510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K251753

B Applicant

Genabio Diagnostics Inc.

C Proprietary and Established Names

GenaCheck COVID-19 Rapid Self-Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QYT	Class II	21 CFR 866.3984 - Over-The-Counter Test To Detect SARS-Cov-2 From Clinical Specimens	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain 510k clearance for the GenaCheck COVID-19 Rapid Self-Test

B Measurand:

SARS CoV-2 nucleocapsid protein antigen

C Type of Test:

Qualitative lateral flow immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The GenaCheck COVID-19 Rapid Self-Test is a visually read lateral flow immunoassay test intended for the rapid, qualitative detection of SARS-CoV-2 virus nucleocapsid protein antigen directly in anterior nasal swab specimens from individuals with signs and symptoms of COVID-19.

This test is for non-prescription home use by individuals aged 14 years or older testing themselves, or adults testing individuals aged 2 years or older.

All negative results are presumptive. Symptomatic individuals with an initial negative test result must be re-tested once between 48 and 72 hours after the first test using either an antigen test or a molecular test for SARS-CoV-2. Negative results do not preclude SARS-CoV-2 infections or other pathogens and should not be used as the sole basis for treatment.

Positive results do not rule out co-infection with other respiratory pathogens.

This test is not a substitute for visits to a healthcare provider or appropriate follow-up and should not be used to determine any treatments without provider supervision. Individuals who test negative and experience continued or worsening COVID-19 like symptoms, such as fever, cough and/or shortness of breath, should seek follow up care from their healthcare provider.

The performance characteristics for SARS-CoV-2 were established from March 2024 to October 2024 when SARS-CoV-2 Omicron was dominant. Test accuracy may change as new SARS-CoV-2 viruses emerge. Additional testing with a lab-based molecular test (e.g., PCR) should be considered in situations where a new virus or variant is suspect.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The GenaCheck COVID-19 Rapid Self-Test Kit is a latex particle based immunochromatography test. The test is designed to detect nucleocapsid protein antigen in self-collected anterior nasal swab specimens from individuals who show symptoms of COVID-19 infection within the first five (5) days of symptom onset. The GenaCheck COVID-19 Rapid Self-Test Kit is validated for use from direct specimens testing without transport media.

The test package is composed of the following components:

- Test Cassette within a Foil Pouch
- Lysis Buffer
- Anterior Nasal Swab
- Quick Reference Instructions

The test cassette contains a test strip (binding pad) in a plastic housing. The binding pad is a nitrocellulose membrane with two regions: a test region (T) and control region (C). A schematic of the test device is shown in Figure 1.

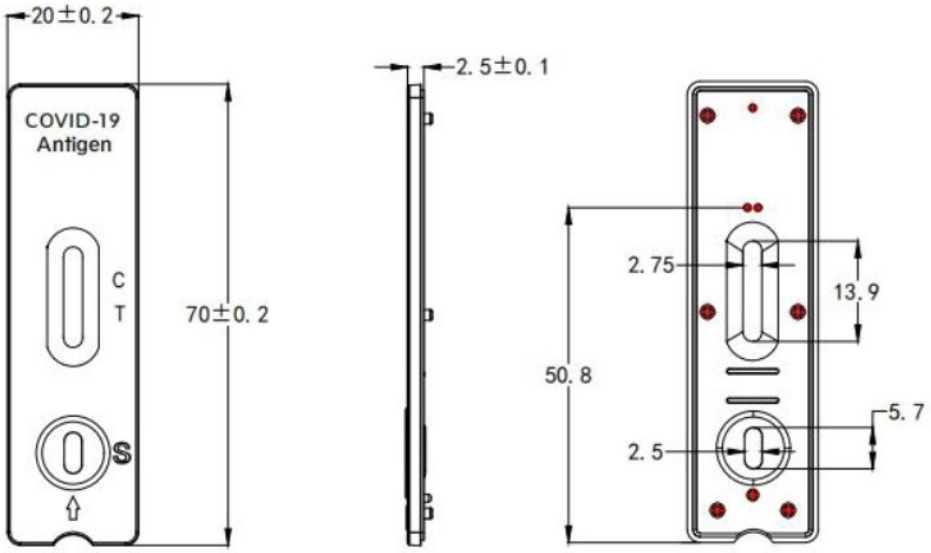


Figure 1: Schematic of Genabio Genacheck COVID-19 Test Cassette

B Principle of Operation:

