February 19, 2025

Visby Medical, Inc.
Jennifer Albrecht
Director of Regulatory Affairs
3010 North First Street
San Jose, California 95134

Re: K242526
Trade/Device Name: Visby Medical Respiratory Health Test
Regulation Number: 21 CFR 866.3981
Regulation Name: Device to detect and identify nucleic acid targets in respiratory specimens from microbial agents that cause the SARS-CoV-2 respiratory infection and other microbial agents when in a multi-target test
Regulatory Class: Class II
Product Code: QOF
Dated: August 23, 2024
Received: August 26, 2024

Dear Jennifer Albrecht:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Anna M. Mielech -S

Anna Mielech, Ph.D.
Deputy Branch Chief (Acting)
Viral Respiratory and HPV Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K242526

Device Name
Visby Medical Respiratory Health Test

Indications for Use *(Describe)*
The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, automated Reverse Transcription Polymerase Chain Reaction (RT-PCR) in vitro diagnostic test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A, and influenza B RNA in nasopharyngeal swab and anterior nasal swab specimens from individuals with signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2, influenza A, and influenza B can be similar.

The Visby Medical Respiratory Health Test is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B infection if used in conjunction with other clinical and epidemiological information, and laboratory findings. SARS-CoV-2, influenza A, and influenza B viral RNA are generally detectable in nasopharyngeal swab and anterior nasal swab specimens during the acute phase of infection. This test is not intended to detect influenza C virus infections.

Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other organisms not detected by the test. The agent(s) detected by the Visby Medical Respiratory Health Test may not be the definitive cause of disease. Negative results do not preclude SARS-CoV-2, influenza A, or influenza B infection. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

A. Submitter

Name:	Visby Medical, Inc.
Address:	3010 N. First Street San Jose, CA 95134
Phone:	1-833-468-4729
Contact:	Jennifer Albrecht
Date Prepared:	February 16, 2025

B. Device

Name of Device:	Visby Medical Respiratory Health Test
Common Name:	Same
Classification Name:	Multi-Target Respiratory Specimen Nucleic Acid Test Including Sars-Cov-2 And Other Microbial Agents
Regulatory Classification:	Class II
Regulation:	21 CFR 866.3981
Primary Product Code:	QOF

C. Predicate Device

DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct (K220963)

D. Device Description

The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, compact device containing a reverse transcription polymerase chain reaction (RT-PCR) based assay for qualitative detection of influenza A, influenza B, and/or SARS-CoV-2 viral RNA in upper respiratory tract specimens. The device automatically performs all steps required to complete lysis, reverse transcription (RT), PCR amplification, and detection.

Specimen collected using nasopharyngeal (NP) or anterior nasal (AN) swabs (without transport media) are placed in the Visby Medical Respiratory Health Buffer and then transferred into the sample port of the device using the provided fixed volume pipette. The sample enters a lysis module and rehydrates the RT enzyme and RT primers. The mixture then moves through a sample preparation module where viruses and human cells are simultaneously lysed, and RNA is reverse transcribed. The resulting fluid (containing cDNA) is then mixed with lyophilized PCR reagents containing the DNA polymerase enzyme and PCR primers. The PCR mixture (containing cDNA template and reagents) is then thermal cycled to amplify the targets, including human beta-2

microglobulin (B2M) RNA, which serves as a process control. After PCR, the biotinylated product is hybridized to covalently bound capture probes at specific locations along a flow channel. The flow channel is configured to facilitate an enzymatic reaction that uses streptavidin bound horseradish peroxidase (HRP) and a colorimetric substrate that forms a purple precipitate. The operator observes a color change at the specific locations indicating the presence of an amplified target. Test results can be expected in approximately 30 minutes: illumination of a “DONE” status light on the front of the device and a purple color in the “RESULTS VALID” spot, indicate a successful test. A purple spot adjacent to “Flu A”, “Flu B”, and/or “COVID-19” signifies the presence of, influenza A, influenza B, and/or SARS-CoV-2 viral RNA.

