510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I. Background Information:

A 510(k) Number

K240728

B Applicant

CorDx, Inc.

C Proprietary and Established Names

CorDx Tyfast COVID-19 Ag Rapid Test; CorDx COVID-19 Ag Test

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QYT	Class II	21 CFR 866.3984 -	MI - Microbiology

II. Submission/Device Overview:

A Purpose for Submission:

To obtain a 510(k) clearance for the CorDx Tyfast COVID-19 Ag Rapid Test.

B Measurand:

Nucleocapsid protein antigen from SARS-Coronavirus 2 (SARS-CoV-2).

C Type of Test:

Qualitative lateral flow immunoassay.

III. Intended Use/Indications for Use:

A Intended Use(s):

The CorDx Tyfast COVID- 19 Ag Rapid Test is a visually read lateral flow immunoassay device 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.

The CorDx Tyfast COVID- 19 Ag Rapid 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 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 September, 2023, to December, 2023, 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 suspected.

B Indication(s) for Use:

See Intended Use above

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 CorDx Tyfast COVID-19 Ag Rapid Test is a manually performed and visually read lateral flow immunoassay device 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 when tested at least twice over three (3) days with at least 48 hours between tests. This test is for non-prescription home use by individuals aged 14 years or older testing themselves, or adults testing individuals aged two (2) years or older. This test does not differentiate between SARS-CoV and SARS-CoV-2.

B Principle of Operation:

The test strip enclosed in a cassette housing is comprised of the following components: sample pad, reagent pad, reaction membrane, and absorbing pad. The reagent pad contains colloidal-gold conjugated with a monoclonal antibody against the nucleocapsid protein of SARS-CoV-2; the reaction membrane contains the secondary antibody for the nucleocapsid protein of SARS-CoV-2. The whole strip is fixed inside a plastic cassette.

When the sample extract is added into the sample well, conjugates dried onto the reagent pad are dissolved and migrate along with the sample. If SARS-CoV-2 nucleocapsid antigen is present in the sample, a complex formed between the anti-SARS-2 conjugate and the viral antigen will be captured by the specific anti-SARS-2 monoclonal antibody coated on the test line region (T). Absence of the test line (T) suggests a negative result. To serve as a procedural control, a red line will always appear in the control line region (C) indicating that proper volume of sample has been added and membrane wicking has occurred.

The CorDx Tyfast COVID-19 Ag Rapid Test may give three possible outcomes, positive results, negative results, or an invalid test that would require retesting with a new device.

V. Substantial Equivalence Information:

A Predicate Device Name(s):

Flowflex COVID-19 Antigen Home Test

B Predicate 510(k) Number(s):

K230828

C Comparison with Predicate(s):

Device & Predicate Device(s):	**K240728**	**K230828**
Device Trade Name	**CorDx Tyfast COVID-19 Ag Rapid Test**	**Flowflex COVID-19 Antigen Home Test**
General Device Characteristic Similarities		
Intended Use/		The Flowflex COVID-19 Antigen

Device & Predicate Device(s):	K240728	K230828
Indications For Use	The CorDx Tyfast COVID- 19 Ag Rapid Test is a visually read lateral flow immunoassay device 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. The CorDx Tyfast COVID- 19 Ag Rapid 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 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 September, 2023, to December, 2024, when SARS-CoV-2 Omicron was dominant. Test accuracy may change as new SARS-CoV-2 viruses	Home Test is a visually read lateral flow immunoassay device 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 within the first 6 days of 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. The Flowflex COVID-19 Antigen 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 December 2022 to March 2023 when SARS- CoV-2 Omicron was dominant. Test accuracy may change as new SARS- CoV-2 viruses

Device & Predicate Device(s):	K240728	K230828
	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.	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.
Intended Use Setting	OTC	Same
Regulation Number	21 CFR 866.3984	Same
Classification Regulation	Class II	Same
Product Code	QYT	Same
Organism Detected	SARS-CoV-2	Same
Analyte	Nucleocapsid protein antigen from SARS-CoV-2	Same
Principle of the Technology	Qualitative lateral flow immunoassay	Same
Sample Type	Anterior nasal swab specimens	Same
Detection Format	Test cassette, visually read without an instrument.	Same
Assay Result	Qualitative (positive, negative, invalid)	Same
Reagent Storage	Store at 36~86°F/2~30°C	Same
Method to Obtain Result	Visually read by user	Same
General Device Characteristic Differences		
Development Time	10 minutes	15 minutes

