visby medical™

MD Rx Only

Respiratory Health

Instructions for Use

For qualitative detection and differentiation of
influenza A, influenza B, and SARS-CoV-2 nucleic acid.
For Rx Only.
For Emergency Use Authorization Only.

REF **PS-400005**

Device Name

Visby Medical Respiratory Health Test

Common or Usual Name

Visby Respiratory Health Test

Intended Use

The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, rapid, automated RT-PCR *in vitro* diagnostic test intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A, and influenza B viral RNA in healthcare provider-collected nasopharyngeal and anterior nasal swab specimens, and healthcare provider-instructed self-collected anterior nasal swab specimens (collected on site) from individuals with signs and symptoms of respiratory tract infection consistent with COVID-19. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar. Testing is limited to 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. The Visby Medical Respiratory Health Test is authorized 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.

Results are for the simultaneous detection and differentiation of SARS-CoV-2, influenza A, and influenza B viral RNA in clinical specimens and are not intended to detect influenza C virus. SARS-CoV-2, influenza A, and influenza B viral RNA are generally detectable in nasopharyngeal and anterior nasal swab specimens during the acute phase of infection.

Positive results are indicative of the presence of SARS-CoV-2, influenza A, and/or influenza B nucleic acid, but do not rule out bacterial infection or co-infection with other pathogens not detected by the test. Clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. The agent detected may not be the definitive cause of disease. Laboratories within the United States and its territories are required to report all SARS-CoV-2 results to the appropriate public health authorities.

Negative results for influenza B are presumptive and should be confirmed with an alternative molecular FDA-cleared or authorized assay, if necessary for patient management. Negative results do not preclude SARS-CoV-2, influenza A, and/or influenza B infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and/or epidemiological information.

The Visby Medical Respiratory Health Test is intended for use by operators who have received specific training in the use of the Visby Medical Respiratory Health Test. The Visby Medical Respiratory Health Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation of the Procedure

Influenza (flu) and COVID-19 are both contagious respiratory illnesses that are caused by different viruses. COVID-19 is caused by infection with a coronavirus (called SARS-CoV-2) and flu is caused by infection with influenza viruses. Symptoms of flu and

COVID-19 are similar, so it is not possible to differentiate infections caused by these viruses based on symptoms alone.[1]

Influenza viruses can cause mild to severe illness. Serious outcomes of flu infection can result in hospitalization or death. Older patients, young children, and patients with certain health conditions are at high risk of serious flu complications. There are two main types of influenza virus: types A and B. Influenza A and B viruses primarily circulate during the winter months in temperate climates.[2] Patients with influenza may experience fever, chills, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, and some patients may have vomiting and diarrhea, though this is more common in children than adults.[3]

Coronaviruses are a large family of viruses which may cause illness in animals or humans. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus, SARS-CoV-2, causes COVID-19. This virus and disease were unknown before the outbreak in Wuhan, China, in December 2019 and on March 11, 2020, COVID-19 was characterized as a pandemic by the World Health Organization (WHO).[3]

Patients with COVID-19 can have a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2-14 days after exposure to the virus. Patients with COVID-19 may exhibit fever, chills, cough, shortness of breath, difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion, nausea, vomiting, and/or diarrhea.[4] The virus that causes COVID-19 is easily spread from person to person.[4]

Principles of the Procedure

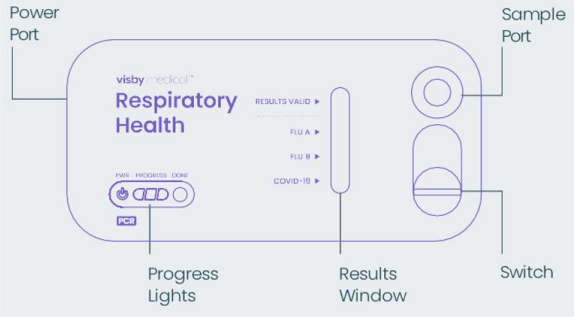
The Visby Medical Respiratory Health Test is a single-use (disposable), fully integrated, fast, compact device containing a reverse transcription polymerase chain reaction (RT-PCR) based assay for qualitative detection of influenza A, influenza B, and/or SARS-CoV-2 viral RNA in upper respiratory tract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

Materials Required

Materials Provided in 10 Pack Test Kit



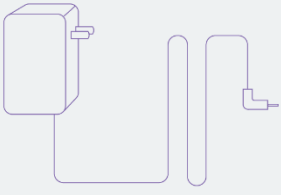
Visby Medical Respiratory Health Test – Quantity 10

Visby Fixed Volume Pipette (650 µl) – Quantity 12

Visby Respiratory Health Buffer Tube with Visby Respiratory Health Buffer (5.85 mL)– Quantity 12

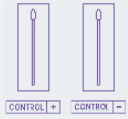
Disposal Bag – Quantity 12

Materials Required and Available as Accessories



Visby Power Adapter

(PS-000855 or PS-000288)



External Controls

Respiratory Health Positive and Negative External Control Swabs (PS-400381)

Materials Required but Not Provided

Gloves

Disposal Bin

Swab

Use sterile nylon, foam, or polyester flocked flexible shaft swabs, only. Cotton and rayon swabs are not compatible with the Visby Respiratory Health Test.

