

BIOFIRE® Respiratory Panels (RP2.1, RP2.1*plus*, RP2.1-EZ, SPOTFIRE R Panel, SPOTFIRE R Panel Mini, SPOTFIRE R/ST and SPOTFIRE R/ST Panel Mini) SARS-CoV-2 Reactivity

Introduction

The BIOFIRE® Respiratory Panel 2.1 (RP2.1), BIOFIRE® Respiratory Panel 2.1 *plus* (RP2.1*plus*), BIOFIRE® Respiratory Panel 2.1-EZ (RP2.1-EZ), BIOFIRE® SPOTFIRE® Respiratory (R) Panel, BIOFIRE® SPOTFIRE® Respiratory (R) Panel Mini, BIOFIRE® SPOTFIRE® Respiratory/Sore Throat (R/ST) Panel and BIOFIRE® SPOTFIRE® Respiratory/Sore Throat (R/ST) Panel Mini are multiplexed nucleic acid tests intended for use with BIOFIRE® FILMARRAY® Systems or BIOFIRE® SPOTFIRE® System, respectively, for the simultaneous, qualitative detection and identification of multiple respiratory pathogen nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals with signs and symptoms or suspected of respiratory tract infections. This includes the detection of SARS-CoV-2 which is identified with two independent assays: SARSCoV2-1 which targets the S (Spike) gene and SARSCoV2-2 which targets the M (Membrane) gene. A positive result from either assay will result in a SARS-CoV-2 Detected result.

Note: BIOFIRE tests do not report cycle threshold (Ct) values and the BIOFIRE SARS-CoV-2 assays are not intended to monitor for novel mutations.

Note: Coronavirus SARS-CoV-2 is not reported on the SPOTFIRE R/ST Panel or SPOTFIRE R/ST Panel Mini when the Throat Swab protocol is selected in countries where the analyte has not been cleared/registered.

Global in silico SARS-CoV-2 Variant Analysis

bioMérieux has performed periodic updates of the in silico analysis provided in the BIOFIRE RP2.1, RP2.1*plus*, RP2.1-EZ, SPOTFIRE R Panel, SPOTFIRE R Panel Mini, SPOTFIRE R/ST Panel and SPOTFIRE R/ST Panel Mini Instructions for Use (IFU) based on available sequences in the GISAID database with the most recent performed on July 21, 2024 as shown in Table 1 below. BIOFIRE has also performed a one month in silico analysis of the most currently deposited GISAID sequences (June 22, 2024 to July 21, 2024) in Table 2 below.



Table 1. In silico Prediction of SARS-CoV-2 Detection by BIOFIRE SARSCoV2-1 and SARSCoV2-2 Assays (December, 2019 to July 21, 2024)

+/+ indicates detected by both assays with no impairment, +/- indicates detection by one assay with no impairment and potential for impaired detection by the other assay, -/- indicates potential for impaired detection by both assays

Predicted Assay Result # sequences		SARSCoV2-1 (S-gene)		# (%) sequences predicted to be detected with no limitations (one or both assays positive)
		+	-	
SARSCoV2-2 (M-gene)	+	13,715,943	246,207	14,017,073/14,017,990 (99.9935%)*
	-	54,923	917*	

*nine hundred and seventeen (208 unique) sequences have mismatches in the 3' half of primer(s) for both the SARSCoV2-1 and SARSCoV2-2 assays or mismatches in the 3' half of the SARSCoV2-1 assay and a 9 base pair deletion in the SARSCoV2-2 assay. The mismatches are predicted to impair detection at low analyte concentration.

Table 2. Single Month in silico Prediction of SARS-CoV-2 Detection by BIOFIRE SARSCoV2-1 and SARSCoV2-2 Assays (June 22, 2024 to July 21, 2024)

+/+ indicates detected by both assays with no impairment, +/- indicates detection by one assay with no impairment and potential for impaired detection by the other assay, -/- indicates potential for impaired detection by both assays

Predicted Assay Result # sequences		SARSCoV2-1 (S-gene)		# (%) sequences predicted to be detected with no limitations (one or both assays positive)
		+	-	
SARSCoV2-2 (M-gene)	+	15,957	20,867	36,880/36,901 (99.9431%)*
	-	56	21*	

*Twenty-one (two unique) sequences have mismatches in the 3' half of primer(s) for both the SARSCoV2-1 and SARSCoV2-2 assays. The mismatches are predicted to impair detection at low analyte concentration.

