

August 16th, 2023

Subject : Notification of internal test results for SARS-CoV-2 variants (Version 7.11)

Dear valued customers,

We, SD Biosensor, Inc., would like to inform you that STANDARD™ Q products for SARS-CoV-2 diagnostic are not affected by **“Alpha(B.1.1.7), Beta(B.1.351), Gamma(P.1), Delta(B.1.617.2), Kappa(B.1.617.1), Epsilon(B.1.429), Iota(B.1.526), Lambda(C.37), Zeta(P.2), Mu(B.1.621), Omicron(B.1.1.529, BA.1, BA.2, BA.3, BA.4.1, BA.5, BA.2.75, BF.7, BF.14, BJ.1, BQ.1.1, BA.4.6, BA.2.75.2, BA.2.12.1, BA.5.1, BA.5.2, BA.2.3.20, XBB, BA.2.10, BM.1.1.1, BS.1, BQ.1, BA.4.4, BA.5.2.6, BN.1, CH.1.1, CJ.1, XBF, XBB.1, XBB.1.5, XBC, XBB.1.16, XBB.1.9.1, XBB.1.16.1, XBB.1.9.2, XBB.2.3, EG.5.1) SARS-CoV-2 variants”**.

The list of applicable STANDARD™ Q products is as follows.

No.	Product Name	Reference No.
1	STANDARD™ Q COVID-19 Ag Test	Q-NCOV-01G
2	STANDARD™ Q COVID-19 Ag Home Test	Q-NCOV-03G
3	STANDARD™ Q COVID-19 Ag Nasal Test	Q-NCOV-04G
4	STANDARD™ Q COVID/Flu Ag Combo Test	Q-CVFL-01C
5	STANDARD™ Q COVID-19 Ag Saliva Test	Q-NCOV-02G
6	STANDARD™ i-Q COVID-19 Ag Home Test	EQ-NCOV-03G
7	STANDARD™ Q COVID-19 Ag Test 2.0	Q-NCOV-07G
8	STANDARD™ i-Q COVID/Flu Ag Combo Test	EQ-CVFL-01C

We verified this through internal test, and detailed information about it is below.

Mutations commonly found in the Alpha (B.1.1.7), Beta(B.1.351), Gamma(P.1), Delta(B.1.617.2), Kappa(B.1.617.1), Epsilon(B.1.429), Iota(B.1.526), Lambda(C.37), Zeta(P.2), Omicron(BA.1, BA.2, BA.3, BA.4.1, BA.5, BF.7, BJ.1) variants as well as the variants listed in part 1, analytical sensitivity, have been wet-lab tested using recombinant proteins, in the combinations indicated in the table in part 1 and no impact was observed in test performance. The mutations commonly found in the respective strains and in the Mu(B.1.621), Omicron(B.1.1.529, BA.2.75, BF.14, BQ.1.1, BA.4.6, BA.2.75.2, BA.2.12.1, BA.5.1, BA.5.2, BA.2.3.20, XBB, BA.2.10, BM.1.1.1, BS.1, BQ.1, BA.4.4, BA.5.2.6, BN.1, CH.1.1, CJ.1, XBF, XBB.1, XBB.1.5, XBC, XBB.1.16, XBB.1.9.1, XBB.1.16.1, XBB.1.9.2, XBB.2.3, EG.5.1) variant (*see the table in part 2, in-silico analysis*) have been analyzed in-silico, and no impact on performance is expected.

0. Monitoring information

0.1 Circulating mutations in nucleocapsid (N) protein

On a monthly basis, viral genomic sequences of the circulating strains will be gathered using GISAID. The most recent 2000 complete and high coverage entries will be analyzed at least monthly against the reference sequence (Wuhan-Hu-1/2019), and all non-synonymous mutations in the N protein will be identified. The percentage of single mutations and mutation combinations in the N protein will be analyzed. All mutations present in > 5% of the circulating isolates will be defined as “Relevant Mutations”.