Warnings and Precautions

General

1. For *in vitro* diagnostic use. Rx only. For use under emergency use authorization (EUA) only.
2. This product has not been FDA cleared or approved but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories.
3. This product has been authorized only for the detection and differentiation of nucleic acid from SARS-CoV-2, influenza A, and influenza B, not for any other viruses or pathogens.
4. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 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.
5. This product is for single use only; do not reuse the Visby Medical Respiratory Health Test.
6. Federal Law restricts this device for sale by or on the order of a licensed practitioner (US only).
7. Color-blind users may be unable to differentiate between green and white status lights. However, they can consult the light location and shape of the light to determine test status. When interpreting results, the purple shade may appear as a dark shade for some users.
8. Results from the Visby Medical Respiratory Health device must be interpreted in accordance with these instructions for use.
9. The Visby Medical Respiratory Health Buffer is a clear, colorless, and odorless solution. Do not use if the solution appears discolored or has a strong odor.

Safety and Contamination Prevention

1. Follow your Institution's safety procedures for working with chemicals and handling biological samples.
2. Visby Respiratory Health Buffer may contain irritants. Do not ingest the contents of the tube. If the contents of the tube are splashed in your eyes, flush your eyes with water. If the contents splash onto your skin, wash with soap and water. If irritation persists, notify a health care provider.
3. Wear gloves while handling samples. If the gloves come in contact with specimen or appear to be wet, change gloves to avoid contaminating other specimens. Change gloves between the processing of each specimen and before leaving the work area and upon entry into work areas.
4. Keep the work area clean to prevent contamination.
5. Do not try to disassemble the Visby Respiratory Health device.
6. Treat all biological specimens, including used Visby Medical Respiratory Health devices, as if capable of transmitting infectious agents. All biological specimens should be treated with standard precautions. Guidelines for specimen handling are available from the U.S. Centers for Disease Control and Prevention and the Clinical Laboratory Standards Institute.[5]
7. If a spill occurs with Visby Medical Respiratory Health Test and/or Visby Respiratory Health Buffer Tube, soak up the spill with an absorbent material. Spray the contaminated area and materials with 10% bleach. Wipe down the surface so that it is saturated with bleach and let rest for at least 10 minutes. Once 10 minutes have passed, wipe the area down with an absorbent material, such as paper towels, followed by rinsing the area with water.

Discard the Visby Medical Respiratory Health device according to your institution's standard practices.

8. If a spill occurs on the Visby power adapter, unplug, and wipe it down vigorously with 70% ethyl or isopropyl alcohol. Allow the power adapter to completely dry before using it again.
9. Safety Data Sheets (SDS) are available at Visby Medical Customer Support 1-833-GoVisby (1-833-468-4729).

Electromagnetic Compatibility (EMC) Safety

1. Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.
2. Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the Visby Medical Respiratory Health Test, including cables specified by the manufacturer. Otherwise, degradation of the performance of this equipment could result.

Visby Medical Respiratory Health Device and Accessories

1. The Visby Medical Respiratory Health device will not run at temperatures outside of the operating conditions and the power light will blink. If this occurs, place the device at the proper temperature and wait for the power light to give a stable white light. Refer to the troubleshooting section of the Quick Reference Guide for additional information.
2. Do not use the Visby Medical Respiratory Health device if it appears broken, has been dropped, or is past its expiration date.
3. Do not use the Visby Respiratory Health Buffer Tube if it appears to be leaking, damaged, opened, or is past its expiration date.
4. Do not shake or tilt the Visby Medical Respiratory Health device after adding a sample.
5. Store the Visby Medical Respiratory Health device sealed in the foil pouch prior to use. Do not unwrap until ready to use; storage of the unwrapped device for an extended time prior to use may result in invalid or false negative results.
6. Do not move or unplug the power cable, adapter, or Visby Medical Respiratory Health device while the test is running.
7. The Visby power adapter should be replaced if an increased number of errors are observed. Failure to do so may result in invalid results.
8. Only use the supplied Visby power adapter (9 V, 3.5 A DC) to power the Visby Medical Respiratory Health device. Using other power adapters will void the safety protection of the device and could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.
9. The Visby Medical Respiratory Health device is best used in a room with adequate lighting and away from glare.
10. Dry swab samples must be placed in Visby Respiratory Buffer within one hour of collection. Exceeding this time period can result in invalid or false negative results.
11. Testing samples stored in Visby Medical Respiratory Health Buffer for more than 120 minutes (2 hours) at room temperature or 48 hours under refrigeration can result in invalid or false negative test results.
12. The results of Visby Medical Respiratory Health Test must be read within 120 minutes (2 hours) after the "Done" Green status light appears.

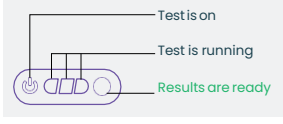
13. The purple switch on the Visby Respiratory Health device must be fully closed to start the test. Failure to completely close the switch will result in failure to start the test and will cause invalid test results.
14. The Visby Medical Respiratory Health device should be operated on a flat surface, placing the device at 90° can result in invalid or false negative test results.
15. After use, the Visby Respiratory Health device should be placed in the provided disposal bag prior to disposal.
16. The Visby Medical Respiratory Health Test should be disposed of in the appropriate specimen waste containers according to your Institution's standard practices.
    Note: Dispose of the power adapter per your local, federal, and institutional guidelines.