NOTE: The number of sequences analyzed and the number of sequences that are predicted to impair detection at low analyte concentrations in the June 22, 2024 to July 21, 2024 single month analysis are comparable to the November 22, 2023 to December 31, 2023 numbers, suggesting stable performance.

This analysis indicates that the BIOFIRE Respiratory family of products will be able to amplify and detect >99.9% of sequences retrieved on July 21, 2024. The analysis includes sequences from the lineages listed below:



A.23 lineage (Uganda)
 A.27 (France) / HMN.19B
 AV.1 / VUI-21MAY-01
 B.1 + 214insQAS
 B.1.1.7 / VOC-20DEC-01 / Alpha (United Kingdom)
 B.1.1.7 + S494P (United Kingdom)
 B.1.1.7 + Q677H (United Kingdom)
 B.1.1.28 and descendants
 B.1.1.28 + N501T + E484Q (Brazil)
 B.1.1.318 lineage / VUI-21FEB-04 variant (UK)
 B.1.1.529 lineage / Omicron
 B.1.214 lineage / Belgium variant (Belgium)
 B.1.214.2 (Belgium)
 B.1.243.1 / Arizona variant (United States)
 B.1.351 lineage / VOC-20DEC-02 variant / Beta (South Africa)

B.1.427/B.1.429 lineage / CAL.20C variant / Epsilon (United States)
 B.1.525 / VUI-21FEB-03 variant / Eta (UK)
 B.1.526 / Iota (United States)
 B.1.526.1 (United States)
 B.1.616 / Breton variant (France)
 B.1.617.1 / VUI-21APR-02 / Kappa (India)
 B.1.617.2 / VOC-21APR-02 / Delta (India)
 B.1.1.529 / BA.1 / Omicron
 B.1.617.3 / VUI-21APR-03 (India)
 C.36.3 / VUI-21MAY-02 (Thailand ex Egypt)
 C.37 / B.1.1.1 + L452Q + F490S / Lambda
 P.1 lineage / VOC-21JAN-02 variant / Gamma (Brazil)
 P.2 lineage / VUI-21JAN-01 variant / Zeta (Brazil)
 P.3 lineage / VUI-21MAR-02 / Theta (Philippines/Japan)

AY.1	AY.115	AY.123.1	AY.17
AY.10	AY.116	AY.124	AY.18
AY.100	AY.116.1	AY.124.1	AY.19
AY.101	AY.117	AY.124.1.1	AY.2
AY.102	AY.118	AY.125	AY.20
AY.103	AY.119	AY.125.1	AY.20.1
AY.103.1	AY.119.1	AY.126	AY.21
AY.103.2	AY.119.2	AY.127	AY.22
AY.104	AY.12	AY.127.1	AY.23
AY.105	AY.120	AY.127.2	AY.23.1
AY.106	AY.120.1	AY.127.3	AY.23.2
AY.107	AY.120.2	AY.128	AY.24
AY.108	AY.120.2.1	AY.129	AY.24.1
AY.109	AY.121	AY.13	AY.25
AY.11	AY.121.1	AY.130	AY.25.1
AY.110	AY.122	AY.131	AY.25.1.1
AY.111	AY.122.1	AY.132	AY.25.1.2
AY.112	AY.122.2	AY.133	AY.25.2
AY.112.1	AY.122.3	AY.134	AY.25.3
AY.112.2	AY.122.4	AY.14	AY.26
AY.112.3	AY.122.5	AY.15	AY.26.1
AY.113	AY.122.6	AY.16	AY.27
AY.114	AY.123	AY.16.1	AY.28