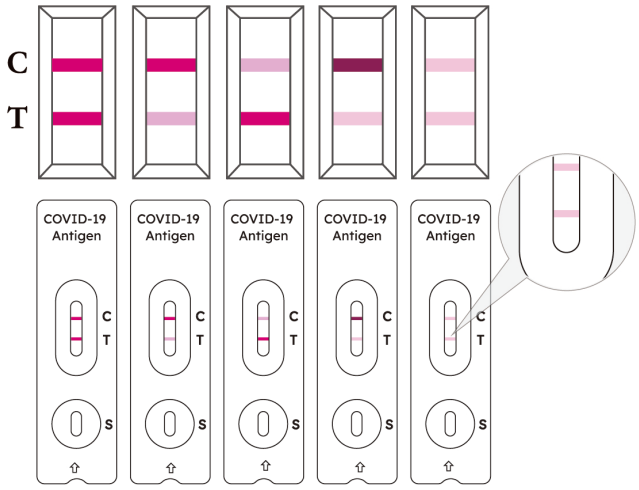
To perform the test, an anterior nasal swab is obtained by the lay user. Swabs can be self-collected by the user (age ≥14 years) or collected by an adult from another individual (age ≥2 years). For sample processing, the swab is first inserted into the lysis buffer during which the buffer disrupts the virus particles in the specimen, exposing internal viral nucleocapsid antigens. Three (3) drops of the lysed specimen are added to the sample well on the test cassette, which migrate from the sample well over the binding pad via capillary action.

The binding pad is coated with anti-SARS-CoV-2 antibodies which are labeled with a latex bead marker. The test region is coated with monoclonal anti-SARS-CoV-2 antibodies. The control region is coated with goat anti-mouse IgG antibodies. During testing, the anti-SARS-CoV-2 antibodies labeled with the latex bead marker form immune complexes with the antigen protein of the virus in the specimen, if present. The immune complexes move along the membrane via capillary action and are captured by the anti-SARS-CoV-2 monoclonal antibodies coated in the test region to form a visible pink colored line. The anti-SARS-CoV-2 antibodies or immune

complexes continue to move forward and specifically bind to the goat anti-mouse antibody coated in the control region to form a visible line with pink color.

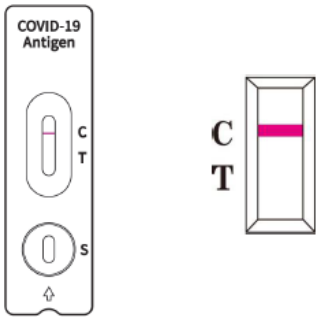
C Interpretation of Results

1. Positive Result



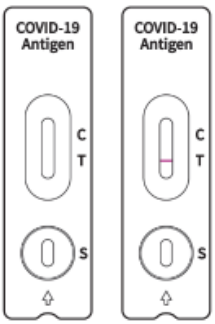
The Control line (C line) and Test line (T line) both appear as pink-colored lines in the window. A positive test result is interpreted as protein antigen from the virus that causes COVID-19 was detected in the specimen. The individual is likely positive for COVID-19. There is a very small chance that this test can give a positive result that is incorrect (a false positive).

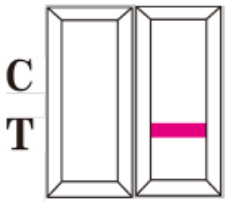
2. Negative Result



A negative test means that antigen from the virus that causes COVID-19 is not detected in the sample. Negative results do not rule out SARS-CoV-2 infection. Individuals without symptoms that test negative should be tested again within at least 24 hours and no more than 48 hours between tests. All negative results are considered presumptive, and confirmation with a molecular assay, if necessary for patient management, may be performed.

3. Invalid Result





If no line appears in the Control (C) area, the test result is invalid regardless of the presence or absence of a line in the Test (T) area. The test should be repeated with a new GenaCheck COVID-19 Rapid Self-Test.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Flowflex Plus COVID-19 Home Test

B Predicate 510(k) Number(s):

K233373

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251753	K233373
Device Trade Name	GenaCheck COVID-19 Rapid Self-Test	Flowflex Plus COVID-19 Home Test
General Device Characteristic Similarities		
Intended Use/Indications For Use	The GenaCheck COVID-19 Rapid Self-Test is a visually read lateral flow immunoassay test intended for the rapid, qualitative detection of SARS-CoV-2 virus nucleocapsid protein antigen directly in anterior nasal swab specimens from individuals with signs and symptoms of COVID-19. This test is for non-prescription home use by individuals aged 14 years or older testing themselves, or	The Flowflex Plus COVID-19 Home Test is a visually read lateral flow immunoassay device intended for the rapid, qualitative detection of SARS CoV-2 nucleocapsid protein antigens directly in anterior nasal (nares) swab specimens from individuals with signs and symptoms of COVID-19 within the first 6 days from symptom onset. This test is for non-prescription home use by individuals aged 14 years or older testing themselves, or adults testing individuals aged 2 years or older.