Specimen

1. Follow your institution's and CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19).[5]
2. Visby Medical Respiratory Health Test is intended for testing NP or AN swabs collected in Visby Respiratory Health Buffer.
3. Collect the NP or AN swab specimens only with the recommended swab types (i.e., sterile nylon, foam, or polyester flocked flexible shaft swabs). Cotton and rayon swabs are not compatible with the Visby Respiratory Health Test.
4. Always process patient specimens with the Visby Respiratory Health Buffer in accordance with the instructions for use.
5. Do not place the swab in viral transport media, saline, water, or alternate media prior to testing.
6. The Visby Respiratory Health Buffer Tube is used to process a single specimen only. If a retest is required, refer to the retesting procedure section.
7. Failure to add sufficient specimen volume to the test can lead to invalid results.
8. The Visby Medical Respiratory Health device requires a specific volume of specimen. Use the provided fixed-volume pipette to transfer specimen to the device.
9. Clinical specimens can contain inhibitors that may generate invalid results.
10. Ensure tube caps are tightened prior to inverting the Visby Respiratory Health Buffer Tube containing the patient specimen. Inverting the Visby Buffer Tube with a patient specimen less than 5 times can result in inaccurate results.

Color Blindness Precaution

While colorblind users may be unable to differentiate green and white status lights, they can consult the light location and shape of the light to determine test status.



Test Kit and Device Storage

Store Visby Medical Respiratory Health Test kit between 36°F-86°F (2°C-30°C), and between 5% and 80% humidity. Do not freeze. In case of refrigeration or other exposure to cold temperatures, ensure that the Visby Medical Respiratory Health device is allowed to come to at least its minimum operating temperature of 55°F (13°C) prior to use.

Specimen Collection and Storage

The Visby Respiratory Health Test is intended for testing NP or dual-nostril AN swabs collected without transport media. Patient samples should be collected by an HCP using an NP or AN swab (without transport media); or self-collected (by individuals 14 years of age or older, under the supervision of an HCP) using an AN swab (without transport media) according to the provided recommended collection instructions or your institution's standard practices. Use sterile nylon, foam, or polyester flocked flexible shaft swabs, only.

For best results, patient samples should be tested as soon as possible. If the sample cannot be immediately tested, it can be stored as shown in the following table.

WARNING: Testing samples beyond these conditions can lead to invalid or inaccurate results.

Patient Sample Storage Specifications

IN DRY TUBE	IN VISBY BUFFER	IN VISBY BUFFER
Up to 1 hour at room temperature **59°F - 86°F** (15°C - 30°C)	Up to 120 minutes (2 hours) at room temperature **59°F - 86°F** (15°C – 30°C)	Up to 48 hours at refrigerated temperature **36°F - 46°F** (2°C - 8°C)

Visby Medical Respiratory Health Test Procedure

Follow these instructions carefully. This test is designed for use by health care professionals.

Operating Conditions

TEMPERATURE
55°F - 88°F
(13°C - 31°C)

HUMIDITY
5% - 80%

Setup | Prepare the Workspace Place device on a level surface.

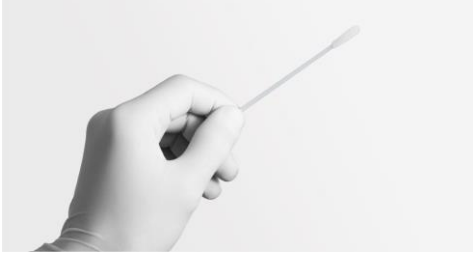
A. Clean your workspace and gather all the required materials, then **unwrap** the device. **Wear gloves** while handling samples and **change gloves** between testing each specimen.
Note: Use the device **immediately after unwrapping** to ensure accurate results.

B. Plug the **Visby Power Adaptor** into the device power port.
Note: If the power light blinks, refer to the Troubleshooting Section.

C. Remove the sticker over the sample port.

Step 1 | Add Patient Swab to Visby Respiratory Health Buffer

A. Open the Visby Respiratory Health Buffer Tube and **place it** in tube holder.



B. Take the patient swab.

C. Place the patient swab into Visby Respiratory Health Buffer Tube.
Note: Break the handle of the swab.

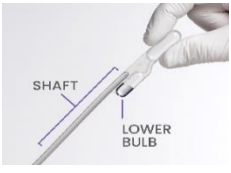
D. With the swab in the tube, screw cap back onto the Visby Respiratory Health Buffer Tube. Label the tube. **Note the time.**

Step 2 | Mix and Add Patient Sample

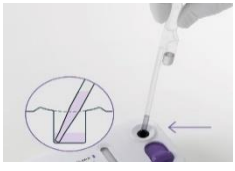
A. Mix the sample by **gently inverting** the tube **5 times**.
Note: Failure to invert may lead to inaccurate results.

B. Squeeze the **upper bulb** of the provided pipette and submerge the tip to the **bottom** of the sample tube.

C. Release the upper bulb **slowly** to fill the shaft. **Keep pipette tip submerged** until shaft is full. Extra fluid should enter the lower bulb.



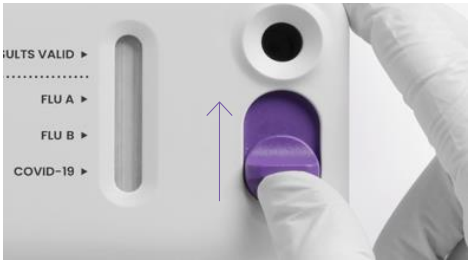
D. Ensure the shaft is filled with liquid sample. **Note:** Do not squeeze lower bulb or invert the pipette.



E. Place the tip at the **bottom** of the sample port and then squeeze the **upper bulb** of the pipette to release **all** of the sample.

F. Some fluid will remain in the lower bulb. Discard the pipette according to your institution's guidelines immediately. **Do not set down.**

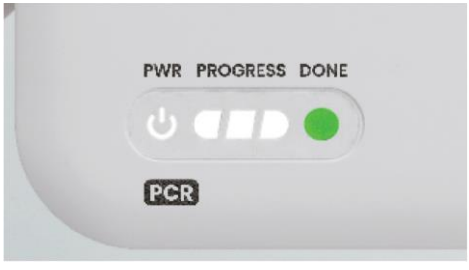
Step 3 | Run the Test Do not move test while running. Run the test immediately after adding patient sample.