E. Intended Use

The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, automated Reverse Transcription Polymerase Chain Reaction (RT-PCR) in vitro diagnostic test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A, and influenza B RNA in nasopharyngeal swab and anterior nasal swab specimens from individuals with signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2, influenza A, and influenza B can be similar.

The Visby Medical Respiratory Health Test is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B infection if used in conjunction with other clinical and epidemiological information, and laboratory findings. SARS-CoV-2, influenza A, and influenza B viral RNA are generally detectable in nasopharyngeal swab and anterior nasal swab specimens during the acute phase of infection. This test is not intended to detect influenza C virus infections.

Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other organisms not detected by the test. The agent(s) detected by the Visby Medical Respiratory Health Test may not be the definitive cause of disease. Negative results do not preclude SARS-CoV-2, influenza A, or influenza B infection. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

F. Substantial Equivalence

The Visby Medical Respiratory Health test is substantially equivalent to DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct, K220963.

The following table compares the Visby Medical Respiratory Health Test to DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct and outlines the similarities and differences between the two tests.

Characteristic	Predicate Device: DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct (K220963)	Subject Device: Visby Medical Respiratory Health (K242526)
Regulation	21 CFR 866.3981	Same
Product Code	QOF	Same
Device Class	Class II	Same
Technology/ Detection	Real-time Reverse Transcription Polymerase Chain Reaction (RT-PCR) system, qualitative	Same

Characteristic	Predicate Device: DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct (K220963)	Subject Device: Visby Medical Respiratory Health (K242526)
Intended Use	The DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct is a real-time RT-PCR assay intended for use on the LIAISON MDX instrument for the in vitro qualitative detection and differentiation of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A virus and influenza B virus in nasopharyngeal swabs (NPS) from individuals with signs and symptoms of respiratory tract infection. The Simplexa COVID-19 & Flu A/B Direct assay is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A and influenza B infection. Negative results do not preclude SARS-CoV-2, influenza A or influenza B infection and should not be used as the sole basis for patient management decisions. Positive results do not rule out coinfections with other organisms. Results should be combined with clinical observations, patient history, and epidemiological information. The Simplexa COVID-19 & Flu A/B Direct assay is intended for use by qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures.	The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, automated Reverse Transcription Polymerase Chain Reaction (RT-PCR) in vitro diagnostic test intended for the simultaneous qualitative detection and differentiation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A, and influenza B RNA in nasopharyngeal swab and anterior nasal swab specimens from individuals with signs and symptoms of respiratory tract infection. Clinical signs and symptoms of respiratory tract infection due to SARS-CoV-2, influenza A, and influenza B can be similar. The Visby Medical Respiratory Health Test is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B infection if used in conjunction with other clinical and epidemiological information, and laboratory findings. SARS-CoV-2, influenza A, and influenza B viral RNA are generally detectable in nasopharyngeal swab and anterior nasal swab specimens during the acute phase of infection. This test is not intended to detect influenza C virus infections. Positive results are indicative of the presence of the identified virus, but do not rule out bacterial infection or co-infection with other organisms not detected by the test. The agent(s) detected by the Visby Medical Respiratory Health Test may not be the definitive cause of disease. Negative results do not preclude SARS-CoV-2, influenza A, or influenza B infection. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Characteristic	Predicate Device: DiaSorin Molecular Simplexa COVID-19 & Flu A/B Direct (K220963)	Subject Device: Visby Medical Respiratory Health (K242526)
Indication for Use	Symptomatic patients; Rx - For Prescription Use Only	Same
Assay Targets	SARS-CoV-2, influenza A virus and influenza B virus	Same
Sample to answer system	Automated	Same
Specimen Types	Nasopharyngeal Swab	Nasopharyngeal Swab; Anterior Nasal Swab
Sample Extraction	Self-contained and automated after specimen sample elution	Same
Assay Results	Qualitative	Same
Instrument System	LIAISON MDX	N/A, self-contained assay and instrument system
Assay Controls	Internal processing control (IPC), External controls available.	Same
Turn-around Time	Approximately 90 minutes to results.	Approximately 30 minutes to results.