	adults testing individuals aged 2 years or older. All negative results are presumptive. Symptomatic individuals with an initial negative test result must be re-tested once between 48 and 72 hours after the first test using either an antigen test or a molecular test for SARS-CoV-2. Negative results do not preclude SARS-CoV-2 infections or other pathogens and should not be used as the sole basis for treatment. Positive results do not rule out co-infection with other respiratory pathogens. This test is not a substitute for visits to a healthcare provider or appropriate follow-up and should not be used to determine any treatments without provider supervision. Individuals who test negative and experience continued or worsening COVID-19 like symptoms, such as fever, cough and/or shortness of breath, should seek follow up care from their healthcare provider. The performance characteristics for SARS-CoV-2 were established from March 2024 to October 2024 when SARS-CoV-2 Omicron was dominant. Test accuracy may change as new SARS-CoV-2 viruses emerge. Additional testing with a lab-based molecular test (e.g., PCR) should be considered in situations where a new virus or variant is suspect.	The Flowflex Plus COVID-19 Home Test does not differentiate between SARS-CoV and SARS-CoV-2. All negative results are presumptive. Symptomatic individuals with an initial negative test result must be re-tested once between 48 and 72 hours after the first test using either an antigen test or a molecular test for SARS CoV-2 Negative results do not preclude SARS-CoV-2 infections or other pathogens and should not be used as the sole basis for treatment. Positive results do not rule out co infection with other respiratory pathogens. This test is not a substitute for visits to a healthcare provider or appropriate follow-up and should not be used to determine any treatments without provider supervision. Individuals who test negative and experience continued or worsening COVID-19 like symptoms, such as fever, cough and/or shortness of breath, should seek follow up care from their healthcare provider. The performance characteristics for SARS-CoV-2 were established from June 2022 to April 2023 when the COVID-19 variant Omicron was dominant. Test accuracy may change as new SARS-CoV-2 viruses emerge. Additional testing with a lab-based molecular test (e.g., PCR) should be considered in situations where a new virus or variant is suspected.
Target Analyte	SARS CoV-2 nucleocapsid antigen	Same
Specimen type	Anterior nasal swab samples	Same
Result interpretation	Visually read	Same
Test principle	Lateral flow immunoassay	Same
Result type	Qualitative	Same
Intended Use Setting	OTC	Same

General Device Characteristic Differences		
Time to Result	10-30 min	15-30 min

VI Standards/Guidance Documents Referenced:

Document	Title	Publisher	Applicable Study
ISO 11135:2014/A1:2018	Sterilization of health-care products - Ethylene oxide - Requirements for the development validation and routine control of a sterilization process for medical devices -	ISO	Sterility
ISO 10993-10:2021	Biological evaluation of medical devices - Part 10: Tests for skin sensitization	ISO	Biocompatibility
ISO 10993-23:2021	Biological evaluation of medical devices - Part 23: Tests for irritation	ISO	Biocompatibility
ISO 10993-7:2008	Biological evaluation of medical devices - Part 7: Ethylene Oxide Sterilization Residuals	ISO	Sterility
ISO 10993-5:2009	Biological evaluation of medical devices - Part 5: Tests for In vitro Cytotoxicity	ISO	Biocompatibility

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

a. Multi-Lot Precision

A precision study was conducted to evaluate variability across days, operators, and device lots. The study used a single internal site with two trained operators and three lots of test kits. Each day, three sample levels (Negative, 1.5 X LoD, and 3 X LoD) were tested with two replicates per run, per operator, and per kit lot. Two runs were conducted each day (at least four hours apart, typically morning and afternoon) by each operator with each lot. This exact testing scheme was followed for 12 days, with the same three sample levels tested across the same three lots by the same two operators in two runs per day, yielding a total of 864 tests (288 per level tested).

Samples with three concentrations of UV-inactivated SARS-CoV-2 virus material (USA-WA1/2020) were prepared by spiking the virus material into negative clinical matrix (NCM), resulting in the following sample types:

- Negative Sample
- Low Positive Sample at 1.5 X LoD
- Positive Sample at 3 X LoD

For the testing, a 50 µL volume of each sample was applied to dry nasal swabs. After blinding and randomization, samples were processed according to the Instructions for Use of the candidate device.

The results of this study are summarized in Table 1. All results matched the expected outcomes for the virus concentrations in the samples (all negative samples tested negative, all low positive and moderate positive samples tested positive). No variability was observed across different conditions, operators, lots, or days.

Table 1: Lot to Lot Precision Study Results

Analyte Concentration	Lot 1		Lot 2		Lot 3		Total Lot-to-Lot Precision		
	n/N	% Agmt	n/N	% Agmt	n/N	% Agmt	n/N	% Agmt	95% CI
Negative	96/96	100%	96/96	100%	96/96	100%	288/288	100%	98.7-100%
1.5X LoD	96/96	100%	96/96	100%	96/96	100%	288/288	100%	98.7-100%
3X LoD	96/96	100%	96/96	100%	96/96	100%	288/288	100%	98.7-100%

b. Supplemental Precision Study

This study was specifically conducted to further evaluate potential differences between distinct lots, because the initial precision study resulted in 100% agreement across all sources of variation and did not allow a conclusive assessment of lot-to-lot variability of the test. The study was performed using a negative sample, one low positive sample at 0.8 X LoD (i.e., below the concentration tested in the initial study, and near the analyte's C_{95} concentration) and one positive sample at 3 X LoD.