A. Slide the **switch upwards** in a firm, swift motion to close the sample port to start the test. **Do not move test while running.** **Note:** Make sure the switch is pushed all the way up.

B. Check that the first **progress indicator light is blinking**. Lights will initially blink and then become stable as the test progresses. **Note:** If something different happens to the lights, please refer to the Troubleshooting Section.

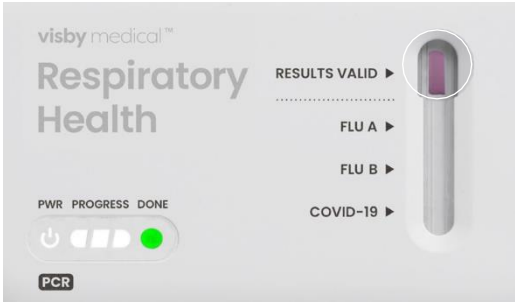
C. The second progress indicator light should become stable within **20 minutes**.



D. Wait approximately **30 minutes** for a green light to appear indicating the test is finished running.

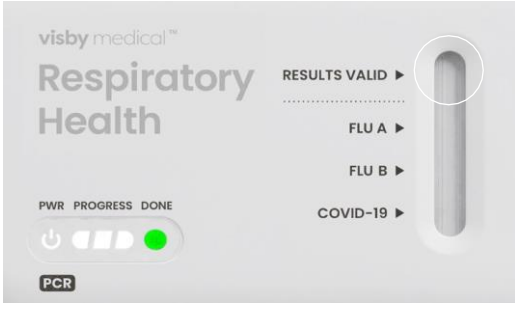
Step 4 | Interpret Results If the test is invalid, stop, and retest!

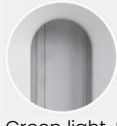
A. Determine if the test is valid.



Green light + Results Valid spot = **Valid Test**

Read Results



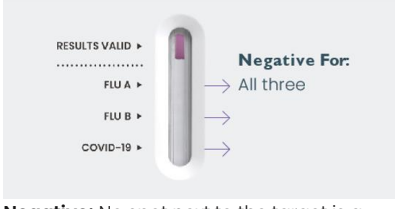


Green light + No Results Valid spot = **Invalid Test**

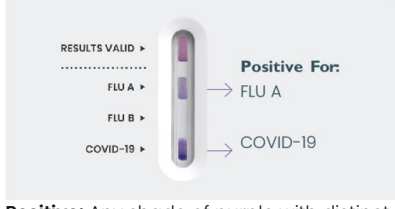
Stop and Retest

B. Read the test results.

Note: Results may be read up to 2 hours after the test is completed. **Do not read** results if test is invalid.



Negative: No spot next to the target is a negative result.



Positive: Any shade of purple with distinct edges next to the target is a positive result.

Intensity of the spot may vary. Any shade of color with distinct edges should be considered positive.

Result Interpretation and Action Table

The following table provides guidance on test interpretation and result reporting. Refer to the Appendix for more information on test interpretation.

Indicator Lights	"RESULTS VALID" Spot	Flu A Spot	Flu B Spot	COVID-19 Spot	Result Interpretation	Action Step
Green Done Light does not illuminate	N/A	N/A	N/A	N/A	Invalid See Troubleshooting Section in the Appendix	
N/A	Absent	N/A	N/A	N/A	Invalid	Retest
Green Done Light	**Present**	**Present**	Absent	Absent	**Flu A Detected** Flu B Not Detected COVID-19 Not Detected	Report results
Green Done Light	**Present**	Absent	**Present**	Absent	Flu A Not Detected **Flu B Detected** COVID-19 Not Detected	Report results
Green Done Light	**Present**	Absent	Absent	**Present**	Flu A Not Detected Flu B Not Detected **COVID-19 Detected**	Report results
Green Done Light	**Present**	**Present**	**Present**	Absent	**Flu A Detected** **Flu B Detected** COVID-19 Not Detected	Report results
Green Done Light	**Present**	**Present**	Absent	**Present**	**Flu A Detected** Flu B Not Detected **COVID-19 Detected**	Report results
Green Done Light	**Present**	Absent	**Present**	**Present**	Flu A Not Detected **Flu B Detected** **COVID-19 Detected**	Report results
Green Done Light	**Present**	**Present**	**Present**	**Present**	**Flu A Detected**, **Flu B Detected** **COVID-19 Detected**	Report results
Green Done Light	**Present**	Absent	Absent	Absent	Flu A Not Detected Flu B Not Detected COVID-19 Not Detected	Report results

Retest Procedure

If a retest is required, obtain the leftover sample from the Visby Respiratory Health Buffer tube. If the leftover sample has been stored for ≤ 120 minutes at room temperature or for ≤ 48 hours at refrigerated temperature, then is it stable and can be re-tested with a new device. If the leftover sample has exceeded the storage recommendations, and/or if the sample volume is insufficient, collect a new sample and repeat the test with a new Visby Medical Respiratory Health Test.

If a repeat test with a patient sample fails, collect a new sample for testing or contact Visby Medical Customer Support at 1-833-468-4729 (1-833-GoVisby).

Quality Control

The Visby Medical Respiratory Health Test has built-in procedural controls. These include an internal process control and built-in electronic control. The result of the process control is displayed in the results window while the results of the electronic controls are displayed using the status lights.

