

EMERGENCY USE AUTHORIZATION (EUA) SUMMARY FOR THE GENETWORx Covid-19 Nasal Swab Test

For *in vitro* Diagnostic Use
Rx Only
For 18 years of age or older
For Use Under Emergency Use Authorization (EUA) Only

The GENETWORx Covid-19 Nasal Swab Test will be performed at RCA Laboratory Services LLC located at 4060 Innslake Drive, Glen Allen, VA 23060 and Testing Centers of America LLC located at 411 Swedeland Road, King of Prussia, PA 19406 that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a and meet requirements to perform high complexity tests as described in the Laboratory Standard Operating Procedures that were reviewed by the FDA under this EUA.

INTENDED USE

The GENETWORx Covid-19 Nasal Swab Test is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasal swab specimens that are self-collected unsupervised at home using the GENETWORx Covid-19 Nasal Swab Test Kit, by individuals (18 years of age or older) suspected of COVID-19, when determined to be appropriate by a healthcare provider. Specimens collected using the GENETWORx Covid-19 Nasal Swab Test Kit can be transported at ambient temperature for testing.

Testing is limited to RCA Laboratory Services LLC located at 4060 Innslake Drive, Glen Allen, VA 23060 and Testing Centers of America LLC located at 411 Swedeland Road, King of Prussia, PA 19406, that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high complexity tests.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in nasal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2 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 epidemiological information. Self-collected specimens from SARS-CoV-2 positive individuals may yield negative results if the specimen was not collected properly.

The GENETWORx Covid-19 Nasal Swab Test is intended for use by qualified laboratory personnel specifically instructed and trained in molecular testing and *in vitro* diagnostic procedures. The GENETWORx Covid-19 Nasal Swab Test and the GENETWORx Covid-19 Nasal Swab Test Kit are only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

1. Device Description

The GENETWORx Covid-19 Nasal Swab Test for use with the GENETWORx Covid-19 Nasal Swab Test Kit enables the self-collection of nasal swab specimens by individuals (18 years of age and older) suspected of COVID-19 when determined to be appropriate by a healthcare provider. The GENETWORx Covid-19 Nasal Swab Test kit consists of the Aptima Multitest Swab Kit (comprising a collection swab and Aptima Specimen Transport Medium in a collection tube) or the Hologic Direct Load Tube Collection kit (comprising the same collection tube, Aptima Specimen Transport Medium, and swab), specimen biohazard bag, absorbent sheet, kit cardboard box, a shipping package/envelope with return shipping label, instructions for specimen collection and shipping (**Table 1**).

Table-1: Components of the GENETWORx Covid-19 Nasal Swab Test Kit

| Name | Description | Quantity | Material Supplier |
|-----------------------------------|---|----------|---|
| GENETWORx Covid-19 Nasal Swab kit | Collection containing transport medium vial (barcoded) and swab | 1 | Aptima Multitest Swab Kit (Part # PRD-03546) or Aptima Direct Load Tube Collection Device (Part# PRD-06997) |
| Instruction for Use | Collection and shipping Instructions | 1 | GENETWORx (Part # N/A) |
| Shipping Box | 7.5" wide x 5.5" deep x 2.25" tall box for shipping sample | 1 | Foley, Inc (Part # N/A) |
| Biohazard Bag | Biohazard bag with absorbent pad. | 1 | VWR (Part # - BioHazard Bag 225) |
| FedEx Clinical Pak | UN3733 Clinical Pak, FedEx Return shipping label attached | 1 | Federal Express |

The GENETWORx Covid-19 Nasal Swab Test Kit was reviewed for adherence to the Department of Transportation's shipping requirements (IATA Dangerous good Regulations; Edition 61, Addendum 1, packing instruction 620; Effective 1 January – 31st December 2020). The kit was found to be acceptable and appropriate for shipping within the United States. The Specimen Transport Medium used in the GENETWORx Covid-19 Nasal Swab Test kit contains a substance that inactivates SARS-CoV-2 and might be a human health hazard if it accidentally comes in contact with eyes or skin. Appropriate cautionary and advisory statements were added in the user instructions to mitigate that risk.