G. Summary of Performance Data

Clinical Evaluation

Performance characteristics of the Visby Medical Respiratory Health Test were established in a clinical study that included testing of prospectively collected fresh specimens. The objective of this study was to establish the clinical performance of the Visby Medical Respiratory Health Test for the detection and differentiation of SARS-CoV-2, influenza A, and influenza B viral RNA in clinical specimens when in the intended use setting. This study was conducted at five CLIA Waived testing settings in the US. All study specimens were tested with the Visby Medical Respiratory Health Test by typical CLIA Waived operators according to the Quick Reference Guide (QRG) and Instructions for Use (IFU). Specimens were collected and tested between May 2022 and Feb 2024.

Prospective Sample Testing

Subjects presenting with signs and symptoms of a viral respiratory infection were prospectively enrolled at five CLIA Waived study sites in the US including urgent care and family care clinics. One NP or dual nostril AN swab specimen was placed directly in Visby Respiratory Health Buffer and tested with the Visby device. The samples were also tested with an FDA-cleared influenza molecular test and an FDA-EUA authorized SARS-CoV-2 RT-PCR test as a comparator.

A total of 1,592 subjects were enrolled in the study. Ninety one (91) study specimens were excluded from the performance analysis due to of lack of a valid comparator result

(n=53), lack of a valid Visby test result (n=21), the subject did not meet inclusion criteria (n=10), or for protocol deviations (n=6). One subject withdrew from the study. This left 1,501 subjects for performance analysis of the Visby Medical Respiratory Health Test. The distribution of subjects in the performance analysis by sex and age range is presented in Table 1.

Table 1. Demographic Summary – Enrollment from May 2022 to Feb 2024

Category		Number Evaluated (as %)
Sex	Male	573 (38.2%)
	Female	928 (61.8%)
Age	≤ 5 years	85 (5.7%)
	6 - 21 years	325 (21.7%)
	22 - 59 years	883 (58.8%)
	≥60 years	208 (13.9%)
Total		**1501**

A total of 1,575 Visby tests were performed on subjects that met the inclusion criteria, did not experience a protocol deviation, did not withdraw from the study. Of these 79 (5.0%) had an initial invalid test result of which 21 (1.3%) were invalid when retested. Of the 840 NP swab specimens tested, 30 (3.6%) had an initial invalid test result of which 5 (0.6%) were invalid when retested. Of the 735 AN swab specimens tested, 49 (6.7%) had an initial invalid test result of which 16 (2.2%) were invalid when retested.

The positive percentage agreement (PPA) and negative percentage agreement (NPA) of influenza A, influenza B, and SARS-CoV-2 are shown in Table 2 below.

Table 2. Prospective Fresh NP and AN Swab Specimen Performance – Enrollment from May 2022 to Feb 2024 (Visby vs. Comparator Assays)

	Specimen Type (NP/AN)	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Influenza A	NP	33	4[a]	791	1[c]	97.1% (85.1-99.5%)	99.5% (98.7-99.8%)
	AN	61	5[b]	604	2[d]	96.8% (89.1-99.1%)	99.2% (98.1-99.7%)
	NP+AN	94	9	1395	3	96.9% (91.3-98.9%)	99.4% (98.8-99.7%)
Influenza B	NP	15	2[e]	812	0	100% (79.6-100%)	99.8% (99.1-99.9%)
	AN	15	1[f]	656	0	100% (79.6-100%)	99.9% (99.1-100%)
	NP+AN	30	3	1468	0	100% (88.7-100%)	99.8% (99.4-99.9%)
SARS-CoV-2	NP	130	7[g]	687	5[i]	96.3% (91.6-98.4%)	99.0% (97.9-99.5%)
	AN	116	5[h]	549	2[j]	98.3% (94.0-99.5%)	99.1% (97.9-99.6%)
	NP+AN	246	12	1236	7	97.2% (94.4-98.7%)	99.0% (98.3-99.5%)

