 detection.

2. Test a control material from Table 3. Many materials from Table 3 will require dilution prior testing; a suggested dilution is provided in the table.

3. Test one or more control materials from Table 4. Consult your laboratory director to determine if one or more of the materials listed in Table 4 is appropriate for your laboratory's quality control plan.

Technical Support Contact Information

BioFire 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.

BioFire Technical Support
Email: support@biofiredx.com
Phone: +1-801-736-6354, select Option 5