The differences in the CorDx Tyfast COVID-19 Ag Rapid Test (the candidate device) and the ACON Flowflex COVID-19 Antigen Home Test (the predicate device, K230828) are limited and the biggest difference is the development time. These differences do not affect the overall substantial equivalence of the proposed device to the predicate device in terms of the technological similarity, intended use, safety and effectiveness.

VI. Standards/Guidance Documents Referenced:

Document Title	Issued by	Applicable study
Reclassification order for DEN220028 and special controls under 21 CFR 866.3984 for Over- the-counter tests to detect SARS-CoV-2 from clinical specimens	FDA/CDRH	All Studies
ISO11135:2014, Sterilization of health care products - Ethylene oxide - Requirements for development, validation and routine control of a sterilization process for medical devices	ISO	Sterility
ISO 10993-7, Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals	ISO	Sterility

Document Title	Issued by	Applicable study
ISO 10993-1, Biological Evaluation of Medical Devices – Part 1: Evaluation and testing within a risk management process	ISO	Biocompatibility
EP5-A3 Evaluation of Precision of Quantitative Measurement Procedures	CLSI	Precision
EP12-A2 User Protocol for Evaluation of Qualitative Test Performance	CLSI	Precision
EP25A Evaluation of Stability of In Vitro Diagnostic Reagents	CLSI	Reagent stability
EP37 Supplemental Tables for Interference Testing in Clinical Chemistry	CLSI	Interference

VII. Performance Characteristics:

A Analytical Performance:

1. Multi-lot Precision:

A precision study was conducted to assess variability with respect to days, operators, and device lots. The study included three device lots, each tested by two operators in triplicates for each sample concentration. The study was conducted over 10 consecutive days (i.e., 3 lots x 2 operators x 3 replicates x 10 days = 180 measurements/sample). Samples with three concentrations of heat inactivated SARS-CoV-2 virus material (Isolate: USA-WA1/2020) were generated by spiking the virus material into negative nasal wash matrix (NWM) as follows:

1. Negative Sample
2. Low Positive Sample at 2xLoD
3. Positive Sample at 4xLoD

50µL of each sample was applied to dry nasal swabs. After blinding and randomizing, samples were processed per the IFU of the candidate device. All results were concordant with the expected results for the virus concentrations of the samples (**Table 1**), and no variability was observed across the conditions, operators, lots, and days.

Table 1. Precision Study Summary Results.

Lot	Negative		Low Positive (2xLoD)		Positive (4xLoD)	
	Operator 1	Operator 2	Operator 1	Operator 2	Operator 1	Operator 2
230201	0/30	0/30	30/30	30/30	30/30	30/30
230202	0/30	0/30	30/30	30/30	30/30	30/30
230203	0/30	0/30	30/30	30/30	30/30	30/30
Total	0/90	0/90	90/90	90/90	90/90	90/90
Agreement	**NPA**	**NPA**	**PPA**	**PPA**	**PPA**	**PPA**
%	100	100	100	100	100	100
95%CI	95.91-100	95.91-100	95.91-100	95.91-100	95.91-100	95.91-100

2. Linearity:

Not applicable, the device is a binary qualitative assay that is visually read.

3. Analytical Specificity/Interference:

a. Cross-Reactivity and Microbial Interference

A panel of microorganisms commonly found as either pathogens or normal flora in respiratory samples were individually spiked into a negative clinical nasal wash matrix (NWM). The used matrix was supported by a matrix equivalency study and found to be equivalent to negative clinical nasal swab matrix. The organisms were then evaluated for their ability to cross-react with the antibodies of the test by adding 50µl of each sample directly to the test swab and then processing the sample swabs per the test's QRI. The study was performed with three replicates per microorganism.

Microbial Interference testing was done in the same manner but in the presence of SARS-CoV-2 (USA-WA1/2020) co-spiked into the samples at 3xLoD.