[a] 3 of 4 false positive NP specimens tested positive and one tested negative with an alternate molecular assay
[b] 5 of 5 false positive AN specimens tested positive with an alternate molecular assay
[c] 1 false negative NP specimen tested positive with an alternate molecular assay
[d] 2 false negative AN specimen tested positive with an alternate molecular assay
[e] 2 of 2 false positive NP specimens tested positive with an alternate molecular assay
[f] 1 of 1 false positive AN specimens tested positive with an alternate molecular assay
[g] 5 of 7 false positive NP specimens tested positive and 2 tested negative with an alternate molecular assay
[h] 4 of 5 false positive AN specimens tested positive, and 1 tested negative with an alternate molecular assay
[i] 3 of 5 false negative NP specimens tested negative and 2 tested positive with an alternate molecular assay
[j] 1 of 2 false negative AN specimen tested negative and 1 tested positive with an alternate molecular assay

Reproducibility

A study was performed to evaluate the reproducibility of the Visby Medical Respiratory Health Test when used by untrained users in CLIA Waived settings. The operators performing the testing were non-laboratorians representing healthcare professionals that may be encountered at such sites. The study evaluated a seven (7) member panel composed of NP swabs seeded with unspiked clinical matrix (negative) and NP swabs seeded with clinical matrix individually spiked with low (1x LoD) or moderate (3-5x LoD) concentrations of the three target viruses.

A total of six (6) study operators (2 operators at each site) tested the panel three (3) times each testing day, over six (6) non-consecutive days. Three reagent lots were used in the study. Each lot was used for two (2) days of testing. The composition of the panel

members along with a summary of results (correct count / total count) and percent agreement with the expected results for each panel member is presented in Table 3 below.

Table 3. Summary of Reproducibility Results with the Visby Medical Respiratory Health Test

Panel Member	Site 1	Site 2	Site 3	Overall Agreement	
	% Agreement (count)	% Agreement (count)	% Agreement (count)	% Agreement (count)	95% CI
Influenza A Moderate Positive	100.0% (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%
Influenza A Low Positive	94.4% (34/36)	100.0% (36/36) [a]	88.9% (32/36)	94.4% (102/108) [a]	88.4%-97.4%
Influenza B Moderate Positive	97.2% (35/36)	100.0% (36/36)	100.0% (36/36)	99.1% (107/108)	94.9%-99.8%
Influenza B Low Positive	97.2% (35/36)	100.0% (36/36)	91.7% (33/36)	96.3% (104/108)	90.9%-98.6%
SARS-CoV-2 Moderate Positive	100.0% (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%
SARS-CoV-2 Low Positive	97.2% (35/36)	100.0% (36/36)	88.9% (32/36)	95.4% (103/108)	89.6%-98.0%
Negative	100.0% (36/36)	100.0% (36/36)	100.0% (36/36)	100.0% (108/108)	96.6%-100.0%

[a] One sample was positive for influenza A, but unexpectedly positive for SARS-CoV-2

Analytical Evaluation

Limit of Detection

The limit of detection (LoD) is the lowest concentration of viral nucleic acid that is reliably detected by the Visby Respiratory Health Test. Influenza A, influenza B, and SARS-CoV-2 were tested in a range-finding study of 3-fold dilutions in negative clinical matrix, and the lowest concentration with 100% detection was established as the estimated LoD. The estimated LoD was confirmed by testing 20 replicates, where confirmation of the LoD was achieved when at least 19 of the 20 replicates returned a positive result for the virus tested. All viruses were tested individually in single-positive samples. The LoD of the Visby Medical Respiratory Health Test for influenza A, influenza B, and SARS-CoV-2 are summarized in Table 4 below.

Table 4. Limit of Detection (LoD) for the Visby Medical Respiratory Health Test Analytes

Virus	LoD Concentration
Influenza A/H1N1 2009, Brisbane/02/18	**106 copies/swab** 4.89 $TCID_{50}$/swab
Influenza A/H3N2, Kansas/14/2017	**125 copies/swab** 2.01 FFU[a]/swab
Influenza B/Washington/02/19	**728 copies/swab** 9.20 $TCID_{50}$/swab
Influenza B/Oklahoma/10/2018	**778 copies/swab** 88.37 $TCID_{50}$/swab
SARS-CoV-2 (USA-WA1/2020)	**100 copies/swab**

[a] FFU: Fluorescent Focus Units. Titer by Fluorescent Focus Assay in MDCK-SIAT1 Cells.