Upon receipt in the laboratory, the GENETWORx Covid-19 Nasal Swab sample undergoes an accessioning process to verify patient information and the integrity of the specimen prior to testing using the GENETWORx Covid-19 Nasal Swab Test that comprises the FDA-authorized APTIMA SARS-CoV-2 Assay and a parallel RT-PCR assay for the human RNase P gene (GENETWORx RNase P Assay), that is used to monitor the integrity of specimen collection and transport.

2. GENETWORx Covid-19 Nasal Swab Test Kit Ordering and Processing

A. Group orders

GENETWORx will supply the GENETWORx Covid-19 Nasal Swab Kit to businesses, colleges, and other institutions for distribution to individuals as ordered under prescription by a physician or other qualified healthcare provider. Group orders may be initiated through the GENETWORx website, www.genetworx.com, or by contract with GENETWORx. GENETWORx will ship group orders to the ordering entity for distribution to individuals under prescription or, if requested on the order of a physician, will send kits to individuals directly. Under no circumstance will a collection kit be provided to an individual without a prescription.

B. Individual Online Orders

Individuals will order the GENETWORx COVID-19 Nasal Swab Test Kit through the GENETWORx website. To place an order an individual must complete a COVID-19 questionnaire provided by Physician Wellness Network (PWN), a national telehealth provider. The questionnaire aligns with CDC recommendations for testing prioritization. PWN will review questionnaire responses to determine test eligibility. If appropriate, a qualified PWN healthcare provider in the individual's state will write a prescription. Test kits will not be sent to patient without a prescription. PWN will contact all individuals whose results are positive or inconclusive. All patients will receive notice of test result availability by text message or email. Patients will be able to access results online using a mobile and web-based application.

The ordering healthcare provider will have electronic access to test results and will contact patients for follow up as appropriate.

3. GENETWORx Covid-19 Nasal Swab Test Kit Use

Upon receiving the kit by mail, the User must read the package insert carefully and thoroughly to begin the sample collection process. The User Instruction Card includes detailed, step-by-step instructions for kit activation, self-collection and return of a specimen. "Activating" the kit is necessary to associate the self-collected specimen with the individual and ensure appropriate result reporting. Specimens cannot be processed in the laboratory unless the collection kit is activated. Individuals will activate a kit by entering the barcode number provided on the sample tube through a link on the GENETWORx website (<https://genetworx.com/>). Individuals then will follow the instructions provided to self-collect and return the specimen to GENETWORx.

Individuals will receive an email or text notification when their results are ready and will be able to retrieve results and an official lab report through a GENETWORx account.

- Patients who receive negative results are encouraged to follow CDC guidelines for keeping themselves COVID-19 Free.
- Patients who receive positive results are given instructions to seek treatment from a medical provider.
- Patients who receive invalid results are advised to consider re-testing.

Results are also reported via secure portal to the ordering healthcare provider who will provide appropriate follow-up based upon the results in the exercise of professional medical discretion.

4. Laboratory Processing (Registration and accessioning of the samples):

Specimens received by RCA Laboratory Services LLC located at 4060 Innslake Drive, Glen Allen, VA 23060 and Testing Centers of America LLC located at 411 Swedeland Road, King of Prussia, PA 19406, will undergo the GENETWORx registration and accessioning process prior to acceptance for testing. As a first step, GENETWORx will confirm specimen delivery in their proprietary Aura web portal (auratracker.org). Once confirmed, the laboratory will open the package and review the paperwork that includes the specimen confirmation form. The patient identification information on the specimen tube should match with the specimen confirmation form. The laboratory will confirm that the samples were received on time (within the sample stability acceptance window), properly packaged in the biohazard bag and will check for any evidence of package damage or leakage of the sample. If the sample has leaked or changed its color (i.e. purple hue, indicative of a pH change), or the sample collection tube does not contain a swab, it will be discarded in the rejection bins leaving the sample in the biohazard bag.