AY.29	AY.4.2.3	AY.50	AY.88
AY.29.1	AY.4.2.4	AY.51	AY.89
AY.29.2	AY.4.2.5	AY.52	AY.9
AY.3	AY.4.3	AY.53	AY.9.1
AY.3.1	AY.4.4	AY.54	AY.9.2
AY.3.2	AY.4.5	AY.55	AY.9.2.1
AY.3.3	AY.4.6	AY.56	AY.9.2.2
AY.3.4	AY.4.7	AY.57	AY.90
AY.30	AY.4.8	AY.58	AY.91
AY.31	AY.4.9	AY.59	AY.91.1
AY.32	AY.40	AY.6	AY.92
AY.33	AY.41	AY.60	AY.93
AY.33.1	AY.42	AY.61	AY.94
AY.33.2	AY.42.1	AY.62	AY.95
AY.34	AY.43	AY.63	AY.96
AY.34.1	AY.43.1	AY.64	AY.97
AY.34.1.1	AY.43.2	AY.65	AY.98
AY.34.2	AY.43.3	AY.66	AY.99
AY.35	AY.43.4	AY.67	B.1.351.2
AY.36	AY.43.5	AY.68	B.1.351.3
AY.36.1	AY.43.6	AY.69	B.1.620
AY.37	AY.43.7	AY.7	B.1.621
AY.38	AY.43.8	AY.7.1	B.1.621.1
AY.39	AY.43.9	AY.7.2	BA.1
AY.39.1	AY.44	AY.70	BA.1.1
AY.39.1.1	AY.45	AY.71	BA.1.1.1
AY.39.1.2	AY.46	AY.72	BA.1.1.10
AY.39.1.3	AY.46.1	AY.73	BA.1.1.11
AY.39.1.4	AY.46.2	AY.74	BA.1.1.12
AY.39.2	AY.46.3	AY.75	BA.1.1.13
AY.39.3	AY.46.4	AY.75.2	BA.1.1.14
AY.39.4	AY.46.5	AY.75.3	BA.1.1.15
AY.4	AY.46.6	AY.76	BA.1.1.16
AY.4.1	AY.46.6.1	AY.77	BA.1.1.17
AY.4.10	AY.47	AY.78	BA.1.1.18
AY.4.11	AY.48	AY.79	BA.1.1.2
AY.4.12	AY.49	AY.8	BA.1.1.3
AY.4.13	AY.5	AY.80	BA.1.1.4
AY.4.14	AY.5.1	AY.81	BA.1.1.5
AY.4.15	AY.5.2	AY.82	BA.1.1.6
AY.4.16	AY.5.3	AY.83	BA.1.1.7
AY.4.17	AY.5.4	AY.84	BA.1.1.8
AY.4.2	AY.5.5	AY.85	BA.1.1.9
AY.4.2.1	AY.5.6	AY.86	BA.1.10
AY.4.2.2	AY.5.7	AY.87	BA.1.12

BA.1.13	BA.2.14	BA.2.33	BA.2.71
BA.1.13.1	BA.2.15	BA.2.34	BA.2.72
BA.1.14	BA.2.16	BA.2.35	BA.2.73
BA.1.14.1	BA.2.17	BA.2.36	BA.2.74
BA.1.14.2	BA.2.18	BA.2.37	BA.2.75
BA.1.15	BA.2.19	BA.2.38	BA.2.75.1
BA.1.15.1	BA.2.2	BA.2.38.1	BA.2.75.10
BA.1.15.2	BA.2.2.1	BA.2.39	BA.2.75.2
BA.1.15.3	BA.2.20	BA.2.4	BA.2.75.3
BA.1.16	BA.2.21	BA.2.40	BA.2.75.4
BA.1.16.1	BA.2.22	BA.2.40.1	BA.2.75.5
BA.1.16.2	BA.2.23	BA.2.41	BA.2.75.6
BA.1.17	BA.2.23.1	BA.2.42	BA.2.75.7
BA.1.17.1	BA.2.24	BA.2.43	BA.2.75.9
BA.1.17.2	BA.2.25	BA.2.44	BA.2.76
BA.1.18	BA.2.25.1	BA.2.45	BA.2.77
BA.1.19	BA.2.26	BA.2.46	BA.2.78
BA.1.2	BA.2.27	BA.2.47	BA.2.79
BA.1.20	BA.2.28	BA.2.48	BA.2.79.1
BA.1.21	BA.2.29	BA.2.49	BA.2.8
BA.1.21.1	BA.2.3	BA.2.5	BA.2.80
BA.1.22	BA.2.3.1	BA.2.50	BA.2.81
BA.1.23	BA.2.3.10	BA.2.51	BA.2.82
BA.1.24	BA.2.3.11	BA.2.52	BA.2.85
BA.1.3	BA.2.3.12	BA.2.53	BA.2.86
BA.1.4	BA.2.3.13	BA.2.54	BA.2.86.1
BA.1.4.6	BA.2.3.14	BA.2.55	BA.2.9
BA.1.4.8	BA.2.3.15	BA.2.56	BA.2.9.1
BA.1.5	BA.2.3.16	BA.2.56.1	BA.2.9.2
BA.1.6	BA.2.3.17	BA.2.57	BA.2.9.3
BA.1.7	BA.2.3.18	BA.2.58	BA.2.9.4
BA.1.8	BA.2.3.19	BA.2.59	BA.2.9.5
BA.1.9	BA.2.3.2	BA.2.6	BA.2.9.7
BA.2	BA.2.3.20	BA.2.60	BA.3
BA.2.1	BA.2.3.3	BA.2.61	BA.3.1
BA.2.10	BA.2.3.4	BA.2.62	BA.4
BA.2.10.1	BA.2.3.5	BA.2.63	BA.4.1
BA.2.10.2	BA.2.3.6	BA.2.64	BA.4.1.1
BA.2.10.3	BA.2.3.7	BA.2.65	BA.4.1.10
BA.2.11	BA.2.3.8	BA.2.66	BA.4.1.2
BA.2.12	BA.2.3.9	BA.2.67	BA.4.1.3
BA.2.12.1	BA.2.30	BA.2.68	BA.4.1.4
BA.2.12.2	BA.2.31	BA.2.69	BA.4.1.9
BA.2.13	BA.2.31.1	BA.2.7	BA.4.2
BA.2.13.1	BA.2.32	BA.2.70	BA.4.3