Table 2. Cross-Reactivity and Microbial Interference Testing Results.

Microorganism	Concentration Tested	Cross Reactivity Result	Interference Result
Human coronavirus 229E	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Human coronavirus OC43	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Human coronavirus NL63	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
MERS-coronavirus	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
SARS-coronavirus (Gamma-irradiated virus in Vero E6 cells in DMEM)	$1x10^5$ PFU/mL	0/3	N/A
SARS-coronavirus (Gamma-irradiated virus in PBS)	$1x10^7$ PFU/mL	0/3	3/3
Human Adenovirus 1	$1x10^6$ $TCID_{50}$/mL	0/3	3/3
Human Metapneumovirus 3 (hMPV-3) Type B1	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Parainfluenza virus – Type 1	$1x10^7$ $TCID_{50}$/mL	0/3	3/3
Parainfluenza virus – Type 2	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Parainfluenza virus – Type 3	$1x10^7$ $TCID_{50}$/mL	0/3	3/3
Parainfluenza virus – Type 4A	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Influenza A/Perth/16/09 (H3N2)	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Influenza A/California/07/09 (H1N1)	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Influenza B/Brisbane/60/08 (Victoria)	For Cross- reactivity: $4.68 x10^4$ $TCID_{50}$/mL For Interference: $2.34 x10^4$ $TCID_{50}$/mL	0/3	3/3
Influenza B/Wisconsin/01/10 (Yamagata)	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Enterovirus B111 2015 isolate	$1x10^6$ $TCID_{50}$/mL	0/3	3/3
Respiratory syncytial virus	$1x10^6$ $TCID_{50}$/mL	0/3	3/3
Rhinovirus Type 1A	$1x10^5$ $TCID_{50}$/mL	0/3	3/3
Haemophilus influenzae type b (Eagan)	$1x10^7$CFU/mL	0/3	3/3
Streptococcus pneumoniae Z022	$1x10^7$CFU/mL	0/3	3/3
Streptococcus pyogenes Z018	$1x10^7$CFU/mL	0/3	3/3
Candida albicans Z006	$1x10^7$CFU/mL	0/3	3/3

Microorganism	Concentration Tested	Cross Reactivity Result	Interference Result
Pooled human nasal wash – representative of normal respiratory microbial flora	NA	0/3	3/3
Bordetella pertussis A639	$1x10^7$ CFU/mL	0/3	3/3
Mycoplasma pneumoniae M129	$1x10^7$ CCU/mL	0/3	3/3
Chlamydia pneumoniae	$1x10^7$ IFU/mL	0/3	3/3
Legionella pneumophila Philadelphia	$1x10^7$ CFU/mL	0/3	3/3
Staphylococcus aureus MRSA; COL	$1x10^7$ CFU/mL	0/3	3/3
Staphylococcus epidermidis MRSE; PR62A	$1x10^7$ CFU/mL	0/3	3/3

Neither cross-reactivity nor microbial interference was observed for any of the tested microorganisms at the concentration used in the study.

An *in silico* analysis was performed for human coronavirus HKU1, and the lower respiratory pathogens *Mycobacterium tuberculosis* (TB), and Pneumocystis jirovecii to evaluate potential cross-reactivity/interference with these microorganisms in lieu of wet testing. The analysis did not identify significant homology between the SARS-CoV-2 Nucleocapsid protein and *Pneumocystis jirovecii* or *Mycobacterium tuberculosis*.

Homology was identified between the Nucleocapsid proteins of SARS-CoV-2 and Human Coronavirus HKU1. The highest homology was 39.1% for one segment within 76% of available sequences, and cross-reactivity/interference cannot be ruled out.

b. Endogenous / Exogenous Interfering Substances Study

Two separate studies to evaluate interference from endogenous and exogenous substances were performed.

Both studies had a similar study design using three device lots and triplicate measurements of samples contrived in NWM. Samples were contrived by individually adding the substances listed in **Table 3** below and testing with or without virus spiked into the sample. 50 µL of each contrived sample was applied to the head of a swab and processed per the IGU/QRI of the test. No false results were observed (**Table 3**).