5. Specimen Collection Control

Concurrently with the APTIMA SARS-CoV-2 Assay, GENETWORx will run a real-time PCR assay to detect the human RNase P gene which serves to monitor the specimen collection process. For the RNase P assay, samples will be extracted by magnetic bead-based extraction and amplified using the Douglas Intelliqube real time PCR instrument.

REAGENTS AND MATERIALS

a. GENETWORx RNase P Assay

A. **Assay components:** The GENETWORx RNase P Assay uses the RNase P-specific primers and probe contained in the LGC_COVID-19 Kit. Each kit is for up to 6000-7000 tests on the IntelliQube.

rRT-PCR primer/probe COVID-19 kit (LGC-BioSearch; KIT-nCoV-PP1-1000) stored between 2° and 8 °C.

Table-2: RNase P Primer and Probe information

| Target | Sequence | |
|--------------------|------------|---|
| Human RNase P gene | Fwd Primer | 5'-AGATTTGGACCTGCGAGCG-3' |
| | Rev Primer | 5'-GAGCGGCTGTCTCCACAAGT-3' |
| | Probe | 5'-FAM/QUA-TTCTGACCTGAAGGCTCTGCGCG-BHQ-3' |

- TaqPath 1-Step RT-qPCR Master Mix, CG (ThermoFisher; cat # A15299 or A15300) store – 20 °C
- Molecular grade water, nuclease-free
- Disposable powder-free gloves
- P2/P10, P200, and P1000 aerosol barrier tips
- Sterile, nuclease-free 1.7 mL microcentrifuge tubes
- 0.2 mL PCR reaction tube strips or 96-well real-time PCR reaction plates and optical 8-cap strips

- Laboratory marking pen
- Cooler racks for 1.5 microcentrifuge tubes and 96-well 0.2 mL PCR reaction tubes
- Racks for 1.5 ml microcentrifuge tubes
- Acceptable surface decontaminants
 - ✓ RNase Away (Fisher Scientific; cat. #21-236-21 Store 25 °C)
 - ✓ 10% bleach (1:10 dilution of commercial 5.25-6.0% sodium hypochlorite)-make fresh weekly

B. IntelliQube Supplies

Array Tape (Douglas Scientific, IT768-13WP050)

Array Tape Seal (Douglas Scientific)

Greiner 96 well plate with full skirt (VWR, 82050-700, or equivalent)

Greiner 96 deep well plate (VWR, 82051-472)

CyBio Tips 384/40uL (OL 3810-25-231)

CyBio Tips 96/40µl (OL 3810-25-431)

Source of RO-DI Type 1 purified water (ELGA Option-Q)

C. Equipment

IntelliQube Real-time PCR detection system DS-IQ1804 (with IntelliQube® software version 1.13.3.0, Douglas Scientific®)

Central Pneumatic Air Compressor (60 gal, 5 HP, 165 PSI, Oil Lubricated)

ELGA Option-Q Water Purification System

Hand Pipettes (VWR or equivalent, 10-1000 µl)

Multichannel Pipettes (VWR or equivalent, P20 and P200)

PCR Plate Spinner (VWR, 89184-608)

Minifuges (VWR, Cat# C1413 or equivalent)

Racks for 1.5 ml, 0.5 ml microcentrifuge tubes

Refrigerators (4°C)

Freezers (both -20°C and -70°C)

PCR Work Station [UV lamp; Laminar flow (Class 100 HEPA filtered)]

Vortex mixers

Microcentrifuge, for 1.5 mL Eppendorf tubes

Nucleic Acid Extraction for the GENETWORx RNase P Assay

- Samples collected with the Genetworx Covid-19 Nasal swab test kit will be extracted using the Sbeadex extraction kit on the LGC Douglas oKtopure instrument.