BA.4.4	BA.5.2.2	BA.5.6.2	BF.20
BA.4.5	BA.5.2.20	BA.5.6.3	BF.21
BA.4.6	BA.5.2.21	BA.5.6.4	BF.22
BA.4.6.1	BA.5.2.22	BA.5.7	BF.23
BA.4.6.2	BA.5.2.23	BA.5.8	BF.24
BA.4.6.3	BA.5.2.24	BA.5.9	BF.25
BA.4.6.4	BA.5.2.25	BC.1	BF.26
BA.4.6.5	BA.5.2.26	BC.2	BF.27
BA.4.7	BA.5.2.27	BD.1	BF.28
BA.5	BA.5.2.28	BE.1	BF.29
BA.5.1	BA.5.2.29	BE.1.1	BF.3
BA.5.1.1	BA.5.2.3	BE.1.1.1	BF.30
BA.5.1.15	BA.5.2.30	BE.1.1.2	BF.31
BA.5.1.16	BA.5.2.31	BE.1.2.1	BF.31.1
BA.5.1.17	BA.5.2.32	BE.1.3	BF.32
BA.5.1.18	BA.5.2.33	BE.1.4	BF.34
BA.5.1.19	BA.5.2.34	BE.1.4.1	BF.4
BA.5.1.2	BA.5.2.35	BE.1.4.2	BF.5
BA.5.1.20	BA.5.2.36	BE.10	BF.5.1
BA.5.1.21	BA.5.2.37	BE.2	BF.5.2
BA.5.1.22	BA.5.2.38	BE.3	BF.6
BA.5.1.23	BA.5.2.39	BE.4	BF.7
BA.5.1.24	BA.5.2.4	BE.4.1	BF.7.1
BA.5.1.25	BA.5.2.42	BE.4.1.1	BF.7.10
BA.5.1.26	BA.5.2.43	BE.4.2	BF.7.11
BA.5.1.27	BA.5.2.44	BE.5	BF.7.12
BA.5.1.28	BA.5.2.45	BE.6	BF.7.13
BA.5.1.3	BA.5.2.46	BE.7	BF.7.13.2
BA.5.1.30	BA.5.2.47	BE.8	BF.7.14
BA.5.1.31	BA.5.2.48	BE.9	BF.7.15
BA.5.1.4	BA.5.2.49	BF.1	BF.7.2
BA.5.1.5	BA.5.2.5	BF.1.1	BF.7.3
BA.5.10	BA.5.2.6	BF.10	BF.7.4
BA.5.10.1	BA.5.2.7	BF.10.1	BF.7.4.1
BA.5.11	BA.5.2.8	BF.11	BF.7.4.2
BA.5.2	BA.5.2.9	BF.11.1	BF.7.5
BA.5.2.1	BA.5.3	BF.11.2	BF.7.5.1
BA.5.2.10	BA.5.3.1	BF.11.3	BF.7.6
BA.5.2.11	BA.5.3.2	BF.11.4	BF.7.7
BA.5.2.12	BA.5.3.4	BF.11.5	BF.7.8
BA.5.2.13	BA.5.3.5	BF.16	BF.7.9
BA.5.2.14	BA.5.5	BF.17	BF.8
BA.5.2.16	BA.5.5.2	BF.18	BF.9
BA.5.2.18	BA.5.5.3	BF.19	BG.1
BA.5.2.19	BA.5.6	BF.2	BG.2