0.2 Variants of Concern/Interest globally

Additionally, Variants of Concern (VoCs) and Variants of Interest (VoIs) by the WHO and the European Centre for Disease Prevention and Control (ECDC), as well as Variants Being Monitored (VBMs), VOIs, VOCs and Variants of High Consequence (VOHCs) by the US CDC will be monitored regularly. Isolates from all variants listed above will be monitored on GISAID. The most recent 2000 complete and high coverage entries per variant will be analyzed against the reference sequence (Wuhan-Hu-1/2019), and all non-synonymous mutations in the N protein will be identified. The percentage of single mutations and mutation combinations in the N protein will be analyzed. All mutations present in > 5% of the variant will be defined as “Relevant Mutations” as well.

1. Analytical sensitivity

1.1 Purpose of test

The purpose of this test is to verify that the sensitivity of STANDARD™ Q products is not affected by SARS-CoV-2 variants by using synthetic recombinant proteins.

1.2 Specimen of test

1) Specimen (Positive)

Since STANDARD™ Q products target nucleocapsid protein (hereafter, N protein), recombinant N protein of 34 variants were synthesized and used as positive specimen.

#	Pango lineage	GISAID ACCESSION ID. EPI_ISL	WHO label
1-1	B	402125	N/A
1-2	B.1.1.7	835226	Alpha
1-3	B.1.351	660190	Beta
1-4	P.1	792680	Gamma
1-5	B.1.617.1	1360306	Kappa
1-6	B.1.617.1	1789542	Kappa
1-7	B.1.617.1	1620161	Kappa
1-8	B.1.617.1	1545312	Kappa
1-9	B.1.617.1	1823120	Kappa
1-10	B.1.617.1	1904467	Kappa
1-11	B.1.617.1	1660436	Kappa
1-12	B.1.617.1	1913208	Kappa
1-13	B.1.617.1	1969991	Kappa
1-14	B.1.617.2	1970310	Delta
1-15	B.1.617.2	1660458	Delta
1-16	B.1.617.2	1807318	Delta
1-17	B.1.617.2	1913205	Delta
1-18	A.23.1	925892	N/A
1-19	B.1.429	1771435	Epsilon
1-20	B.1.526.2	1080752	N/A
1-21	B.1.526	1227165	Iota
1-22	B.1.617.3	1704494	N/A
1-23	C.36	1936140	N/A
1-24	C.37	1111296	Lambda
1-25	P.2	1182578	Zeta
1-26	B.1.616	1239370	N/A
1-27	C.1.2	3164100	N/A
1-28	BA.1	6640917	Omicron
1-29	BA.2 ¹⁾	7190366	Omicron
1-30	BA.4.1 ²⁾	12043292	Omicron
1-31	BA.5	11903045	Omicron
1-32	BA.5.3.1 ³⁾	12307612 ^a	Omicron
1-33	BF.7	12810243	Omicron
1-34	BJ.1	14167044	Omicron

1) In the case of BA.3 variant, wet-testing is omitted since the mutation sites of N protein are same as BA.2.

2) BA.4.1 (hCoV-19/South Africa/NCV1112/2022) was first designated as BA.4 on April 14, 2022, and re-designated on May 22, 2022 (from pango-designation issue #548).

3) BA.5.3.1 is rearranged from BA.5 (12307612). Its prevalence is 0.39% for last 6 months (2022.07.18-2023.01.12) from covspectrum (Cov spectrum.org).

* Previously circulating Variants of Concerns

** Previously circulating Variants of Interest

*** Formerly Monitored Variants

2) Specimen (Negative)

ID	PCR result
*Negative human swab	Negative

* Negative human swabs were collected from healthy donors and were confirmed to be negative by PCR (US FDA EUA approved, STANDARD M nCoV Real-Time Detection kit, CFX96).

3) Test strip

3 LOTs of test strips were used for the test.

1.3 Method of test

1) Each of the recombinant N proteins was diluted in successive concentrations.

2) The dilutions were spiked with a swab.

3) The spiked swab was tested in the same method as the IFU.