WHO 1st International Standard for SARS-CoV-2

The established analytical sensitivity or LoD of the Visby Medical Respiratory Health Test when tested with the World Health Organization (WHO) 1st International Standard for SARS-CoV-2 RNA (NIBSC code: 20/146) is 2.2 x 10^5 IU/mL of RNA in the sample tested.

Inclusivity

The ability of the Visby Medical Respiratory Health Test to detect 10 H1N1 (pandemic 2009) strains, 13 H3N2 strains, 12 influenza B strains (5 each of Victoria and Yamagata lineages and 2 additional strains), 6 SARS-CoV-2 strains, and 6 avian influenza A strains (RNA only, representing H5N1, H7N9, and H9N2). Each virus was individually spiked into negative clinical matrix at or near 3x LoD (unless otherwise noted) and tested in triplicate. All strains were successfully detected within 3x LoD, with the exception of the Omicron (BA.2.3) Isolate USA/MD-HP24556/2022 (detected at 6x LoD) and A/Egypt/321/2007 (H5N1).

Table 5. Analytical Reactivity (Inclusivity) of the Visby Respiratory Health Test

Virus	Strain	Tested Concentration
Influenza A H1N1 (pdm2009)	A/Brownsville/39H/2009	318 copies/swab
	A/Hong Kong/H090-761-V1(0)/2009	318 copies/swab
	A/Netherlands/2629/2009	318 copies/swab
	A/Massachusetts/15/2013	318 copies/swab
	A/Bangladesh/3002/2015	318 copies/swab
	A/Michigan/45/2015	318 copies/swab
	A/St. Petersburg/61/2015	318 copies/swab
	A/Hawaii/66/2019	318 copies/swab
	A/Wisconsin/588/2019	318 copies/swab
	A/Indiana/02/2020	318 copies/swab

Virus	Strain	Tested Concentration
Influenza A H3N2	A/Netherlands/22/2003	393 copies/swab
	A/New York/55/2004	393 copies/swab
	A/Brisbane/10/2007	393 copies/swab
	A/Uruguay/716/2007	393 copies/swab
	A/Hong Kong/H090-756-V1(0)/2009	393 copies/swab
	A/Perth/16/2009	393 copies/swab
	A/Victoria/361/2011	393 copies/swab
	A/Texas/50/2012	393 copies/swab
	A/Switzerland/9715293/2013	393 copies/swab
	A/Alaska/232/2015	393 copies/swab
	A/California/55/2020	393 copies/swab
	A/Hong Kong/2671/2019	393 copies/swab
	A/Wisconsin/04/2018	393 copies/swab
Avian Influenza A[1]	A/duck/Hunan/795/2002 (H5N1)	1500 pg/mL
	A/chicken/Yunnan/1251/2003 (H5N1)	1500 pg/mL
	A/Vietnam/1194/2004 (H5N1)	1500 pg/mL
	A/Egypt/321/2007 (H5N1)	Not Detected[2]
	A/Anhui/1/2013 (H7N9)	1500 pg/mL
	A/chicken/Hong Kong/G9/1997 (H9N2)	1500 pg/mL
Influenza B	B/Lee/1940	2334 copies/swab
	B/Maryland/1/1959	2334 copies/swab
Influenza B Victoria Lineage	B/Malaysia/2506/2004	2184 copies/swab
	B/St. Petersburg/14/2006	2184 copies/swab
	B/Brisbane/60/2008	2184 copies/swab
	B/Nevada/03/2011	2184 copies/swab
	B/New Jersey/1/2012	2184 copies/swab
Influenza B Yamagata Lineage	B/New York/1061/2004	2334 copies/swab
	B/Florida/4/2006	2334 copies/swab
	B/Texas/06/2011	2334 copies/swab
	B/Phuket/3073/2013	2334 copies/swab
	B/Guangdong-Liwan/1133/2014	2334 copies/swab
SARS-CoV-2	Alpha (B.1.1.7) England/204820464/2020	300 copies/swab
	Beta (B.1.351) South Africa/ KRISP-K005325/2020	100 copies/swab
	Gamma (P.1) Japan/TY7-503/2021	300 copies/swab
	Delta (B.1.617.2) USA/PHC658/2021	300 copies/swab
	B.1.1.529 BA.1 Isolate: USA/MD-HP20874/2021	300 copies/swab
	Omicron (BA.2.3) Isolate: USA/MD-HP24556/2022	600 copies/swab