BG.3	BQ.1.1.1	BQ.1.2	CA.5
BG.4	BQ.1.1.10	BQ.1.20	CA.7
BL.1	BQ.1.1.11	BQ.1.21	CB.1
BL.1.1	BQ.1.1.12	BQ.1.22	CC.1
BL.1.4	BQ.1.1.13	BQ.1.23	CD.1
BL.2	BQ.1.1.14	BQ.1.24	CD.2
BL.3	BQ.1.1.15	BQ.1.25	CE.1
BL.4	BQ.1.1.16	BQ.1.25.1	CG.1
BL.6	BQ.1.1.17	BQ.1.26	CH.1
BM.1	BQ.1.1.18	BQ.1.26.1	CH.1.1
BM.1.1	BQ.1.1.19	BQ.1.27	CH.1.1.1
BM.1.1.1	BQ.1.1.2	BQ.1.28	CH.1.1.2
BM.1.1.3	BQ.1.1.20	BQ.1.3	CH.1.1.3
BM.1.1.4	BQ.1.1.21	BQ.1.4	CH.1.1.4
BM.1.1.5	BQ.1.1.22	BQ.1.5	CH.1.1.5
BM.2	BQ.1.1.23	BQ.1.6	CH.3
BM.2.1	BQ.1.1.24	BQ.1.7	CJ.1
BM.4	BQ.1.1.25	BQ.1.8	CJ.1.1
BM.4.1	BQ.1.1.26	BQ.1.8.2	CK.1
BM.4.1.1	BQ.1.1.27	BQ.1.9	CK.1.1
BN.1	BQ.1.1.28	BQ.2	CK.1.2
BN.1.1	BQ.1.1.29	BR.1	CK.2
BN.1.1.1	BQ.1.1.3	BR.1.2	CK.2.1
BN.1.2	BQ.1.1.30	BR.2	CK.2.1.1
BN.1.2.1	BQ.1.1.31	BR.2.1	CK.3
BN.1.3	BQ.1.1.32	BR.3	CL.1
BN.1.3.1	BQ.1.1.34	BR.4	CM.1
BN.1.3.2	BQ.1.1.4	BS.1	CM.10
BN.1.3.3	BQ.1.1.5	BS.1.1	CM.11
BN.1.3.4	BQ.1.1.6	BT.1	CM.12
BN.1.4	BQ.1.1.7	BT.2	CM.2
BN.1.4.1	BQ.1.1.8	BU.1	CM.2.1
BN.1.5	BQ.1.1.9	BU.2	CM.3
BN.1.6	BQ.1.10	BU.3	CM.4
BN.1.7	BQ.1.10.1	BV.1	CM.4.1
BN.1.8	BQ.1.11	BV.2	CM.5
BN.1.9	BQ.1.12	BW.1	CM.5.1
BN.2	BQ.1.13	BW.1.1	CM.5.2
BN.2.1	BQ.1.13.1	BY.1	CM.6
BN.3	BQ.1.14	BY.1.1.1	CM.6.1
BN.3.1	BQ.1.15	C.36	CM.7
BN.5	BQ.1.16	CA.1	CM.8
BN.6	BQ.1.17	CA.2	CM.8.1
BQ.1	BQ.1.18	CA.3	CM.9
BQ.1.1	BQ.1.19	CA.3.1	CN.1