Testing was conducted using the same protocol as the preliminary study, with the exception that the NCM and 3 X LoD samples were only tested with one replicate per run, whereas the 0.8 X LoD samples were tested twice per run. For the negative and the 3 X LoD, samples the results were in 100% agreement with the expected result. Consistent with the analyte concentration of the low positive sample, the 0.8X LoD sample resulted in percent agreements less than 95%, with similar results for all lots. The results are summarized below in Table 2.

Table 2: Supplemental Lot-to-Lot Precision Study Results

Analyte Concentration	Lot 1		Lot 2		Lot 3		Total Lot-to-Lot Precision		
	n/N	% Agmt	n/N	% Agmt	n/N	% Agmt	n/N	% Agmt	95% CI
Negative	48/48	100%	48/48	100%	48/48	100%	144/144	100%	97.4-100%
0.8X LoD	77/96	80.2%	80/96	83.3%	81/96	84.4%	238/288	82.6%	77.8-86.6%
3X LoD	48/48	100%	48/48	100%	48/48	100%	144/144	100%	97.4-100%

2. Linearity:

Not applicable. This device is a qualitative, visually interpreted assay.

3. Analytical Specificity/Interference:

a. Cross Reactivity Microbial Interference

The analytical specificity of the GenaCheck COVID-19 Rapid Self-Test was evaluated by testing various microorganisms and viruses, for cross-reactivity (in the absence of SARS-CoV-2) and microbial interference (in the presence of SARS-CoV-2 at 3 X LoD, or 4.57 x 10^3 $TCID_{50}$/mL). Respiratory viral pathogens were tested at a final concentration of ≥1 x 10^5 units/mL, or at the highest available concentrations. Common respiratory bacterial and yeast pathogens were tested at a final concentration of ≥1 x 10^6 units/mL, or at the highest available concentrations. Each organism was assessed for potential cross-reactivity with the test antibodies by adding 50 µL of each sample directly to the test swab, followed by processing in accordance with the test's IFU. Three replicates per microorganism were tested in this study. Microbial interference testing was conducted similarly, with SARS-CoV-2 (USA-WA1/2020) co-spiked into the samples at 3 X LoD.

The results of these studies are summarized in Table 3. Neither cross-reactivity nor microbial interference was observed for any of the tested microorganisms at the concentrations used in the study.

Table 3: Cross Reactivity/Microbial Interference Study Results

Microbe Added	Concentration Tested	Cross Reactivity (Positive/Tested)	Microbial Interference (Positive/Tested)
Adenovirus Type 1	2.23E+05 TCID50/mL	0/3	3/3
Adenovirus Type 2	2.13E+06 TCID50/mL	0/3	3/3
Adenovirus Type 7A	1.58E+05 TCID50/mL	0/3	3/3
Bordetella pertussis	2.90E+08 CFU/mL	0/3	3/3
Candida albicans	1.21E+07 CFU/mL	0/3	3/3
Chlamydia pneumoniae	4.33E+06 IFU/mL	0/3	3/3
Enterovirus Type 68	2.23E+05 TCID50/mL	0/3	3/3
Haemophilus influenzae	9.68E+06 CFU/mL	0/3	3/3

Microbe Added	Concentration Tested	Cross Reactivity (Positive/Tested)	Microbial Interference (Positive/Tested)
Human coronavirus 229E	1.58E+05 TCID50/mL	0/3	3/3
Human coronavirus NL63	8.00E+04 TCID50/mL	0/3	3/3
Human coronavirus OC43	7.00E+05 TCID50/mL	0/3	3/3
Human Metapneumovirus	1.40E+05 TCID50/mL	0/3	3/3
Influenza A H1N1	1.85E+08 CEID50/mL	0/3	3/3
Influenza A H3N2	6.50E+06 FFU/mL	0/3	3/3
Influenza B Victoria	1.58E+05 TCID50/mL	0/3	3/3
Influenza B Yamagata	1.90E+06 TCID50/mL	0/3	3/3
Legionella pneumophila	6.50E+06 CFU/mL	0/3	3/3
MERS-coronavirus	1.40E+05 TCID50/mL	0/3	3/3
Mycobacterium tuberculosis avirulent	3.03E+06 CFU/mL	0/3	3/3
Mycoplasma pneumoniae	2.50E+07 CFU/mL	0/3	3/3
Parainfluenza virus 1	2.00E+05 TCID50/mL	0/3	3/3
Parainfluenza virus 2	1.40E+05 TCID50/mL	0/3	3/3
Parainfluenza virus 3	7.00E+05 TCID50/mL	0/3	3/3
Parainfluenza virus 4	2.39E+05 TCID50/mL	0/3	3/3
Pooled Nasal Wash	N/A	0/3	3/3
Respiratory syncytial virus Type A	3.50E+05 TCID50/mL	0/3	3/3
Respiratory syncytial virus Type B	2.29E+05 TCID50/mL	0/3	3/3
Rhinovirus 1A	7.05E+04 TCID50/mL	0/3	3/3
Rhinovirus B14	1.31E+05 TCID50/mL	0/3	3/3
SARS-CoV	1.25E+05 PFU/mL	0/3	3/3
Staphylococcus aureus	2.60E+08 CFU/mL	0/3	3/3
Staphylococcus epidermidis	9.00E+07 CFU/mL	0/3	3/3
Streptococcus pneumoniae	1.81E+07 CFU/mL	0/3	3/3
Streptococcus pyogenes	7.50E+07 CFU/mL	0/3	3/3
HKU1 clinical sample 1	Ct value: 31.8	0/3	3/3
HKU1 clinical sample 2	Ct value: 27.4	0/3	3/3
HKU1 clinical sample 3	Ct value: 23.1	0/3	3/3