4) Dilutions of the recombinant N proteins were tested repeatedly 20 times for each LOT of test strips.

1.4 Result of test

The recombinant N protein of 34 variants showed a similar limit of detection to the Wuhan-Hu-1 recombinant N protein (#1-1) used as a positive control. Therefore, it was confirmed that the sensitivity of the STANDARD™ Q product was not affected by the 34 variants.

2. In-silico analysis

2.1 Purpose of test

The purpose of this test is to theoretically verify that STANDARD™ Q products are not affected by SARS-CoV-2 variants.

2.2 Method of test

- 1) Compare the region where the variant was mutated (hereinafter, mutation site) with the region that STANDARD™ Q targets to detect SARS-CoV-2 (hereinafter, epitope region).
- 2) If the mutation site corresponds to the epitope region, it is predicted that there is a possibility of affecting the STANDARD™ Q product, and the evaluation result is marked with 'P'.
- 3) If the mutation site does not correspond to the epitope region, it is predicted that there is no possibility of affecting the STANDARD™ Q product, and the evaluation result is marked with 'N'.

2.3 Result of test

As a result of in-silico analysis of 90 variants (Table 1), the mutation sites of 3 variants (#1-14: 1239370, #1-31: 1969991, #1-62: 14167044) corresponded to the epitope region. However, it was confirmed that #1-14, #1-31, #1-62 did not affect the sensitivity of SARS-CoV-2 products through the test for analytical sensitivity (#2-26, #2-13, #2-34). It is important to note that the N protein sequences evaluated in the in-silico analysis include mutations and patterns of mutations commonly present in relevant and newly emerging Omicron variants. Therefore, although not all omicron variants are listed in following table, relevant circulating Omicron variants are covered within the scope of this analysis.

#	Pango lineage	GISAID ACCESSION ID. EPI_ISL	Dominant Mutation site (amino acid number)	Result (P or N)
2-1	B	402125	N/A (as standard)	N/A
2-2	A.23.1	925892	202	N
2-3	AT.1	2385327	67, 203, 204	N
2-4	AT.1	1259283	203, 204	N
2-5	B.1.1.7	835226	3, 203, 204, 235	N
2-6	B.1.351	660190	205	N
2-7	B.1.427	1060793	205	N
2-8	B.1.429	1771435	205, 234	N
2-9	B.1.429	1194304	205	N
2-10	B.1.525	2432518	12, 205	N
2-11	B.1.526.1	2204920	205, 234	N
2-12	B.1.526.2	1080752	13, 202	N
2-13	B.1.526	1227165	199, 234	N
2-14	B.1.616	1239370	325	P
2-15	B.1.617.1	1360306	203, 377	N
2-16	B.1.617.2	1508996	63, 203, 215, 377	N
2-17	B.1.617.3	1704494	67, 203, 377	N
2-18	B.1.621	1582980	205	N
2-19	C.36	1936140	203, 204, 212	N
2-20	C.37	1111296	13, 203, 204, 214, 366	N
2-21	P.1	792680	80, 203, 204	N
2-22	P.2	1182578	119, 203, 204, 234	N
2-23	P.3	1213573	203, 204	N
2-24	B.1.617.1	1789542	203, 377, 385	N
2-25	B.1.617.1	1620161	3, 203, 377	N
2-26	B.1.617.1	1545312	203, 204	N
2-27	B.1.617.1	1823120	203, 236, 377	N
2-28	B.1.617.1	1904467	3, 13, 203, 243, 377	N
2-29	B.1.617.1	1660436	3, 63, 203, 377	N
2-30	B.1.617.1	1913208	30, 203, 377	N
2-31	B.1.617.1	1969991	203, 310, 377	P
2-32	B.1.617.2	1970310	63, 203, 377, 385	N
2-33	B.1.617.2	1660458	63, 203, 377	N
2-34	B.1.617.2	1807318	63, 203, 204, 205, 206, 207, 208, 377, 385	N
2-35	B.1.617.2	1913205	63, 203, 215, 377	N
2-36	AY.1	3244751	63, 203, 215, 377	N