Table 3. Endogenous / Exogenous Interfering Substances Summary Data

Potential Interfering Substance	Concentration	Without SARS-CoV-2	With SARS-CoV-2
No other substance	N/A	0/6*	6/6*
Whole Blood	4%	0/3	3/3
Mucin	0.5%	0/3	3/3
Chloraseptic (Menthol/ Benzocaine)	3mg/mL	0/3	3/3
Chloraseptic (Menthol/Benzocaine)	1.5 mg/mL	0/3	3/3
Naso GEL (NeilMed)	5% v/v	0/3	3/3
CVS Nasal Drops (Phenylephrine)	15% v/v	0/3	3/3
Afrin (Oxymetazoline)	15% v/v	0/3	3/3
CVS Nasal Spray (Cromolyn)	15% v/v	0/3	3/3
Zicam	5% v/v	0/3	3/3
Homeopathic (Alkalol)	10% v/v	0/3	3/3
Sore Throat Phenol Spray	15% v/v	0/3	3/3
Tobramycin	4 µg/mL	0/3	3/3
Mupirocin	10 mg/mL	0/3	3/3
HealthA2Z Fluticasone Propionate Nasal Spray	15% v/v	0/3	3/3
Fluticasone Propionate	5% v/v	0/3	3/3

Tamiflu (Oseltamivir Phosphate)	5 mg/mL	0/3	3/3
Chloraseptic (Menthol/ Benzocaine)	3mg/mL	0/3	3/3
Gericare Saline Nasal Spray (Sodium chloride with preservatives)	15% v/v	0/3	3/3
CVS Health Budesonide Allergy Nasal Spray (Budesonide)	15% v/v	0/3	3/3
Nasonex 24HR Allergy Nasal Spray (Mometasone)	15% v/v	0/3	3/3
Luffeel Nasal Spray (Luffa opperculata, Sulfur)	1.25% v/v	0/3	3/3
Boiron Galphimia glauca	15% v/v	0/3	3/3
Boiron Histaminum Hydrochloricum	15% v/v	0/3	3/3

*Conglomerate results from both independent studies.

4. Assay Reportable Range:

Not applicable, the device is a binary qualitative assay that is visually read.

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

a. Controls

Internal Control:

The CorDx Tyfast COVID-19 Ag Rapid Test has a built-in internal procedural control. A red line should always appear in the control line region (C) indicating that proper volume of sample has been added and that membrane wicking has occurred. The anti-SARS-CoV-2 antibodies are conjugated with colloid gold nanoparticles leading to the coloration of the C line.

External Controls:

This test is for OTC distribution. As such the test kits will not contain external controls as lay users are not required to perform external control testing. However, for professional use setting, the CorDx Tyfast COVID-19 Ag Rapid Test External Control Kit can be obtained separately as an accessory to the test.

b. Device Stability:

Real Time Stability (Shelf life):

The stability of the CorDx Tyfast COVID- 19 Ag Rapid Test was determined for the intended storage conditions, 2-30°C (36-86°F), and an intended shelf life of 24 months. Within one month of manufacture three device lots were transferred to five different temperatures (-20°C, 2°C, 15°C, 30°C and 40°C), where they were stored for 27 months. Testing of the kit lots was performed every 3 months with 5 replicates/timepoint, lot and test sample concentration. Two test samples, corresponding to 3.6xLoD and at 4.6xLoD, were tested at each time point. All study data were 100% concordant with expected results and thereby supportive of the 24 months shelf life at 2-30°C (36-86°F).

Shipping Stability:

The effects of shipping on the integrity of the test device were evaluated with three device lots that were manufactured within one month of study start. These were exposed to either cycles of temperature and humidity fluctuations or mechanical stress. Temperature cycles

included temperatures from -20 to +55°C with relative humidities between 20 and 90%, depending on the cycle. All results were concordant with expected results supporting stability during the anticipated shipping conditions for the test.

6. Detection Limits:

a. Limit of Detection (LoD):

The LoD study was performed in parallel with NWM and NSM to demonstrate the equivalency of both matrices. NWM was used in most of the analytical validation studies. In this study a heat inactivated SARS-CoV-2 virus culture fluid (Isolate: USA-WA1/2020; ZeptoMetrix) was spiked into the negative matrices, and samples were then diluted in 10-fold steps. 50µl of each dilution was added directly to the test swab and the swab samples processed per the QRI. The LoD was assessed with three device lots.