CN.2	DV.7.1.1	GE.1.2.1	JN.1.16
CP.1	DV.7.1.2	GE.1.3	JN.1.18
CP.1.1	DV.7.1.3	GS.1	JN.1.18.3
CP.1.2	DY.2	GS.4.1	JN.1.19
CP.1.3	EG.1	GW.5.1.1	JN.1.22
CP.2	EG.1.2	HF.1	JN.2
CP.3	EG.1.3	HF.1.1	JN.2.1
CP.4	EG.1.4	HK.1	JN.2.2
CP.5	EG.10.1	HK.11	JN.2.4
CP.6	EG.2	HK.2	JN.2.5
CQ.1	EG.5	HK.3	JN.3
CQ.1.1	EG.5.1	HK.3.1	JN.4
CQ.2	EG.5.1.1	HK.3.2	JN.6
CR.1	EG.5.1.2	HK.6	JN.10
CR.1.1	EG.5.1.3	HK.7	KP.1
CR.1.3	EG.5.1.4	HK.9	KP.1.1
CR.2	EG.5.1.5	HN.1	KP.2
CT.1	EG.5.1.6	HV.1	KP.2.2
CV.1	EG.5.1.7	JD.1.1	KP.2.3
CV.2	EG.5.1.8	JD.1.1.1	KP.2.6
CY.1	EG.5.1.9	JD.1.1.2	KP.3
CZ.2	EG.5.2	JD.1.1.3	KP.3.1
DA.1	EG.6.1	JF.1	KP.3.1.1
DB.1	EG.7	JG.1	KP.3.1.4
DB.2	FD.1.1	JG.2	KP.3.2.2
DC.1	FL.1.5	JG.3	KP.3.2.3
DE.2	FL.1.5.1	JM.1	KP.3.2.4
DF.1	FL.1.5.2	JM.2	KP.3.3
DF.1.1	FL.2	JN.1	KP.4.1
DG.1	FL.3	JN.1.1	LB.1
DJ.1	FL.3.1	JN.1.1.1	LB.1.3
DJ.1.1	FL.4	JN.1.1.2	P.1.1
DK.1	FL.9	JN.1.1.3	P.1.2
DL.1	FS.1	JN.1.2	P.1.4
DM.1	FU.1	JN.1.4	P.1.6
DN.1	FU.2	JN.1.4.1	P.1.7
DN.1.1	FU.3	JN.1.4.2	Q.1
DQ.1	FU.4	JN.1.5	Q.2
DR.1	FW.1.1	JN.1.7	Q.3
DS.1	FY.1.1	JN.1.7.1	Q.4
DT.1	FY.1.2	JN.1.7.2	Q.5
DU.1	FY.4.1	JN.1.8	Q.6
DV.6	GE.1	JN.1.8.1	Q.7
DV.7	GE.1.1	JN.1.9	Q.8
DV.7.1	GE.1.2	JN.1.11.1	R.1

XAA	XBB.1.16.17	XBB.1.8	XBJ
XAB	XBB.1.16.19	XBB.1.9	XBK
XAC	XBB.1.16.2	XBB.1.9.1	XBL
XAD	XBB.1.16.21	XBB.1.9.2	XBM
XAE	XBB.1.16.3	XBB.2	XD
XAF	XBB.1.16.4	XBB.2.2	XDK
XAG	XBB.1.16.5	XBB.2.3	XDK.1
XAH	XBB.1.16.6	XBB.2.3.1	XE
XAJ	XBB.1.16.9	XBB.2.3.11	XF
XAN	XBB.1.17.1	XBB.2.3.2	XG
XAW	XBB.1.2	XBB.3	XH
XAY	XBB.1.22.1	XBB.3.1	XJ
XAY.1	XBB.1.3	XBB.3.2	XK
XAY.1.1	XBB.1.4	XBB.4	XL
XAY.2	XBB.1.4.1	XBB.5	XM
XAY.3	XBB.1.5	XBB.6	XN
XAZ	XBB.1.5.11	XBB.6.1	XP
XBB	XBB.1.5.12	XBC	XQ
XBB.1	XBB.1.5.13	XBC.1	XR
XBB.1.1	XBB.1.5.18	XBC.1.1	XT
XBB.1.11.1	XBB.1.5.28	XBC.1.2.1	XU
XBB.1.16	XBB.1.5.59	XBC.2	XV
XBB.1.16.1	XBB.1.5.7	XBD	XW
XBB.1.16.10	XBB.1.5.71	XBE	XY
XBB.1.16.11	XBB.1.6	XBF	XZ
XBB.1.16.15	XBB.1.7	XBG	