2-37	AY.2	3123565	63,203,377	N
2-38	AY.3	3352221	63, 203, 215, 377	N
2-39	AY.3.1	2920875	63, 203, 215, 377	N
2-40	B.1.621	3477571	205	N
2-41	C.1.2	2695610	13, 204, 384, 203	N
2-42	B.1.1.529	6647959	13, 31(del), 32(del), 33(del), 203, 204	N
2-43	BA.1 (B.1.1.529.1)	6640917	13, 31(del), 32(del), 33(del), 203, 204	N
2-44	BA.2 (B.1.1.529.2)	7190366	13, 31(del), 32(del), 33(del), 203, 204, 413	N
2-45	BA.3 (B.1.1.529.3)	7526186	13, 31(del), 32(del), 33(del), 203, 204, 413	N
2-46	B.1.640.1	6700813	63, 205, 378	N
2-47	B.1.640.2	7181977	22, 205	N
2-48	XD* (Delta and BA.1)	9879437	63, 203, 215, 377	N
2-49	XE* (BA.1 and BA.2)	9177743	13, 31(del), 32(del), 33(del), 203, 204, 413	N
2-50	XF* (Delta and BA.1)	8894978	13, 31(del), 32(del), 33(del), 203, 204	N
2-51	BA.1.1	9754508	P13L, E31(del), R32(del), S33(del), R203K, G204R	N
2-52	BA.2.2	12417574	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-53	BA.2.12	10842022	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-54	BA.2.12.1	11490263	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-55	BA.4.1 ^{a)}	12043292	P13L, E31(del), R32(del), S33(del), P151S, R203K, G204R, S413R	N
2-56	BA.5	11903045	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-57	BA.5.3.1 ^{b)}	12307612**	P13L, E31(del), R32(del), S33(del), E136D, R203K, G204R, S413R	N
2-58	BA.2.75	13826295***	P13L E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-59	BA.2.75	13711333***	P13L, G204R, R203K, S413R	N
2-60	BF.7	12810243	P13L, G30(del), E31(del), R32(del), S33F, R203K, G204R, S413R	N
2-61	BF.14	13490388	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-62	BJ.1	14167044	P13L, E31(del), R32(del), S33(del), R203K, G204R, T282I, S413R	P
2-63	BQ.1.1	15155651	P13L, E31(del), R32(del), S33(del), E136D, R203K, G204R, S413R	N
2-64	BA.4.6	12475182	P13L, E31(del), R32(del), S33(del), P151S, R203K, G204R, S413R	N
2-65	BA.2.75.2	14290506	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-66	BA.2.12.1	9801346	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-67	BA.5.1	11941796	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-68	BA.5.2	11763535	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-69	BA.2.3.20	15031190	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-70	XBB	14891630	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-71	BA.2.10	8092783.2	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-72	BM.1.1.1	13949278	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-73	BS.1	14853841	P13L, E31(del), R32(del), S33(del), T135I, R203K, G204R	N

2-74	BQ.1	14294806	P13L, E31(del), R32(del), S33(del), E136D, R203K, G204R, S413R	N
2-75	BA.4.4	12012915	P13L, E31(del), R32(del), S33(del), P151S, R203K, G204R, S413R	N
2-76	BA.5.2.6	12845553	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-77	BN.1	15027018	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-78	CH.1.1	15316879	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-79	CJ.1	15157635	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-80	XBF	15414358	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-81	XBB.1	14917652	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-82	XBB.1.5	15687648	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-83	XBC	15057246	D63G, R203M, D377Y	N
2-84	XBB.1.16	16835403	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-85	XBB.1.9.1	17300463	P13L, E31(del), R32(del), S33(del), R203K, G204R, T362I, S413R	N
2-86	XBB.1.9.1 ^{C)}	16093023	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-87	XBB.1.16.1	17206435	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-88	XBB.1.9.2	16508753	P13L, E31(del), R32(del), S33(del), R203K, G204R, L219F (10.22%), S413R	N
2-89	XBB.2.3	16382405	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N
2-90	EG.5.1	17308785	P13L, E31(del), R32(del), S33(del), R203K, G204R, S413R	N

* XD, XE, XF are characterized by combining with the other two lineages (Delta + Omicron) by considering all mutation site including both spike protein and nucleocapsid protein. However, if only the sequence of nucleocapsid protein is considered, a single lineage can be characterized.