For the preliminary LoD study, testing was performed with five replicates per lot. The lowest concentration with >95% detection was then tested with 20 randomized replicates to confirm the LoD (**Table 4**). The LoD for both matrices was confirmed at $1x10^4$ $TCID_{50}$/ml with 57/60 (C_{95}) positive results, and both matrices were determined to be equivalent. This LoD was independently confirmed by a second study conducted as part of the ITAP program.

Table 4. LoD Study Summary - UV Inactivated SARS-CoV-2 (USA-WA1/2020)

Matrix	Concentration		Lot: 230201		Lot: 230202		Lot: 230203	
	$TCID_{50}$/ml	$TCID_{50}$/Swab	P	C	P	C	P	C
NWM	$1x10^7$	$5x10^5$	5/5	N/A	5/5	N/A	5/5	N/A
	$1x10^6$	$5x10^4$	5/5	N/A	5/5	N/A	5/5	N/A
	$1x10^5$	$5x10^3$	5/5	20/20	5/5	20/20	5/5	20/20
	$1x10^4$	**$5x10^2$**	**5/5**	**19/20**	**5/5**	**19/20**	**5/5**	**19/20**
	$1x10^3$	$5x10^1$	0/5	0/20	0/5	0/20	0/5	0/20
	$1x10^2$	5	0/5	N/A	0/5	N/A	0/5	N/A
	$1x10^1$	$5x10^{-1}$	0/5	N/A	0/5	N/A	0/5	N/A
NSM	$1x10^7$	$5x10^5$	5/5	N/A	5/5	N/A	5/5	N/A
	$1x10^6$	$5x10^4$	5/5	N/A	5/5	N/A	5/5	N/A
	$1x10^5$	$5x10^3$	5/5	20/20	5/5	20/20	5/5	20/20
	$1x10^4$	**$5x10^2$**	**5/5**	**19/20**	**5/5**	**19/20**	**5/5**	**19/20**
	$1x10^3$	$5x10^1$	0/5	0/20	0/5	0/20	0/5	0/20
	$1x10^2$	5	0/5	N/A	0/5	N/A	0/5	N/A
	$1x10^1$	$5x10^{-1}$	0/5	N/A	0/5	N/A	0/5	N/A

P: Preliminary Study. C: Confirmatory LoD Study.

b. NIBSC 21/368 – WHO International Standard

The sponsor tested the sensitivity of the test against the 1st WHO International Standard for SARS-CoV-2 antigen (NIBSC code: 21/368) spiked into NSM. The unitage of this material has an assigned value of 5,000 International Units of SARSCoV-2 antigen per ampoule when reconstituted per instructions. A 2-fold dilution series was made to determine the preliminary LoD, which was measured using one device lot and triplicate measurements (n=3). The measurements were done by adding 50µl of each dilution directly to the test swab and processing the sample per the test's QRI (**Table 5**). The preliminary LoD was determined to be 5x102 IU/ml.

The LoD confirmatory study was performed using 20 replicates (n=20) per dilution (**Table 5**). The lowest concentration at which a minimum of 95% of results were positive was confirmed to be $5x10^2$ IU/ml or $2.5x10^1$ IU/Swab.

Table 5. LoD Study Summary – 1st WHO International Standard for SARS-CoV-2 antigen (NIBSC code: 21/368)

Preliminary LoD		Confirmatory LoD	
Dilution (IU/ml)	**Results**	**Dilution (IU/ml)**	**Results**
$4x10^3$	3/3	N/A	N/A
$2x10^3$	3/3	N/A	N/A
$1x10^3$	3/3	$1.5x10^3$	20/20
$5x10^2$	**3/3**	**$5x10^2$**	**20/20**
$2.5x10^2$	1/3	$1.67x10^2$	8/20
$1.25x10^2$	0/3	N/A	N/A
$6.25x10^1$	0/3	N/A	N/A
$3.13x10^1$	0/3	N/A	N/A