Sbeadex Viral RNA extraction kit: Kit number NAP40-026-03 (storage temperature 25°C).

oKtopure liquid handling workstation Model name: oKtopure (KBS-0009-001)

PC with Liquid Handler software

Software version for oKtoPure Instrument: oKtopure software v8.6

b. APTIMA SARS-CoV-2 Assay

Aptima SARS-CoV-2 Assay Kit PRD-06419

For contents, see product insert (Aptima SARS-CoV-2 - Panther System, AW-21492-001 Rev. 005)

Table- 3

Aptima SARS-CoV-2 Refrigerated Box (Box 1 of 2)
(store at 2°C to 8°C upon receipt)

| Symbol | Component | Quantity 250 test kit |
|--------|--|--------------------------|
| A | Aptima SARS-CoV-2 Amplification Reagent <i>Non-infectious nucleic acids dried in buffered solution containing < 5% bulking agent.</i> | 1 vial |
| E | Aptima SARS-CoV-2 Enzyme Reagent <i>Reverse transcriptase and RNA polymerase dried in HEPES buffered solution containing < 10% bulking reagent.</i> | 1 vial |
| P | Aptima SARS-CoV-2 Probe Reagent <i>Non-infectious chemiluminescent DNA probes dried in succinate buffered solution containing < 5% detergent.</i> | 1 vial |
| IC | Aptima SARS-CoV-2 Internal Control | 1 vial |

Table- 4

Aptima SARS-CoV-2 Room Temperature Box (Box 2 of 2)
(store at 15°C to 30°C upon receipt)

| Symbol | Component | Quantity 250 test kit |
|--------|---|--------------------------|
| AR | Aptima SARS-CoV-2 Amplification Reconstitution Solution <i>Aqueous solution containing preservatives.</i> | 1 x 27.7 mL |
| ER | Aptima SARS-CoV-2 Enzyme Reconstitution Solution <i>HEPES buffered solution containing a surfactant and glycerol.</i> | 1 x 11.1 mL |
| PR | Aptima SARS-CoV-2 Probe Reconstitution Solution <i>Succinate buffered solution containing < 5% detergent.</i> | 1 x 35.4 mL |
| S | Aptima SARS-CoV-2 Selection Reagent <i>600 mM borate buffered solution containing surfactant.</i> | 1 x 108 mL |
| TCR | Aptima SARS-CoV-2 Target Capture Reagent <i>Buffered salt solution containing solid phase and capture oligomers.</i> | 1 x 54 mL |
| | Reconstitution Collars | 3 |
| | Master Lot Barcode Sheet | 1 sheet |

Materials Required But Not Provided

Aptima Assay Fluids Kit (Aptima Wash Solution, Aptima Buffer for Deactivation Fluid, and Aptima OilReagent) 303014 (1000 tests)
 Aptima Auto Detect Kit 303013 (1000 tests)
 Multi-tube units (MTUs) 104772-02
 Panther Waste Bag Kit 902731
 Panther Waste Bin Cover 504405

Or Panther Run Kit contains MTUs, waste bags, waste bin covers, assay fluids, and auto detects 303096 (5000 tests)

Tips, 1000 µL conductive, liquid sensing 10612513 (Tecan)

Aptima SARS-CoV-2 Controls Kit

PC - Aptima SARS-CoV-2 Positive Control. Non-infectious nucleic acid in a buffered solution containing < 5% detergent. Quantity 5 x 1.7 mL

NC - Aptima SARS-CoV-2 Negative Control. A buffered solution containing < 5% detergent. Quantity 5 x 1.7 mL PRD-06420

Aptima Multitest Swab Specimen Collection Kit PRD-03546

Bleach, 5% to 7% (0.7M to 1.0M) sodium hypochlorite solution

Disposable gloves (VWR)

Hologic Solid Cap for use with PRD-06554*, 100 caps per bag

Panther System Aptima SARS-CoV-2 Aptima SARS-CoV-2 - Panther System 16 AW-21492-001 Rev. 005

Aptima SARS-CoV-2 Assay Kit Configuration:

- **Negative and Positive Control Kit**
- 5 tubes of each control in the box (2°C to 8°C)
- Aptima SARS-CoV-2 Positive Control (5 x 1.7mL)
- Aptima SARS-CoV-2 Negative Control (5 x 1.7mL)
 - 1 Positive Control per Worklist
 - 1 Negative Control per Worklist
 - Not Master Lot Specific
 - Controls are single use only
 - Control results may be configured with up to 24 hours of validity
- **Stable for 30 days after reconstitution when stored at 15°C to 30°C**
 - Working Target Capture Reagent (wTCR)
- **Stable for 30 days after reconstitution when stored at 2°C to 8°C**
 - Enzyme Reagent
 - Amplification Reagent
 - Probe Reagent (Photosensitive) **Note:** Protect from light during storage and preparation for use.
- **Stable for 30 days after opening when stored at 2°C to 30°C**
 - Selection Reagent
- **Reagents are Stable for 72 hours when stored on-board the Panther system,**

Do not freeze reagents

CONTROLS

a. RNase P Assay Controls

Detection of the human RNase P gene is used to monitor the integrity of specimens collected

with the GENETWORx Covid-19 Nasal Swab Test Kit. Two assay controls are required to perform the GENETWORx RNase P Assay and must be tested with each batch of patient specimens:

- ❖ **NTC (No Template Control):** UltraPure DNase/RNase free water (ThermoFisher, Catalog # 10977015) used to monitor for cross-contamination during nucleic acid extraction and/or RT-PCR set-up.
 - NTC reaction should be negative and not exhibit fluorescence growth curves that cross the threshold line.
 - If a false positive result occurs with the RNase P primers and probe for NTC reactions, sample contamination may have occurred.
 - Invalidate the run and repeat the assay with stricter adherence to the procedure guidelines.
- ❖ **HSC (Human Specimen Control):** A COVID-19 negative human specimen prepared in a Multitest Aptima tube used to verify the integrity of nucleic acid extraction and RT-PCR amplification.
 - RNase P should be positive at or before 45 cycles for the HSC, thus indicating the presence of sufficient nucleic acid from the human RNase P gene. This validates the integrity of the reagents and extraction system.

b. Aptima Assay Controls

Aptima SARS-CoV-2 Controls Kit

PC - Aptima SARS-CoV-2 Positive Control. Non-infectious nucleic acid in a buffered solution containing < 5% detergent. Quantity 5 x 1.7 mL

NC - Aptima SARS-CoV-2 Negative Control. A buffered solution containing < 5% detergent. Quantity 5 x 1.7 mL PRD-06420

The APTIMA SARS-CoV-2 Assay is performed according to the manufacturer's instructions using the assay controls supplied with the kit. One Positive and one Negative Control must be processed each time a new kit is loaded onto the Panther System or when the existing controls have expired. An exogenous Internal Control is added to each sample prior to nucleic acid extraction to monitor specimen processing and nucleic acid amplification/detection. The Internal Control must be detected in all samples that are negative for SARS-CoV-2 in order for a negative test result to be reported.

INTERPRETATION OF RESULTS

All assay controls for the GENETWORx Covid-19 Nasal Swab Test will be evaluated and found to meet the specified acceptance criteria prior to interpretation of patient results. If the controls are not valid, patient results cannot be interpreted.

a. Interpretation of RNase P results and Sample Evaluation

- ❖ RNase P should be positive at or before 45 cycles for all clinical samples and the HSC, thus indicating the presence of sufficient nucleic acid from the human RNase P gene and that the specimen is of acceptable quality.
 - Failure to detect RNase P in HSC may indicate:
 - Improper assay set up and execution
 - Reagent or equipment malfunction
 - Detection of RNase P in HSC but failure to detect RNase P in any of the clinical samples may indicate:
 - Improper extraction of nucleic acid from clinical materials resulting in loss of nucleic acid or carry-over of PCR inhibitors from clinical specimens
 - Absence of sufficient human cellular material in the sample to enable detection
- ❖ Any samples that are reported invalid on an initial run need to be retested beginning with extraction. If the result from the rerun remains the same, the result is reported as Invalid.