Internal Process Control

The Visby Medical Respiratory Health device contains an internal process control assay that targets human beta-2 microglobulin (B2M) RNA. The internal process control monitors lysis, reverse transcription, PCR amplification, and detection. If these steps are completed successfully, then a purple spot will develop next to "Results Valid" in the results window. If the purple spot does not appear, the test result is Invalid, and the test must be repeated with a new Visby Medical Respiratory Health device.

Electronic Control

The electronic controls monitor the device to ensure proper operation. If the electronic control passes, a green done status light appears. If this control fails, the white status light will fail to illuminate or will flash, as shown below. See the Additional Troubleshooting section in the Appendix for additional information.

If the power light is blinking:

- The device is outside operating temperature (55°F–88°F or 13°C–31°C).
- If the room is in the right temperature range, wait for the device to reach operating temperature. The power light will become stable when that happens.
- If the room is too cold or too hot, move to a different location within the operating temperature range.
- Wait until the power light is stable before loading the sample.

If the power light and progress lights are blinking together:

- The device has encountered an error and is no longer functional.
- Refer to the Retesting Instructions.

External Positive and Negative Controls

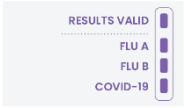
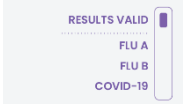
Good laboratory practice suggests the use of external positive and negative controls to ensure that the test is working properly and that the test is correctly performed.

The external control must be run once with each new shipment of test kits and once for each untrained operator. Further controls may be tested to conform with local, state and/or federal regulations, accrediting groups, or your laboratory's standard Quality Control procedures.

Procedure to Run External Controls

1. To run external control swabs, unwrap the swab, place it into the Visby Respiratory Health Buffer Tube, and tap the swab against the bottom of the tube 5 times.
2. Discard the swab according to your institution's guidelines and screw the cap back onto the Visby Respiratory Health Buffer Tube. Proceed to Step 2 of the procedure to run the test.

Respiratory Health Control Swabs (PS-400381)

External Controls	Units in Kit	Control Key
Respiratory Health Positive Control Swab	2 Swabs	Valid Positive Control Run 
Respiratory Health Negative Control Swab	2 Swabs	Valid Negative Control Run 

If the positive or negative external controls fail, repeat the test with a new control swab with a new Visby Medical Respiratory Health device. If a repeat test fails, contact Visby Medical Customer Support at 1-833-468-4729 (1-833-GoVisby).

Limitations

1. The performance of the Visby Medical Respiratory Health Test was established using NP and AN swab specimens.
2. The test is a qualitative test and does not provide the quantitative value of detected organism present.
3. Cross-reactivity with respiratory tract organisms other than those tested in the Analytical Specificity Study may lead to erroneous results.
4. Negative results for influenza B are presumptive and should be confirmed with an alternative molecular FDA-cleared or authorized assay, if necessary for patient management.
5. Influenza B performance was assessed by testing surrogate samples only; it was not assessed by testing unmanipulated natural influenza B clinical samples.
6. Erroneous results may occur from improper specimen collection, technical error,

sample mix-up, or if the viral load in the patient sample is below the limit of detection of the Visby Medical Respiratory Health Test.

7. Careful compliance with the instructions in this insert and the Quick Reference Guide Instructions are necessary to avoid inaccurate results.
8. Because the detection of influenza A, influenza B, and SARS-CoV-2 is dependent on the viral load present in the sample, reliable results are dependent on proper sample collection, sample processing, handling, and storage.
9. This test has been evaluated with human specimen material only.
10. The effect of interfering substances has been evaluated only for those listed in the interfering substances section of this document.
11. Mutations within the target region of influenza A, influenza B, and SARS-CoV-2 could affect primer and/or probe binding, resulting in failure to detect the presence of virus.
12. This test cannot rule out diseases caused by other bacterial or viral pathogens.
13. Performance has not been established in asymptomatic individuals.
14. Viral nucleic acid may persist *in vivo*, independent of virus viability. Detection of influenza A, influenza B, and SARS-CoV-2 nucleic acid does not imply that the corresponding virus is infectious or is the causative agents for clinical symptoms.
15. The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of influenza A, influenza B, and SARS-CoV-2 and their prevalence, which change over time.
16. The Visby Medical Respiratory Health Test is predicted to have decreased ability to detect non-H1N1 or non-H3N2 influenza A strains of zoonotic origin that are not currently known to be widely circulating in humans (e.g., H1N2, H3N8, H5N1, H5N6, H5N8, H7N4, H7N9, H9N2, H10N3).
17. This test is not intended to differentiate influenza A subtypes or influenza B lineages. If differentiation of influenza subtypes and strains is needed, additional testing, in consultation with state or local public health departments, is required.
18. Positive and negative predictive values are dependent upon prevalence. False negative results are more likely during peak activity when disease prevalence is high and false positive results are more likely during periods of low activity.
19. Recent patient exposure to FluMist® or other live attenuated influenza vaccines may cause inaccurate positive results.

Conditions of Authorization for Laboratories

The Visby Medical Respiratory Health Test Letter of Authorization, along with the authorized Fact Sheets for Healthcare Providers, the authorized Fact Sheets for Patients, and authorized labeling are available on the FDA website: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas.

However, to assist clinical laboratories and/or Point of Care Settings using the Visby Medical Respiratory Health Test (referred to in the Letter of Authorization as "Your Product"), the relevant Conditions of Authorization are listed below:

1. Authorized laboratories* using the Visby Medical Respiratory Health Test must include with test result reports, all authorized Fact Sheets. Under exigent

circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.