7. Inclusivity

An evaluation of the sensitivity of the test for the detection of relevant SARS-CoV-2 variants was done by testing the detection limits of the test with seven heat inactivated virus variant reagents that show diverging mutations in the nucleocapsid protein. Specifically, variants B.1.1.7 (Alpha), P.1 (Gamma), B.1.595 (Gamma), B.1.351 (Beta), B.1.617.2 (Delta), B1.1.529 (Omicron), and XBB (Omicron). The virus reagents were spiked into NSM and serial diluted 2-fold in NSM were performed thereafter. Each dilution was tested with five replicates by adding 50µl contrived sample directly onto each test swab and processing the swab samples per the test's QRI. The number of positive replicates for the tested variants are shown in **Table 6** below with highlight on the lowest concentration that detected >95% of all replicates.

Table 6. LoD of SARS-CoV-2 Variants.

Concentration ($TCID_{50}$/ml)	B.1.1.7 (Alpha)	P.1 (Gamma)	B.1.595 (Gamma)	B.1.351 (Beta)	B.1.617.2 (Delta)	B1.1.529 (Omicron)	XBB (Omicron)
$1x10^5$	5/5	5/5	5/5	5/5	5/5	5/5	5/5
$5x10^4$	5/5	5/5	5/5	5/5	5/5	5/5	5/5
$2.5x10^4$	**5/5**	**5/5**	5/5	**5/5**	5/5	5/5	**5/5**
$1.25x10^4$	2/5	0/5	5/5	0/5	5/5	5/5	0/5
$6.25x10^3$	0/5	0/5	5/5	0/5	5/5	5/5	0/5
$3.13x10^3$	0/5	0/5	5/5	0/5	**5/5**	**5/5**	0/5
$1.56x10^3$	0/5	0/5	5/5	0/5	0/5	0/5	0/5
$7.81x10^2$	0/5	0/5	5/5	0/5	0/5	0/5	0/5
$3.91x10^2$	0/5	0/5	**5/5**	0/5	0/5	0/5	0/5
$1.95x10^2$	0/5	0/5	0/5	0/5	0/5	0/5	0/5

Beyond the testing described above, Omicron JN.1.1 was independently evaluated with the test showing detection down to an average Ct of 25.4 (139015.1 GE/ml).

As an extension of the inclusivity testing, a deep mutational screen was performed to identify amino acid residues in the SARS-CoV-2 nucleocapsid antigen that are critical for the paratope-epitope affinity for the antibodies used in the test. This knowledge will help identify future and emergent variants that may not be sufficiently detected by the test.

8. High Dose Hook Effect:

An assessment of whether a high dose hook effect exists for the test was done using a serial dilution of UV-inactivated SARS-CoV-2 virus (Stock concentration: $4.57x10^6$ $TCID_{50}$/ml). The virus was spiked into negative NWM, and 50µl of sample was added directly to the head of the swabs. Swabs were processed per the test's IFU/QRI. Testing was done across three device lots. Each of the 3 operators performed a single measurement for each concentration per lot (**Table 7**). No high dose hook effect was observed in the study, up to the maximum concentration tested herein.

Table 7. High Dose Hook Effect Data Summary.

Virus Concentration ($TCID_{50}$/ml)	xLoD	Results
$4.57x10^6$	365.6	3/3
$2.5x10^6$	200	3/3
$1.25x10^6$	100	3/3
$6.25x10^5$	50	3/3
$1.25x10^5$	10	3/3
$2.5x10^4$	2	3/3

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable. See "C. Clinical Studies" for performance comparison with a clinical comparator.

2. Matrix Comparison:

The CorDx COVID-19 Ag Test is only intended for use with direct anterior nasal swab specimens. As no other specimen or sample type is used with this device, a matrix comparison study to support other sample types for clinical testing with this device was not performed.

However, as part of the LoD study (see section VII. A. 6.a) the sponsor conducted a matrix equivalency study between pooled negative nasal swab matrix and the surrogate negative clinical nasal wash matrix (NWM) that was used in the analytical studies. The data demonstrated the equivalent performance of the test with both matrices.