b. Exogenous Endogenous Interference Studies

Thirty (30) potentially interfering substances were evaluated using the GenaCheck COVID-19 Rapid Self- Test. Each substance was tested in triplicate, both in the absence and presence of SARS-CoV-2 at 3 X LoD (4.57 x 10^3 $TCID_{50}$/mL). The results of this

study are summarized in Table 4. Among all the substances tested, hand sanitizer cream lotion was the only one to cause a false-positive result when tested at concentrations of 5% w/v or above. All other substances yielded expected results, indicating they do not impact the performance of the GenaCheck COVID-19 Rapid Self-Test at the concentrations specified.

Table 4:Exogenous/ Endogenous Interference Study Results

Interfering Substances Tested	Test Concentration	SARS-CoV-2 Negative Sample (Positive/Tested)	SARS-CoV-2 Positive Sample (Positive/Tested)
Throat Lozenges (Benzocaine, Menthol)	3 mg/mL	0/3	3/3
Sore Throat Spray (Phenol)	5% v/v	0/3	3/3
Mucin (Purified mucin protein)	2.5 mg/mL	0/3	3/3
Whole Blood (Human)	2.5% v/v	0/3	3/3
Leukocytes	2×10^6 cells/mL	0/3	3/3
Throat Spray (Zinc)	15% v/v	0/3	3/3
Nasal Drops (Phenylephrine)	15% v/v	0/3	3/3
Nasal Spray (Cromolyn)	15% v/v	0/3	3/3
Nasal Spray (Oxymetazoline)	15% v/v	0/3	3/3
Nasal Spray (Saline)	15% v/v	0/3	3/3
Nasal corticosteroids (Beclomethasone)	15% v/v	0/3	3/3
Nasal corticosteroids (Dexamethasone)	15% v/v	0/3	3/3
Nasal corticosteroids (Flunisolide)	15% v/v	0/3	3/3
Nasal corticosteroids (Triamcinolone)	15% v/v	0/3	3/3
Nasal corticosteroids (Budesonide)	15% v/v	0/3	3/3
Nasal corticosteroids (Mometasone furoate)	15% v/v	0/3	3/3
Nasal corticosteroids (Fluticasone propionate)	15% v/v	0/3	3/3
Nasal Spray (Zicam, Luffa opperculata, Galphimia glauca, Histaminum hydrochloricum)	15% v/v	0/3	3/3
Alkalol	15% v/v	0/3	3/3
Oseltamivir Phosphate (Tamiflu)	5 mg/mL	0/3	3/3
Remdesivir	10 mg/mL	0/3	3/3
Molnupiravir	10 mg/mL	0/3	3/3
Mupirocin	10 mg/mL	0/3	3/3
Nasal gel	5% v/v	0/3	3/3
Body Lotion (Dimethicone)	0.5% w/v	0/3	3/3
Hand Sanitizer (62% Ethyl alcohol)	5% v/v	0/3	3/3
Hand Sanitizer Cream Lotion* (Benzalkonium chloride)	5% w/v	3/3	3/3
Hand Sanitizer (80% Ethyl alcohol)	15% v/v	0/3	3/3
Hand Soap	10% w/v	0/3	3/3
Biotin	3,500 ng/mL	0/3	3/3

* Hand Sanitizer Cream Lotion was found to not interfere with testing at 1.67% w/v, giving negative results in 3 out of 3 replicates tested.