Table-5: Interpretation of RNase P results and Sample Evaluation

| Control/Clinical Sample | Used to Monitor | RP | Expected Ct value | Expected QC Result/ interpretation |
|-------------------------|---|----|-------------------|---------------------------------------|
| NTC | Reagent and/or environmental contamination | - | None detected | Negative (no contamination) |
| HSC | Failure in lysis and/or extraction procedure | + | ≤45 Ct | Positive (Extraction step went well) |
| Sample | Sufficient Nucleic Acid from human RNase P gene (sample collection control) | + | ≤45 Ct | Positive (sample collection adequate) |
| | | - | >45 Ct | Negative (Retest or recollect sample) |

Final interpretation of the GENETWORx Covid-19 Nasal Swab Test

Final interpretation of the GENETWORx Covid-19 Nasal Swab Test will be determined based on the combined results of the GENETWORx RNase P Assay and APTIMA SARS-CoV-2 Assay using the following matrix given in Table-6.

Table-6. Interpretation of results from clinical specimens **

| APTIMA SARS-COV2 Result | RNase P Assay Result | Final Result Interpretation | Report | Actions |
|--------------------------------|-----------------------------|------------------------------------|---------------|---|
| Negative | Detected | SARS-COV-2 not detected | Negative | Report results to sender; Both positive and negative results should be reported to appropriate public health authorities. |
| Positive | Detected | SARS-COV-2 detected | Positive | Report results to sender; Both positive and negative results should be reported to appropriate public health authorities. |
| Negative | Not Detected | Invalid | Invalid | Recollection and Retest the sample |
| Positive | Not Detected | SARS-COV-2 detected | Positive | Report results to sender; Both positive and negative results should be reported to appropriate public health authorities. |
| Invalid | Detected/Not Detected | Invalid | Invalid | Recollection and Retest the sample |

**** Addition of the RNase P Assay result in the interpretation of the GENETWORx Covid-19 Nasal Swab Test is only intended to evaluate specimen adequacy.**

PERFORMANCE EVALUATION

Note: GENETWORx has obtained a Right of Reference from Hologic Inc. for the analytical and clinical validation information submitted to FDA with respect to Emergency Use Authorization of the Aptima SARS-CoV-2 Assay, including use of the Aptima Multitest Swab Collection Kit for specimen collection, transport and storage.

1) Shipping Study: sample stability study for GENETWORx Covid-19 Nasal swab Test

In order to perform the Shipping study, GENETWORx determined the LoD by serially diluting SARS-CoV-2 positive human nasopharyngeal (NP) specimens into Aptima Specimen Transport Medium and negative specimen matrix. The final LoD was determined to be 274 copies/mL. GENETWORx performed two shipping stability studies for the GENETWORx Covid-19 Nasal Swab Test Kit using both contrived positive and negative samples to demonstrate the stability of the SARS-CoV-2 RNA under summer and winter conditions.

To prepare the specimens for spiking, a SAR-CoV-2 positive nasopharyngeal specimen at

100,000 copies per mL was diluted in Aptima Specimen Transport Medium (STM) containing SARS-CoV-2 negative clinical matrix to the following concentrations:

- 274 copies (1x LoD) per mL
- 1370 copies (5x LoD) per mL

For each shipping condition,

- 20 contrived samples at 274 copies / mL (1x LoD, Low)
- 10 contrived samples at 1370 copies / mL (5x LoD, High)
- 10 Negative controls (SARS-CoV-2 negative clinical matrix in Aptima STM)

The samples were incubated as indicated in Table 7 (Summer Profile) and Table 8 (Winter Profile). The samples were tested at the end of the thermal profile only and were not tested at any other time point in the study.

Acceptance Criteria:

Low Positive Samples: $\geq 95\%$ agreement with expected results.

High Positive Samples: 100% agreement with expected results.

Negative Samples: 100% agreement with expected results.