C Clinical Studies:

1. Clinical Sensitivity and Specificity:

A prospective lay person clinical study was conducted to assess the performance of the candidate test in a simulated at-home setting when compared to a highly sensitive 510(k)-cleared SARS-CoV-2 RT-PCR assay with an extraction step. The study enrolled symptomatic subjects at four clinical study sites between September 09, 2023, and December 11, 2023, when Omicron was the most prevalent SARS-CoV-2 strain in the U.S.

Both, the comparator and the candidate test, used anterior nasal swab samples, and the collection order was alternated (randomized) by study subject. Comparator test samples were collected by health care professionals at the clinical study site and inserted into Universal Transport Media per the IFU of the comparator test. Samples for the candidate antigen test

were collected per the test's QRI and were either self-collected by a lay user aged ≥14 years or collected by an adult (parent/guardian) from individuals aged 2 to <14 years. 751 study subjects were enrolled in total, of which 740 subjects between 0 and 7 days post symptom onset (DPSO) had valid comparator test results and were evaluable per the study protocol. Detailed study subject demographics are listed below (**Table 8**).

Table 8: Demographics - Age Distribution and Education of the Clinical Study Cohort

Age group	Percent total	Total
2-13 years*	22%	163
14-21 years	9.1%	67
22-64 years	60.1%	445
≥65 years	8.8%	65
Total	**100%**	**740**

Education	Lay user	Total
<high school**	14.9%	110
High school	45.1%	334
Some college	16.5%	122
Associates	7.7%	57
Bachelor	12.4%	92
Master	1.4%	10
Professional Degree	0.1%	1
Doctorate	0.1%	1
Other	1.8%	13
Total	**100%**	**740**

*Tested by adult >14 years old per the intended use statement.
**32 users age 14 to <18 did not finish high school yet

The clinical performance estimates are based on 693 study subjects between 0 and 5 DPSO.

The clinical study included approximately 29% low positive samples based upon the comparator's Ct values. The CorDx Tyfast COVID-19 Ag Rapid Test detected SARS-CoV-2 with a Positive Percent Agreement (PPA) of 85.6% (95% CI: 78.1 - 90.8) and a Negative Percent Agreement (NPA) of 99.5% (95% CI: 98.5 - 99.8) when compared to the result of the SARS-CoV-2 RT-PCR comparator assay. Results are listed in the **Table 9** below.

Table 9. Clinical Performance Estimates

Candidate Test	Comparator Test		
	Positive	**Negative**	**Total**
Positive	101	3	104
Negative	17	572	589
Total	118	575	693
Positive Percent Agreement (PPA)		**85.6% (95% CI: 78.1 - 90.8)**	
Negative Percent Agreement (NPA)		**99.5% (95% CI: 98.5 - 99.8)**	

Table 10. Clinical Performance Stratified by DPSO

DPSO	TN	FP	TP	FN	Total	PPA	NPA
0	14	0	7	0	21	100	100
1	107	1	15	1	124	93.8	99.1
2	182	0	23	3	208	88.5	100
3	143	1	25	9	178	73.5	99.3
4	98	1	17	1	117	94.4	99
5	28	0	14	3	45	82.4	100
Total	**572**	**3**	**101**	**17**	**693**	**85.6**	**99.5**

Table 11. Clinical Performance Stratified by Age

Age Bin	TN	FP	TP	FN	Total	% of Study Cohort	PPA [%]	PPA [%]
0-14	142	1	20	4	167	24.1	83.3	99.3
14-25	62	0	16	3	81	11.7	84.2	100
25-35	89	0	10	2	101	14.6	83.3	100
35-45	72	2	18	3	95	13.7	85.7	97.3
45-55	76	0	22	0	98	14.1	100	100
55-65	80	0	8	5	93	13.4	61.5	100
65-110	51	0	7	0	58	8.4	100	100
Total	572	3	101	17	693	100	85.6	99.5

2. Usability

The usability of the test was assessed by observers as part of the clinical study. The observers recorded the proper execution of each task described in the QRI when the enrolled lay user study subject (n=751) conducted the test in the simulated at-home setting (**Table 12**). The observers did not otherwise interfere with the study subject's sample collection and testing. The acceptance criterion for critical tasks is ≥90% correct execution, and ≥80% for non-critical tasks.