4. Assay Reportable Range:

Not applicable, qualitative assay.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

a. Controls

The GenaCheck COVID-19 Rapid Self-Test has a built-in internal procedural control. A built-in internal control is needed to indicate the test is working and is automatically run onboard within the development time of each test run. This procedural control consists of goat anti-mouse IgG antibodies and generates a colored line at the "C" marked control region of the test window. The control line should always appear to demonstrate that the test procedure was performed properly, reagents are working as intended, and for a result to be valid.

b. Stability

i. Shelf-life

The shelf-life of the GenaCheck COVID-19 Rapid Self-Test under the intended storage conditions (2-30℃) was assessed in a real-time stability study using three (3) lots of test kits stored at 2-8℃ and 30℃ and 85% Relative Humidity (RH). The test kits were assessed with negative samples (NCM) and contrived positive samples prepared at 3 X LoD (4.57E+03 $TCID_{50}$/mL) using SARS-CoV-2 (USA-WA1/2020). Replicate samples were generated by spiking 50µL of virus diluted in NCM onto dry swabs. For each lot, five replicates per time point per storage condition were tested. Data collected to date in this study (baseline, 14 days, 4 months, 7 months, 10 months, 14 and 18 months) supports a test kit shelf-life of 14 months when stored at the intended storage temperature of 2- 30°C at the time of clearance.

ii. Shipping Stability:

In order to evaluate the stability of the test kit under high temperature shipping conditions, kits from three lots were stored at: 60℃ with 85% ±5% relative humidity for periods from 1 to 8 days. The stored test kits were tested in five (5) replicates daily through the entire test system including the sample application and processing step for each storage condition. All negative samples tested negative; all positive samples (3 X LoD) tested positive over the 8-day time course.

In order to determine the effect of variable extreme temperature shipping conditions on the performance of the test, kits from three (3) different lots were subjected to three freeze thaw cycles and stored at or 55°C for periods of 7, 21, or 35 days. All negative samples tested negative; all positive samples (3 X LoD) tested positive in all storage conditions.

iii. Sample Stability:

Samples in the OTC environment will not undergo storage as the IFU instructs the user to immediately proceed from sample collection to the testing steps.

6. Detection Limit:

a. Limit of Detection (LoD)

The Limit of Detection (LoD) of the GenaCheck COVID-19 Rapid Self-Test was determined by evaluating different dilutions of heat-inactivated SARS-CoV-2 (isolate USA-WA1/2020) in NCM. The LoD was determined as the lowest virus concentration that was detected >95% of the time (e.g., concentration at which at least 19 out of 20 replicates tested positive). The limit of detection was established in two phases.

i. Preliminary LoD Study:

Five 10-fold serial dilutions were prepared from heat-inactivated SARS-CoV-2 virus into NCM. Five replicates of each serial dilution were tested to determine the preliminary LoD concentration of the device. The lowest concentration with 3/3 positive results from each lot was considered the preliminary LoD of the virus strain. For each replicate, 50 µl of the virus dilution was applied to the swab and the swab was processed according to the test's Instructions for Use. The results are summarized below in Table 5 below.

Table 5: Preliminary LoD Study Summary

Concentration ($TCID_{50}$/mL)	Positive Results (n/N)
4.57E+06 (Stock)	3/3
4.57E+05	3/3
4.57E+04	3/3
4.57E+03	**3/3**
4.57E+02	0/3
4.57E+01	0/3

ii. Confirmatory LoD Study:

The preliminary LoD concentration was tested with a total of twenty (20) replicates for each of 3 kit lots with at least two 2-fold dilutions tested below to demonstrate that the concentration above the LoD were 100% positive and the concentration below the LoD were <95% positive. The results are summarized in Table 6 below.

Table 6: Confirmatory LoD Study Summary

Concentration ($TCID_{50}$/mL)	Positive results (n/N)		
	Kit Lot 1	Kit Lot 2	Kit Lot 3
4.57E+03	20/20	20/20	20/20
1.52E+03	**20/20**	**20/20**	**20/20**
5.08E+02	0/20	2/20	0/20

The limit of detection for the GenaCheck COVID-19 Rapid Self-Test was determined to be 1.52 x 10^3 $TCID_{50}$/mL of sample and was achieved by all tested lots. This is equivalent to 7.6 X 10^1 $TCID_{50}$/swab.

b. International Standard for SARS-CoV-2 Antigen (NIBSC code: 21/368)

The LoD of the GenaCheck COVID-19 Rapid Self-Test was also determined by evaluating different dilutions of SARS-CoV-2 antigen (NIBSC code: 21/368) in negative clinical matrix (NCM). Two vials of SARS-CoV-2 Antigen (NIBSC 21/368) were reconstituted in 250 µL ultra-pure water each and then combined for testing one (1) lot of the GenaCheck COVID-19 Rapid Self-Test. The LoD was determined as the lowest virus concentration that was detected ≥95% of the time (i.e., concentration at which at least 19 out of 20 replicates tested positive). The limit of detection was established in two (2) phases.

i. Preliminary LoD Study

The SARS-CoV-2 antigen stock solution (concentration 2 x 10^4 IU/mL) was diluted 1:5, 1:10, and 1:20 into NCM. An addtional 2-fold series of dilutions was prepared from the 1:20 dilution to a level of 62.5 IU/mL (1:320). Three (3) replicates were tested for each dilution level. For each replicate, 50 µL of virus dilution was applied to a swab and the swab was processed according to the IFU. The lowest concentration with 3/3 positive results was considered the preliminary LoD (i.e., 250 IU/mL). The results are summarized below in Table 7.