The nine hundred and seventeen very rare sequences represent only two hundred and eight unique sequences that indicate a potential for impaired detection by both assays (indicated in Table 1). Ninety-three sequences have been evaluated using synthetic nucleic acid template to estimate the impact of the observed mismatches on amplification and detection by both assays. Table 3 below shows the observed effect of the mismatches found in the 93 unique sequences tested with synthetic templates. The BIOFIRE RP2.1, RP2.1*plus*, RP2.1-EZ, SPOTFIRE R Panel, SPOTFIRE R Panel Mini, SPOTFIRE R/ST Panel and SPOTFIRE R/ST Panel Mini SARS-CoV-2 test only requires one assay to be positive in order to report “SARS-CoV-2 Detected” therefore these nine hundred and seventeen very rare sequences are expected to be detected by the BIOFIRE Respiratory family of products but could demonstrate a reduction in analytical sensitivity near the limit of detection.

Table 3. Results of completed synthetic template testing of sequences with possible impairment in both SARS-CoV-2 assays.

Effect on pouch	Number of unique sequences tested	Total number of sequences
No effect	46 / 93	545 / 14,017,990
Minor (2-10 fold reduction)	38 / 93	172 / 14,017,990
Mild (10-100 fold reduction)	8 / 93	14 / 14,017,990
Moderate (≥ 100 fold reduction)	1 / 93	1 / 14,017,990

This analysis supports the conclusion that all of the 14,017,990 sequences evaluated as of July 21, 2024 can be amplified and detected by the BIOFIRE Respiratory family of tests, though a limitation or impairment on detection is predicted at low concentrations ($\leq 10x$ the limit of detection) for less than 0.007% of the sequences (917/14,017,990) with only nine unique sequences identified with detection likely affected greater than 10 fold.



Conclusions

1. The BIOFIRE Respiratory 2.1 Panels (RP2.1, RP2.1*plus* and RP2.1-EZ) and the SPOTFIRE Respiratory Panels (R Panel, R Panel Mini, R/ST Panel and R/ST Panel Mini) SARS-CoV-2 assays are not affected by any circulating SARS-CoV-2 lineages identified as of July 21, 2024 sequences.
2. Global in silico analysis (as of July 21, 2024) predicts that the BIOFIRE Respiratory Panels (RP2.1, RP2.1*plus*, RP2.1-EZ, SPOTFIRE R Panel, SPOTFIRE R Panel Mini, SPOTFIRE R/ST Panel and SPOTFIRE R/ST Panel Mini) SARS-CoV-2 assays will detect all sequences evaluated, including FLiRT variant sequences.
3. BIOFIRE tests do not report cycle threshold (Ct) values and the BIOFIRE Respiratory Panels SARS-CoV-2 assays are not intended to monitor for novel mutations.

Bioinformatics for the SARS-CoV-2 virus is expanding at a rapid rate since the emergence of the virus in human infection in late 2019. Thousands of viral whole genome sequences are being evaluated and submitted to public and private databases on a monthly basis. As the pandemic persists and viral genomes evolve, monitoring of assay reactivity with new sequences is important for understanding the state-of-the-art for performance of the SARS-CoV-2 assays in the BIOFIRE Respiratory family of products (RP2.1, RP2.1*plus*, RP2.1-EZ, SPOTFIRE R Panel, SPOTFIRE R Panel Mini, SPOTFIRE R/ST Panel and SPOTFIRE R/ST Panel Mini).

bioMérieux continues to monitor these new sequences and is performing regular in silico analyses of the BIOFIRE Respiratory Panels SARS-CoV-2 assays.

Note: The BIOFIRE RP2.1-EZ test is for in vitro diagnostic use under Emergency Use Authorization only.

BIOFIRE RP2.1-EZ has not been FDA cleared or approved but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA) for use by laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high, moderate, or waived complexity tests. This product is for use at the Point of Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation.

BIOFIRE RP2.1-EZ has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms.

The emergency use of BIOFIRE RP2.1-EZ is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated, or authorization is revoked sooner.

Technical Support Contact Information

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

Customer and Technical Support

Web: www.BioFireDX.com

Email: BioFireSupport@biomerieux.com

Phone: +1-800-735-6544, toll free

+1-801-736-6354,

All product names, trademarks and registered trademarks are property of their respective owners.