2. Authorized laboratories using the Visby Medical Respiratory Health Test must use the Visby Respiratory Health Test as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents, and authorized materials required to use the Visby Medical Respiratory Health Test are not permitted.
3. Authorized laboratories that receive the Visby Medical Respiratory Health Test must notify the relevant public health authorities of their intent to run the Visby Medical Respiratory Health Test product prior to initiating testing.
4. Authorized laboratories using the Visby Medical Respiratory Health Test must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
5. Authorized laboratories must collect information on the performance of the Visby Medical Respiratory Health Test and report to DMD/OHT7 /OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and Visby Medical Inc. (support@visby.com) any suspected occurrence of false positive or false negative results and significant deviations from the established performance characteristics of the Visby Medical Respiratory Health Test of which they become aware.
6. All operators using the Visby Medical Respiratory Health Test must be appropriately trained in performing and interpreting the results of the Visby Medical Respiratory Health Test, use appropriate personal protective equipment when handling this kit, and use the Visby Medical Respiratory Health Test in accordance with the authorized labeling.
7. Visby Medical, Inc., authorized distributor(s), and authorized laboratories using the Visby Medical Respiratory Health Test must ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

* The Letter of authorization refers to "authorized laboratories" as "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. The Visby Medical Respiratory Health Test is authorized 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."

Quality Systems Evaluation

The Quality Systems of Visby Medical, Inc. were independently evaluated. The evaluation has provided evidence to establish that the quality systems and manufacturing capability are likely to achieve the performance noted in this labeling.

Expected Values

The performance of the Visby Medical Respiratory Health Test included 1,115 prospectively collected respiratory (NP and AN) swab specimens. The number and percentage of cases positive for influenza A and SARS-CoV-2, as determined by the Visby Medical Respiratory Health Test, are shown by age and sex categories in Table 1 below. There was 1 influenza B positive specimen during the study from a 54 year old male subject.

Table 1. Positivity Rate by Age and Sex of the Visby Medical Respiratory Health Test for Detection of Influenza A and SARS-CoV-2 in Respiratory Swab Specimens (NP and AN) During the Prospective Clinical Study

Age	N (%)	% Positive (# Positive / # Tested)			
		Female		Male	
		Influenza A	SARS-COV-2	Influenza A	SARS-COV-2
0-5	72 (6.5%)	0.0% (0/35)	8.6% (3/35)	0.0% (0/37)	8.1% (3/37)
6-21	247 (22.2%)	6.0% (8/134)	9.0% (12/134)	12.4% (14/113)	7.1% (8/113)
22-59	649 (58.2%)	4.5% (19/418)	19.9% (83/418)	5.2% (12/231)	21.6% (50/231)
≥ 60	147 (13.2%)	0.0% (0/92)	21.7% (20/92)	1.8% (1/55)	32.7% (18/55)
Total	**1115**	**4.0% (27/679)**	**17.4% (118/679)**	**6.2% (27/436)**	**18.1% (79/436)**

Performance Characteristics

Clinical Evaluation

Performance characteristics of the Visby Medical Respiratory Health Test were established in a two-armed clinical study that included testing of (1) prospectively collected fresh specimens, and (2) previously characterized banked frozen 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 used by typical CLIA Waived operators. This study was conducted at three POC sites in 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 March 2023.

Prospective Sample Testing

Subjects presenting with signs and symptoms of a viral respiratory infection were prospectively enrolled at three POC 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 ("direct swab") and tested with the Visby device by study operators according to the QRG and IFU. The remaining sample was sent to the reference laboratory for comparator testing with an FDA-cleared influenza molecular test and an FDA-EUA authorized SARS-CoV-2 RT-PCR test.

A total of 1,171 subjects were enrolled in the study. Fifty-six (56) study specimens were excluded from the performance analysis due to of lack of a valid comparator result (n=21), lack of a valid Visby test result (n=19), the subject did not meet inclusion criteria (n=10), or for protocol deviations (n=5). One subject withdrew from the study. This left 1,115 subjects for performance analysis of the Visby Medical Respiratory Health Test.

A total of 1,155 Visby tests were performed on subjects that met the inclusion criteria, did not experience a protocol deviation, and did not withdraw from the study. Of these

61 (5.3%) had an initial invalid test result of which 19 (1.6%) were invalid when retested. Of the 631 NP swab specimens tested, 20 (3.2%) had an initial invalid test result of which 5 (0.8%) were invalid when retested. Of the 524 AN swab specimens tested, 41 (7.8%) had an initial invalid test result of which 14 (2.7%) 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 March 2023 (Visby vs. Comparator Assays)

	Specimen Type (NP/AN)	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Influenza A	NP	21	3[a]	597	0	100.0% (84.5-100.0%)	99.5% (98.5-99.8%)
	AN	26	4[b]	463	1[c]	96.3% (81.7-99.3%)	99.1% (97.8-99.7%)
	NP+AN	47	7	1060	1	97.9% (89.1-99.6%)	99.3% (98.7-99.7%)
Influenza B	NP	1	0	620	0	100% (20.7-100%)	100% (99.4-100%)
	AN	0	0	494	0	N/A	100% (99.2-100%)
	NP+AN	1	0	1114	0	100% (20.7-100%)	100% (99.7-100%)
SARS-CoV-2	NP	107	6[d]	504	4[f]	96.4% (91.1-98.6%)	98.8% (97.5-99.5%)
	AN	79	5[e]	409	1[g]	98.8% (93.3-99.8%)	98.8% (97.2-99.5%)
	NP+AN	186	11	913	5	97.4% (94.0-98.9%)	98.8% (97.9-99.3%)

[a] 2 of 3 false positive NP specimens tested positive and 1 tested negative with an alternate EUA-authorized molecular assay