Table 7: Preliminary LoD for SARS-CoV-2 Antigen (NIBSC code: 21/368)

Concentration of the International Standard (IU/mL)	Positive results (n/N)
20,000	3/3
4,000	3/3
2,000	3/3
1,000	3/3
500	3/3
250	**3/3**
125	0/3
62.5	0/3

ii. Confirmatory LoD Study

The NIBSC 21/368 material was tested at one 3-fold concentration above and one 3-fold concentration below the preliminary LoD concentration in 20 replicates for each. To confirm the preliminary concentration as the LoD, at least 19 of 20 replicates (95%) should be positive. The results of the confirmatory testing are summarized below in Table 8.

Table 8: Confirmatory LoD for SARS-CoV-2 Antigen (NIBSC code: 21/368)

Concentration of the International Standard (IU/mL)	Positive results (n/N)
750	20/20
250	**20/20**
83.3	0/20

The LoD for the GenaCheck COVID-19 Rapid Self-Test using the International Standard for SARS-CoV-2 antigen (NIBSC code: 21/368) in nasal matrix was confirmed

to be 250 IU/mL (12.5 IU/swab).

7. Assay Cut-Off:

   Not applicable. This is a qualitative, visually interpreted assay.

8. High Dose Hook Effect

   No high-dose hook effect was observed with a concentration of 4.57 x 10^6 $TCID_{50}$/mL of heat-inactivated SARS-CoV-2 virus tested the GenaCheck COVID-19 Rapid Self-Test which corresponded to ~3000X LoD.

9. Inclusivity (Analytical Reactivity)

   The analytical reactivity of the GenaCheck COVID-19 Rapid Self-Test was demonstrated by testing 10 additional human SARS-CoV-2 variants listed in Table 9 below. Each variant was serially diluted 3-fold in negative clinical matrix (NCM) and tested in triplicate. The minimum detectable level of each variant (lowest concentration at which all triplicates tested positive) is summarized in Table 9 below.

Table 9:Inclusivity Study Results

SARS-CoV-2 Variant	Minimum Detectable Level ($TCID_{50}$/mL)
SARS-CoV-2 Lineage B.1.1.7; Alpha Variant	1.18E+04
SARS-CoV-2 Lineage B.1.351; Beta Variant	1.88E+03
SARS-CoV-2 Lineage P.1 Brazil; Gamma variant	1.56E+03
SARS-CoV-2 Lineage B.1.617.2; Delta Variant	1.30E+03
SARS-CoV-2 Lineage XBB; Omicron Variant	7.35E+03
SARS-CoV-2 Lineage BA.2.3; Omicron Variant	1.44E+02
SARS-CoV-2 Lineage BA.5; Omicron Variant	8.15E+02
SARS-CoV-2 Lineage B.1.1.529; Omicron Variant	4.80E+01
SARS-CoV-2; Hong Kong/VM20001061/2020	5.19E+02
SARS-CoV-2; Italy-INMI1	3.93E+03

B Comparison Studies:

1. Method Comparison with Predicate Device:

   See Section C. Clinical Studies

2. Matrix Comparison:

   Not applicable, the test uses anterior nasal swabs only.

C Clinical Studies:

1. Clinical Sensitivity:

The performance of the GenaCheck COVID-19 Rapid Self-Test was compared to an FDA-cleared SARS-CoV-2 molecular assay in a prospective clinical study completed at nine (9) sites in the United States. Samples were collected by lay users from themselves or collected for a household member. A total of 678 subjects who were currently experiencing symptoms associated with COVID-19 were enrolled into the study. Of those, 643 were within 6 days of symptom onset (i.e., 5 days post symptom onset) and evaluable based upon the inclusion and exclusion criteria for analysis. The demographics of the enrolled clinical study subjects are summarized in Table 10 below.

Table 10: Clinical Study Demographics (All Enrolled Subjects)

Demographic characteristic	n (%)
Age Group	
2-13 years	103 (16.0%)
14-21 years	52 (8.1%)
22-64 years	403 (62.7%)
≥65 years	85 (13.2%)
Gender	
Male	249 (38.7%)
Female	394 (61.3%)
Education Level (Lay User)	
Grade 12 or GED	261 (40.6%)
Trade/tech/vocational	136 (21.1%)
Some college, no degree	105 (16.3%)
Bachelor's degree	97 (15.1%)
Graduate or professional	37 (5.8%)
Not reported	7 (1.1%)

An analysis based upon the comparator's Ct values estimates that the study cohort included 30.8 % low positive samples. The GenaCheck COVID-19 Rapid Self-Test detected SARS-CoV-2 with a Positive Percent Agreement (PPA) of 93.3% and a Negative Percent Agreement (NPA) of 98.7% in symptomatic individuals as compared to a highly sensitive FDA 510(k) cleared molecular SARS-CoV-2 assay. Results are provided in Tables 11 (overall) and 12 (broken down by DPSO).