[1] Purified RNA will be tested due to biosafety regulations.
[2] The Visby Medical Respiratory Health Test returned influenza A positive results in 2/3 replicates at 1500 pg/mL for the A/Egypt/321/2007 (H5N1) strain RNA.

In silico analysis of sequences from GISAID are conducted routinely to assess the ability of the Visby Medical Respiratory Health Test to detect the most recent COVID-19 strains. The results of these analyses of 16,852,539 total sequences, as of August 2024, show that the Visby Medical Respiratory Health Test will detect all variants in circulation.

Cross-Reactivity and Microbial Interference

The potential for cross-reactivity from microorganisms that may be found in an upper respiratory sample other than the target respiratory viruses (influenza A, influenza B, and SARS-CoV-2) on the performance of the Visby Medical Respiratory Health Test was evaluated. Forty-three (43) microorganisms were tested in triplicate at high concentrations (>10^5 units/mL for viruses and >10^6 units/mL for bacteria and yeast) in negative samples (negative clinical matrix). No cross-reactivity was observed with any of the organisms at the concentrations tested.

Microbial Interference was evaluated by testing the same 43 microorganisms in triplicate in negative clinical matrix in the presence of low concentrations of the target organisms (3X LoD for influenza A, influenza B, and SARS-CoV-2). No microbial interference was observed with any of the microorganisms at the concentrations tested.

Table 6. Microorganisms Evaluated for Cross-Reactivity and Microbial Interference on Visby Respiratory Health Test

Viruses (ATCC Number)	Bacteria and Yeast (ATCC Number)
Human Coronavirus 229E (VR-740)	*Bordetella parapertussis* (15311)
Human Coronavirus OC43 (VR-1558)	*Bordetella pertussis* (9340)
Human coronavirus HKU1 (VR-3262SD) *	*Candida albicans* (18804)
Human Coronavirus NL63 (VR-3263SD) *	*Chlamydia pneumoniae* (53592)
SARS-Coronavirus (VR-3280SD) *	*Corynebacterium xerosis* (373)
MERS-Coronavirus (VR-3248SD) *	*Escherichia coli* (25922)
Adenovirus strain 1, C1 Ad 71 (VR-1)	*Haemophilus influenzae* (49247)
Adenovirus strain 7 (VR-7)	*Lactobacillus brevis* (14869)
Cytomegalovirus (VR-977)	*Legionella pneumophila* (33152)
Epstein Barr virus (B95-8, ZeptoMetrix)	*Moraxella (Branhamella) catarrhalis* (25238)
Enterovirus 68 (NR-51430, BEI)	*Mycobacterium tuberculosis* (25177)
Human metapneumovirus (hMPV) (NR-22232, BEI)	*Mycoplasma genitalium* (49123)
Human parainfluenza virus 1 (NR-48681, BEI)	*Mycoplasma pneumoniae* (15531)
Human parainfluenza virus 2 (VR-92)	*Neisseria meningitidis* serogroup a (13077)
Human parainfluenza virus 3 (VR-93)	*Neisseria mucosa* (19695)
Human parainfluenza virus 4b (NR-3238, BEI)	*Pneumocystis jirovecii* also called Pneumocystis carinii Delanoe and Delanoe (PRA-159)
Measles (VR-24)	*Pseudomonas aeruginosa* (0801519, ZeptoMetrix)
Mumps (VR-106DQ) *	*Staphylococcus aureus* (12600)
Respiratory syncytial virus (Strain B) (VR-1400)	*Staphylococcus epidermidis* (12228)
Human rhinovirus 1A (strain 2060) (VR-1559)	*Streptococcus pneumoniae* (49619)
	Streptococcus pyogenes (19615)
	Streptococcus salivarius (9759)
	Pooled human nasal wash

* Purified RNA was tested for these viruses.