**Accession number of 12307612 is BA.5 sub lineage with very small portion (7.86 by GISAID, 2022.06.16.)

*** E31, R32 and S33 amino acid deletions of BA.2.75 occur in 74.15%, 74.15% and 72.79% respectively (Cov-spectrum.org, 2022.07.22).

a) BA.4.1 (hCoV-19/South Africa/NCV1112/2022) was first designated as BA.4 on April 14, 2022, and re-designated on May 22, 2022 (from pango-designation issue #548).

b) BA.5.3.1 is rearranged from BA.5 (12307612). Its prevalence is 0.39% for last 6 months (2022.07.18-2023.01.12) from covspectrum (Cov spectrum.org).

c) XBB.1.9.1 was not designated in Covspectrum and GISAID on 4th April (Version.7.10), so we searched for XBB.1.9.1 based on cov-lineages/pango-designation, issue #1819. But, issue #1819 was closed as not planed issue. The information of XBB.1.9.1 was corrected based on Covspectrum, GISAID and cov-lineages/pango-designation, issue #1704 (<https://github.com/cov-lineages/pango-designation/issues/1704>).

3. Final conclusion of the test

As a result of analytical sensitivity and In-silico analysis, it is verified that STANDARD™ Q products are not affected by “Alpha(B.1.1.7), Beta(B.1.351), Gamma(P.1), Delta(B.1.617.2), Kappa(B.1.617.1), Epsilon(B.1.429), Iota(B.1.526), Lambda(C.37), Zeta(P.2), Omicron(BA.1, BA.2, BA.3, BA.4.1, BA.5, BF.7, BJ.1) SARS-CoV-2 variants”. In addition, as a result of In-silico analysis, it is verified that STANDARD™ Q products are not affected by “Mu(B.1.621), Omicron(B.1.1.529, BA.2.75, BF.14, BQ.1.1, BA.4.6, BA.2.75.2, BA.2.12.1, BA.5.1, BA.5.2, BA.2.3.20, XBB, BA.2.10, BM.1.1.1, BS.1, BQ.1, BA.4.4, BA.5.2.6, BN.1, CH.1.1, CJ.1, XBF, XBB.1, XBB.1.5, XBC, XBB.1.16, XBB.1.9.1, XBB.1.16.1, XBB.1.9.2, XBB.2.3, EG.5.1) SARS-CoV-2 variants”.

In version.7.11, the sequence of EG.5.1 (17308785) was investigated, it has same mutations in the N protein as BA.2 (7190366). We have previously wet tested BA.2 (7190366) and no impact on the performance of the test was detected. Therefore, EG.5.1 (17308785) is expected to not have impact on the performance of the test.

4. Interpretation of test result

The result of this test should not be the sole basis for the diagnosis; confirmatory testing is required.

4.1 Negative test result

A negative test result means that it is unlikely that you have COVID-19. However, even if your test is negative, continue to observe all hygiene and safety measures. If you suspect that you have an infection, contact your doctor/primary care physician.

4.2 Positive test result

A positive test result means that it is very likely that you have COVID-19. Please contact your doctor/primary care physician or your local health authority immediately and adhere to the local guidelines regarding self-isolation. Your doctor may require you to undergo a PCR test to confirm the result.

We will continue our efforts to comply with high quality management standards and to maintain a consistent high quality management system to ensure customer's satisfaction and product safety. If you have any questions, please contact our sales representative.

Sincerely,
Jongkwan Ko
QMR
SD BIOSENSOR, Inc