Table 11: Clinical Study Results

GenaCheck Self-Test	Comparator Method		
	Positive	**Negative**	**Total**
Positive	112	7	119
Negative	8	516	524
Total	120	523	643
Positive Percent Agreement (PPA)	93.3% (112/120) (95% CI: 87.4%-96.6%)		
Negative Percent Agreement (NPA)	98.7% (516/523) (95% CI: 97.3%-99.4%)		

Table 12: Clinical Study Results by Days Past Symptom Onset (DPSO)

DPSO	TN[1]	FP[2]	TP[3]	FN[4]	Total	PPA	NPA
1	28	2	4	0	34	100% (51.0-100%)	93.3% (78.7-98.2%)
2	147	3	39	3	192	92.9% (81.0-97.5%)	98.0% (94.3-99.3%)
3	161	1	40	4	206	90.9% (78.8-96.4%)	99.4% (96.6-99.9%)
4	114	1	18	1	134	94.7% (75.4-99.1%)	99.1% (95.2-99.8%)
5	66	0	11	0	77	100% (74.1-100%)	100% (94.5-100%)
Total	**516**	**7**	**112**	**8**	**643**	**93.3% (87.4-96.6%)**	**98.7% (97.3%-99.4%)**

[1]TN: true negative; [2]FP: false positive; [3]TP: true positive; [4]FN: false negative

2. Usability Study:

A usability study was conducted to assess the lay users' ability to understand the instructions for use to adequately execute the GenaCheck COVID-19 Rapid Self-Test workflow accordingly. The study took place at a single clinical site, where lay users followed the IFU to complete the test and subsequently answered questionnaires about the test kit and testing process. The lay user's test process was observed and noted by a research staff member.

A total of 120 lay users (46% male, 54% female) with diverse ages and educational backgrounds participated in the study, including 106 who performed self-tests and 14 who tested children aged 2-13 years. All participants completed user comprehension questionnaires, which were divided into three sections: general questions about the test, questions about using the instruction documents, and questions about performing the test steps.

A total of thirteen (13) predefined tasks were rated by the observer for each study subject participating in the usability study. The usability study obtained an overall success rate of 99.6% (1555/1560 tasks) with almost all critical tasks exhibiting a success rate of 100%. Additionally, 89% of participants reported favorable responses (very easy and easy) and 11% reported neutral responses (OK) , regarding their ability to understand and follow the test's IFU.

3. Lay User Readability Study

The purpose of this study was to determine whether lay users could interpret test results correctly, especially with mock low positive samples from the GenaCheck COVID-19 Rapid Self-Test.

A total of 69 lay users with diversity in ages and educational background participated in the Readability Study. Twenty nine percent of the lay users exhibited some form of visual impairment. Each lay user was asked to interpret one of two panels of 4 mock test devices with three different concentrations (Negative, 1.5 X LoD, 1.5 X LoD, 5 X LoD) or (Negative, Negative, 1.5 X LoD, 5 X LoD).

The results are summarized in Table 13. Out of 276 mock device readings, one negative mock device was interpreted as invalid, and four low-positive mock devices (1.5 X LoD) were incorrectly read as negative. All moderate positive mock devices (5 X LoD) were interpreted correctly. Of the 5 incorrectly interpreted devices, 100% were read by study participants with vision impairment. Therefore, it is recommended that users with conditions affecting their vision, such as far-sightedness, glaucoma, or color blindness, are encouraged to seek assistance to interpret results accurately (e.g., reading glasses, additional light source, or another person). A related warning statement will be included in the labelling documents.

Table 13: Lay User Readability Study Results

Age Group	Negative (n/N)	Low positive (1.5X LoD) (n/N)	Positive (5X LoD) (n/N)	Total (n/N)
14-19	3/3	3/3	2/2	8/8
20-30	26/26	25/25	17/17	68/68
31-50	53/53	49/49	34/34	136/136
51-54	6/6	6/6	4/4	16/16
≥55	16/17	15/19	12/12	43/48
Total	**104/105**	**98/102**	**69/69**	**271/276**
% Agreement with Expected Results	99.0%	96.1%	100.0%	98.2%

D Clinical Cut-Off:

Not applicable, qualitative assay

E Expected Values/Reference Range:

Not applicable. A patient is expected to be negative for SARS CoV-2

F Other Supportive Study/Device Information

1. Flex Studies

   To assess the robustness of the GenaCheck COVID-19 Rapid Self-Test, flex studies were conducted that assessed all major aspects of the test procedure (e.g., sample volume, reading time, extraction buffer volume, swab elution time, and procedure) and variability of environmental test conditions that the test may be subjected to when in use (e.g., device orientation, lighting, various temperature, and humidity stress conditions). Testing was performed with contrived positive nasal swabs generated by diluting heat inactivated SARS-CoV-2 virus into NCM at 2 X LoD. The studies support that the test is robust in the intended use condition with an insignificant risk of erroneous result.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.