Competitive Interference

The potential for high concentrations of one target organism to interfere with detection of low concentrations of another target organism was evaluated. Influenza A, influenza B, and SARS-CoV-2 viruses were spiked into negative clinical matrix at varying concentrations and then tested in triplicate. Low concentrations were prepared at 3x LoD for the respective viruses, and high concentrations were prepared at ≥ 10^5 copies/swab. No competitive interference was observed for any of the three target viruses at the concentrations tested.

Table 7. Competitive Interference for each Target Virus

Viral Targets in Sample			Detection Rate (# Positive / # Tests)		
Influenza A	**Influenza B**	**SARS-CoV-2**	**Influenza A**	**Influenza B**	**SARS-CoV-2**
High	Low	Neg	3/3	3/3	0/3
High	Neg	Low	3/3	0/3	3/3
Low	High	Neg	3/3	3/3	0/3
Neg	High	Low	0/3	3/3	3/3
Low	Neg	High	3/3	0/3	3/3
Neg	Low	High	0/3	3/3	3/3

Endogenous/Exogenous Interfering Substances

Potentially interfering substances that may be found in a clinical nasal sample were evaluated to determine if they interfere with the accuracy of test results. The potential interfering substances were spiked in negative clinical matrix and tested in the presence and absence of low concentrations (3x LoD) of influenza A, influenza B, and SARS-CoV-2 viruses. All samples were tested in triplicate. As shown in Table 8 below, all of the negative samples returned valid results that were negative for influenza A, influenza B, and SARS-CoV-2. All the positive samples returned valid results that were positive for influenza A, influenza B, and SARS-CoV-2. None of the tested substances were found to interfere with test accuracy at the concentrations tested.

Table 8. Potentially Interfering Substances

Substance	Concentration	Negative Samples (# Negative / # Tests)	Low Positive Samples (3x LoD) (# Positive / # Tests)
Afrin	25% (v/v)	3/3	3/3
Biotin	3.5 µg/mL	3/3	3/3
Flonase	25% (v/v)	3/3	3/3
Fresh Whole Blood Pooled Human Donors	5% (v/v)	3/3	3/3
Human lotion	5% (w/v)	3/3	3/3
Hand sanitizer	5% (w/v)	3/3	3/3
Purified mucin protein	1% (w/v)	3/3	3/3
Method all purpose cleaner	5% (v/v)	3/3	3/3
Mupirocin	12 mg/mL	3/3	3/3
Nasacort	25% (v/v)	3/3	3/3
Nasal Saline Spray	25% (v/v)	3/3	3/3
NeoSynephrine Cold & Sinus Extra Strength Spray	25% (v/v)	3/3	3/3
Seventh generation disinfectant	5% (v/v)	3/3	3/3
Softsoap moisturizing hand soap	5% (w/v)	3/3	3/3
Tobramycin	2.43 mg/mL	3/3	3/3
Zanamivir (Relenza)	5 mg/mL	3/3	3/3
Zicam Allergy Relief	25% (v/v)	3/3	3/3

Specimen Stability

The stability of nasal swab specimens after elution into the Visby Respiratory Health Buffer was determined when stored at room temperature (15 - 30°C) or refrigerated (2 - 8°C) conditions. Influenza A, influenza B, and SARS-CoV-2 viruses were spiked into negative clinical matrix at 2x LoD and tested at baseline and at each storage time-point with 20 replicates. All low positive devices returned the expected triple positive results at all time-points tested. Based on the results, the following specimen stability in Visby Respiratory Health Buffer is claimed:

- Room temperature (15 – 30°C) storage up to 120 minutes (2 hours)
- Refrigerated (2 – 8°C) storage up to 48 hours (2 days)

H. Conclusions

The analytical and clinical studies have demonstrated that the Visby Medical Respiratory Health Test is substantially equivalent to the predicate device (K220963).