[b] 4 of 4 false positive AN specimens tested positive when tested with an alternate EUA-authorized molecular assay

[c] 1 false negative AN specimen tested positive with an alternate EUA-authorized molecular assay

[d] 5 of 6 false positive NP specimens tested positive and 1 tested negative with an alternate EUA-authorized molecular assay

[e] 4 of 5 false positive AN specimens tested positive, and 1 tested negative with an alternate EUA-authorized molecular assay

[f] 3 of 4 false negative NP specimens tested negative and 1 tested positive with an alternate EUA-authorized molecular assay

[g] 1 false negative AN specimen tested positive with an alternate EUA-authorized molecular assay

Banked Sample Testing

To increase the number of influenza A positive specimens , previously characterized banked frozen individual NP dry swab specimens were tested at POC study sites. The specimens were randomized with negative banked frozen NP swab specimens and blinded to the study operators. The study operators thawed and tested the specimens with the Visby devices according to the QRG and IFU at the POC study sites. The remaining sample was tested with an FDA-cleared influenza molecular test.

A total of 50 banked frozen specimens were enrolled, of which 3 were excluded because they did not meet study inclusion criteria. Among the 47 tests performed with eligible specimens on the Visby test, one study specimen was excluded from the data analysis due to lack of a valid Visby test result (n=1) for an overall initial invalid rate of 2.1% (1/47). The PPA and NPA of influenza A and influenza B for the previously characterized banked frozen NP dry swab specimens are shown in Table 3 below as compared to the FDA-cleared influenza molecular test.

Table 3. Banked Frozen NP Swab Specimen Performance (Visby vs. Comparator Assay)

	N	TP	FP	TN	FN	PPA (95% CI)	NPA (95% CI)
Influenza A	46	13	1 [a]	31	1 [b]	92.9% (68.5%-98.7%)	96.9% (84.3%-99.4%)
Influenza B	46	0	0	46	0	N/A	100.0% (92.3%-100.0%)

[a] This influenza A false positive specimen was positive when tested with an alternate EUA-authorized molecular assay.
[b] This influenza A false negative specimen was negative when tested with an alternate EUA-authorized molecular assay.

Reproducibility (Includes Around the LoD Testing)

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 unspiked (negative) NP swabs and NP swab samples 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 4 below.

Table 4. 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

Surrogate Sample Testing Study

Surrogate influenza A and influenza B positive specimens were prepared by spiking 50 µL of de-identified unique positive leftover clinical NP swab specimens in viral transport media (VTM) onto two NP swabs. Both swabs were immediately frozen. One swab was eluted into 3 mL of VTM and tested with an FDA-cleared influenza molecular test. Once influenza A or influenza B positivity was confirmed, the paired unused surrogate dry swabs were randomized with negative banked frozen specimens and tested with Visby devices by study operators according to the QRG and IFU at the POC study sites.

A total of 63 surrogate influenza A or influenza B positive specimens and 10 banked influenza A and B negative specimens were enrolled in the study. Among the 73 tests performed on the Visby device, 0 had an invalid result on the first test, for an overall initial invalid rate of 0.0% (0/73). The PPA and NPA of influenza A and influenza B for the surrogate specimens are shown in Table 5 below as compared to the expected results from the FDA-cleared influenza molecular test.

Table 5. Surrogate Specimen Performance (Visby vs. Expected Results)

	N	TP	FP	TN	FN	Positive Agreement with Expected Results (95% CI)	Negative Agreement with Expected Results (95% CI)
Influenza A	73	30	0	42	1	96.8% (83.8%-99.4%)	100.0% (91.6%-100.0%)
Influenza B	73	31	0	41	1	96.9% (84.3%-99.4%)	100.0% (91.4%-100.0%)

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 6 below.

Table 6. 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.

Inclusivity

The ability of the Visby Medical Respiratory Health Test to detect 20 strains of influenza A and 12 strains of influenza B at or near the LoD was evaluated. Each virus was individually spiked into negative clinical matrix at or near 3x LoD and tested in triplicate. All strains were successfully detected within 3x LoD.

Table 7. 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
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
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

***In Silico* Analysis**

Sequences from all available influenza strains collected between August 2017 and August 2022 (5 years) were downloaded from the GSAID and NCBI databases and analyzed. All mismatches present in > 1% of influenza A (H1N1 and H3N2 strains) and influenza B sequences with respect to their corresponding primer/probe set underwent further *in silico* analysis. None of these mismatches are predicted to significantly reduce the percentage of primer/probe bound at the nominal annealing/detection temperatures of the device; the maximum predicted reduction in binding across all analyzed mismatches is < 2%. Therefore, these mismatches are expected to have a minimal impact on device performance.

All mismatches present in > 1% of other influenza subtypes underwent further *in silico* analysis. The mismatches in the probe sequences were predicted to significantly reduce the percentage of amplicon bound to the probe at the nominal detection temperature of the device; the reduction in binding ranged from approximately 70-99%. These mismatches are expected to have an impact on the ability of the device to detect these influenza strains. The device may have a reduced sensitivity for detection of influenza A strains other than H1N1 and H3N2 (e.g., H5N1, H5N6, H5N8, and H9N2, etc.).