Table 7: Summer Profile

| Temperature | Cycle Period | Cycle Period Hours | Total Time Hours |
|-------------|--------------|--------------------|------------------|
| 40°C | 1 | 8 | 8 |
| 22°C | 2 | 4 | 12 |
| 40°C | 3 | 2 | 14 |
| 30°C | 4 | 36 | 50 |
| 40°C | 5 | 6 | 56 |

Table 8: Winter Profile

| Temperature | Cycle Period | Cycle Period Hours | Total Time Hours |
|-------------|--------------|--------------------|------------------|
| -10°C | 1 | 8 | 8 |
| 18°C | 2 | 4 | 12 |
| -10°C | 3 | 2 | 14 |
| 10°C | 4 | 36 | 50 |
| -10°C | 5 | 6 | 56 |

Table 9: Summary of the results from the Shipping sample stability study

| Sample group | Sample profile | Total number of samples | Percent Positive (Aptima SARS-CoV-2) | Percent Positive (RNase P) |
|------------------------|----------------|-------------------------|--------------------------------------|----------------------------|
| Low Positive (1x LoD) | Summer | 20 | 100 (20/20) | 100 (20/20) |
| | Winter | 20 | 100 (20/20) | 100 (20/20) |
| High Positive (5x LoD) | Summer | 10 | 100 (10/10) | 100 (10/10) |
| | Winter | 10 | 100 (10/10) | 100 (10/10) |
| Negative | Summer | 10 | 0 (0/10) | 100 (10/10) |
| | Winter | 10 | 0 (0/10) | 100 (10/10) |

Both summer and winter shipping sample stability study results indicate that specimens will remain stable over a broad range of temperature conditions for up to 56 hours post collection (100% agreement with expected results for SARS-CoV-2 and RNase P) in the Aptima Specimen Transport Medium used in the GENETWORx Covid-19 Nasal Swab Test Kit.

2) Usability Study

GENETWORx performed a human usability study to evaluate whether patients could follow the instructions included in the GENETWORx Covid-19 Nasal Swab Test Kit. Briefly, 30 subjects of varying age, race, and gender participated in this study. All participants were at least 18 years or older and had a minimum high school diploma level of education. The participants' age, race, and gender distribution is given below.

Table 10: Age group distribution

| Age | Count |
|---------|-------|
| 18-35 | 23 |
| 35 - 50 | 5 |
| Over 50 | 2 |

Table 11: Gender distribution

| Gender | Count |
|--------|-------|
| Male | 11 |
| Female | 19 |

Table 12: Race distribution

| Race | Count |
|-------------|--------------|
| Black | 12 |
| White | 16 |
| Hispanic | 2 |

Participants collecting the nasal swab samples using GENETWORx Covid-19 Nasal Swab Test Kit were informed that the study would be recorded on video, and that the footage would be analyzed for the purposes of the study. Following enrollment, participants were invited to a private room where the home collection kits were placed on a table in advance. Each participant was asked to complete self-collection with each kit. At the end of the collection process, the participants were provided with an anonymous survey on their user experience. The results of the usability questionnaire response showed that 60-80% user found the IFU was effective for collecting samples while 10-20% were neutral or opined that the IFU could be further improved to facilitate proper sample collection.

The nasal swabs collected during the Usability Study were tested using GENETWORx RNase P Assay. The results were interpreted using the algorithm described in Table-5.

The RNase P results showed that 4/30 (13%) samples were RNase P negative. Upon review of the video recordings, GENETWORx noted that participants who methodically followed the specimen collection instructions obtained appropriate RNase P results but that the four subjects who had negative RNase P results did not appear to adhere to the expected sample collection procedure.

GENETWORx provided additional data from a clinical study showing 249/250 (99.6%) nasal samples collected by a healthcare provider were positive for RNase P, indicating that the GENETWORx RNase P assay performs as expected with samples that are collected appropriately. This low failure rate suggests that the high rate of RNase P negative results in the Usability Study was due to inadequate sample collection, rather than to the RNase P assay itself. To address this and help ensure that the Instructions for Use are clear and simple to follow, GENETWORx made the following additional modifications to align their Instructions for Use with those of other FDA-authorized nasal swab home collection kits:

Further Modifications to the Instructions for Use:

1. A photograph of the GENETWORx Covid-19 Nasal Swab Test Kit components was added.
2. Graphics revised for clarity and accuracy.
3. Opening and closing of the test vial and insertion of the swab into the test vial was clarified.
4. Handling of the biohazard bag was clarified.

5. Video instructions posted on GENETWORx's website to provide additional guidance. The video is available for viewing at:
<https://www.youtube.com/watch?v=ZBCIQVpobGI&feature=youtu.be>
6. Details of the kit activation and warning statement regarding the exposure to the specimen transport medium moved to front flap.
7. Photographs of the individual components of the GENETWORx COVID-19 Nasal Swab Test Kit were added to second flap.
8. An advisory statement regarding arrangement of the same-day FedEx pickup was added.
9. The steps for sample collection were separated into discrete bullets (only one action in each step).
10. The text size was increased.
11. The text instruction for each step was limited to a maximum of two lines.
12. One-column text format instead of three was adopted.
13. The text for the critical steps was bolded.
14. The graphics of the collection steps showing how far the swab should be inserted in the nostril were modified and revised to include a curved arrow indicating that the swab needs to be circled on the nostril walls.
15. Collection from each nostril was separated into discrete steps with opposite facing images for each nostril.
16. Additional hand washing steps were added.
17. Repackaging of the sample steps were further separated to provide more clarity.
18. GENETWORx' address and applicable regulatory information were added on the back flap.

In addition to making these changes, on March 25, 2021, GENETWORx also reported to the FDA an analysis of data from 655 samples that were prospectively collected at home using GENETWORx Covid-19 Nasal Swab Test Kit, of which 553 (84.4%) met the accessioning criteria for testing. Of the 102 samples that were rejected, 97 (95.1%) were expired at the time of receipt in the laboratory. Of the 553 samples that were accepted for testing, 550 (99.5%) (550/553) tested positive for RNase P and 6 (1.1%) were reported positive for SARS-CoV-2. These data confirmed that the changes GENETWORx made to the IFU were appropriate to ensure an adequate collection of nasal swab samples. GENETWORx will implement additional measures to prevent expiration of specimens prior to receipt in the laboratory and will submit the data for the FDA review.

In a supplement to the original EUA request, to accommodate use of the Aptima Direct Load Tube Collection Kit as an alternative to the Aptima Multitest Swab Kit as a component of the GENETWORx Covid-19 Nasal Swab Test Kit, and to prevent user confusion, GENETWORx updated the graphics of the collection tube in the Instructions For Use to show a white (generic, neutral color) label and a yellow cap.

FDA SARS-CoV-2 Reference Panel Testing

The evaluation of sensitivity and MERS-CoV cross-reactivity was performed using reference material (T1), blinded samples and a standard protocol provided by the FDA. The study included a range finding study and a confirmatory study for LoD. Blinded sample testing was used to establish specificity and to confirm the LoD. The Aptima SARS-CoV-2 Assay was run on the Hologic Panther instrument. For the RNase P assay, samples were extracted using the Sbeadex extraction kit on the LGC Douglas oKtopure instrument and amplified using the Douglas IntelliQube Real-time PCR detection system DS-IQ1804 (with IntelliQube[®] software version 1.13.3.0, Douglas Scientific[®]). The results are summarized in the following Table.

Table 13: Summary of LoD Confirmation Result Using the FDA SARS-CoV-2 Reference Panel

| Reference Materials Provided by FDA | Specimen Type | Product LoD | Cross-Reactivity |
|-------------------------------------|---------------|----------------------------|------------------|
| SARS-CoV-2 | Nasal Swab | 1.8x10 ⁴ NDU/mL | N/A |
| MERS-CoV | | N/A | ND |

NDU/mL: RNA NAAT detectable units/mL

N/A: Not Applicable

ND: Not Detected

LIMITATIONS:

- Detection of RNase P indicates that human nucleic acid is present and implies that human biological material was collected and successfully extracted and amplified. It does not necessarily indicate that the specimen is of appropriate quality to enable detection of SARS-CoV-2.
- The clinical performance has not been established in 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 SARS-CoV-2 and their prevalence, which change over time.

WARNINGS

- For Emergency Use Authorization (EUA) only.
- Caution: Federal Law restricts this device to sale by or on the order of a licensed practitioner.
- For *in vitro* diagnostic use.
- For prescription use.
- 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.
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens.
- 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 diagnostic tests for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetics Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.