Visby follows the FDA's Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests by monitoring SARS-CoV-2 sequences for mutations in the N or *Orf1ab* genes that may impact the Visby Medical Respiratory Health Test performance. As of August 29, 2022, Visby has screened 11,758,691 global SARS-CoV-2 sequences submitted to the GISAID database. These analyses included sequence submissions from all common spike gene variants in circulation in the US, including the current WHO designated Variant of Concern Omicron (B.1.1.529 and BA) variants. All mismatches present in > 1% of SARS-CoV-2 sequences underwent further *in silico* analysis. None of these mismatches are predicted to significantly reduce the percentage of primer/probe bound at the nominal annealing/detection temperatures of the device; the maximum predicted reduction in binding across all analyzed mismatches is < 8%. These minor reductions in primer/probe binding, in combination with the redundancy of the ORF and N primer/probe sets, are expected to have a minimal impact on the ability of the Visby Medical Respiratory Health Test to detect variants for SARS-CoV-2.

Cross-Reactivity

An *in silico* analysis was performed to determine if the primers or probes in the Visby Medical Respiratory Health Test would be expected to react with related pathogens, high prevalence disease agents, and normal or pathogenic flora that are reasonably likely to be encountered in a clinical sample. The analysis searched for homology of 80% or more between one of the oligos and the genetic sequence of any of the organisms. The search uncovered only two interactions that met this criterion. Further analysis showed that the homology of each of these does not affect the other primer or probe for the respective amplicons, and therefore would not lead to false positive signals, and both were included in the laboratory testing described below. Overall, there are no interactions of the primers or probes of the Visby Respiratory Health Test to the analyzed organisms that would lead to a false positive signal.

The potential for cross-reactivity from organisms 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 (40) organisms (viral and bacterial) were tested in triplicate at high concentrations (>10^5 units/mL for viruses (e.g., >10^5 TCID50/mL, etc.) and >10^6 units/mL for bacteria and yeast (e.g., >10^6 CFU/mL, etc.)) in negative clinical matrix. None of the 40 organisms caused false positive results when tested using the Visby Medical Respiratory Health Test. No cross-reactivity was observed with any of the organisms tested.

Table 8. Organisms Evaluated for Cross-Reactivity on Visby Respiratory Health Test

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

* Purified RNA was tested for these viruses.
** Purified DNA was tested for these bacteria.

Microbial Interference

The potential for microbial interference from organisms that may be found in an upper respiratory sample on detection of low concentrations of the target respiratory viruses (influenza A, influenza B, and SARS-CoV-2) was evaluated. Forty (40) organisms (viral and bacterial) were tested in triplicate at high concentrations (>10^5 units/mL for viruses and >10^6 units/mL for bacteria and yeast) in negative clinical matrix spiked with low concentrations (3x LoD) of influenza A, influenza B, and SARS-CoV-2. 40 non-target organisms did not interfere with detections of low levels of influenza A, influenza B, and/or SARS-CoV-2.

Table 9. Organisms Evaluated for Microbial Interference on Visby Respiratory Health Test

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

* Purified RNA was tested for these viruses.
** Purified DNA was tested for these bacteria.

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 inactivated 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 1000x LoD. No competitive interference was observed for any of the three target viruses.

Table 10. 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 11 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.

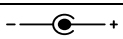
Table 11. Potentially Interfering Substances

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
Purified mucin protein	1% (w/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
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

References

1. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/. Accessed September 22, 2021.
2. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed September 22, 2021.
3. Centers for Disease Control and Prevention. https://www.cdc.gov/flu/symptoms/index.html. Accessed September 22, 2021.
4. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species *Severe acute respiratory syndrome-related coronavirus*: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* **5,** 536–544 (2020). https://doi.org/10.1038/s41564-020-0695-z
5. Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19). https://www.cdc.gov/coronavirus/2019-ncov/lab/lab-biosafety-guidelines.html

Index of Symbols

Symbol	Meaning	ISO 15223-1 Ref. Number
	Power supply	N/A
	Catalog number	5.1.6
	Do not reuse	5.4.2
	Handle with care	5.3.1
	Batch code	5.1.5
	Caution	5.4.4
	Consult instructions for use	5.4.3
	Manufacturer	5.1.1
	Expiration date	5.1.4
	Temperature limitation	5.3.7
	Humidity limitation	5.3.8
	Biological risk	5.4.1
	*In vitro* diagnostic medical device	5.5.1
	Do not use if package is damaged	5.2.8
	Nemko 61010	N/A
	Positive / negative controls	5.5.4 / 5.5.3
	Prescription Use Only	N/A

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Appendix

More Information on Result Interpretation

The following are occasionally observed:

Background Staining	Speckling and Bubbles	Spot Shadow
		
The background color in the results window may turn a light shade of blue or purple over time. This is a normal feature of chemistry. This should not be considered a positive result.	Non-specific small flakes in the results window should not be interpreted to be a positive result. It is also normal for bubbles to appear in the results window during test processing.	An extremely faint spot without distinct edges may be seen in the results window. This should not be interpreted to be a positive result.

Additional Troubleshooting

Status Light Behavior	Cause of error	User instructions
None of the white lights illuminate 	The device is not receiving power or there was a power interruption during the run	• If the error occurs prior to the start of the run, the user can ensure the device is properly plugged in and proceed with testing • If a power interruption occurred after the run starts, the test will not progress. The sample must be tested with a new device.
The white power light is blinking 	The device is being operated outside of its temperature range	The device can be allowed to reach operating temperature or moved to a more appropriate location prior to the start of the run
The white power light is on, but the progress lights do not turn on 	The purple slider was not completely closed or did not activate the test	Confirm the slider is completely closed. If it is, the test will not progress, and the sample must be tested with a new device.
All of the white lights blink 	The device has experienced an error	The test will not complete, and the sample must be tested with a new device.

If you are unsure how to interpret a result, please contact **Visby Medical Customer Support** at 1-833-GoVisby (1-833-468-4729).