Table 12. Usability Study Results

Procedural Step	Critical/Non-Critical	Risk	% Correct Execution	
Wash or sanitize hands prior to testing	NC	Low	61.8% (462/748)	FAIL
Check test expiration date	C	Medium	71% (531/748)	FAIL
Place the test device on a flat surface	NC	Low	98.1% (734/748)	PASS
Remove the swab from the packaging without touching the swab head	C	High	99.3% (743/748)	PASS
Swab both nostrils, at least 5 times in each nostril	C	High	96.1% (719/748)	PASS
Insert swab into the extraction buffer	C	High	99.6% (745/748)	PASS
Stir the swab at least 10 times	C	Medium	94.8% (709/748)	PASS
Squeeze both sides of the tube applying pressure on both sides of the tube while removing the swab	NC	Low	79.1% (592/748)	FAIL
Seal the tube securely with the nozzle cap	C	Medium	98.3% (735/748)	PASS
Add 3 drops to the sample well	C	Medium	95.9% (717/748)	PASS
Read the results between 10 and 30 minutes	C	Medium	96.7% (723/748)	PASS
Did the subject perform any other errors in completing the study procedures?	N/A	N/A	98.4% (736/748)	PASS

3. Readability and Comprehension:

A readability and comprehension study with lay persons was conducted as part of the clinical study to evaluate the ability of the intended lay user to use read low positive results and their ability to interpret the test results. 104 study participants across three study sites of the clinical study were enrolled in the readability and comprehension study. Each study subject

was provided with five randomized mock tests of different concentration, which they were asked to interpret per the test's QRI (**Table 13**). The mock tests were either Invalid, Negative, 1.9xLoD Positive, or 5xLoD Positive. After interpreting the mock tests, the study subjects were provided with a questionnaire to assess their comprehension of the test results.

Table 13. Mock Test Interpretation Summary Results

	Concentration	**TN**	**FN**	**TP**	**FP**	**TI**	**FI**	**Total**	**NPA**
Negative	N/A	148	N/A	N/A	2	N/A	2	152	97.4%
	Concentration	**TN**	**FN**	**TP**	**FP**	**TI**	**FI**	**Total**	**PPA**
Positive	1.9x	N/A	5	154	N/A	N/A	1	160	96.3%
	5x	N/A	1	102	N/A	N/A	1	104	98.1%
	Concentration	**TN**	**FN**	**TP**	**FP**	**TI**	**FI**	**Total**	**IPA**
Invalid	N/A	N/A	7	N/A	0	97	N/A	104	93.3%

D Clinical Cut-Off:

The test is a qualitative test with a binary positive/negative signal and does not provide quantitative raw data. There is no clinical cutoff for the presence of SARS-CoV-2 in patient samples. Analyte negative samples must not have any visible signal at the test lines.

E Expected Values/Reference Range:

When the test is valid, it produces binary values, positive or negative for SARS-CoV-2 antigens. Patient samples are expected to be negative for SARS-CoV-2

F Other Supportive Performance Characteristics Data:

1. OTC Flex Studies:

   To assess the robustness and risk for false results of the test when deviating from the IFU/QRI test steps, flex studies were conducted that assessed all major aspects of the test procedure (sample volume, reading time, swab extraction time and procedure [swab rotation and tube squeezing], bubbles in the reagent tube, sample hold time before and during processing) and variability of environmental test conditions that the test may be subjected to when in use (lighting, disturbance during use, temperature and humidity stress conditions). Testing was performed with contrived positive nasal swabs generated by diluting SARS-CoV-2 virus into negative NWM at 2xLoD.

   False results were observed with too little sample volume and insufficient incubation time, specifically with less than two drops of sample and with less than eight minutes incubation. The studies support that the test is robust in the intended use condition with an insignificant risk of erroneous result.

2. Serial Testing:

   As a mitigation for the lower sensitivity of the device after Day 5 of symptom onset, the Intended Use for this test device (and associated Instructions for Use) includes recommendations for repeat testing (i.e., test at least twice over three days with at least 48 hours between tests). Although the data, when stratified by symptom onset have performance estimates with insufficient statistical confidence, the clinical study data set of this and similar studies for test devices of a similar principle and design, indicate that such mitigation is

needed. This mitigation is supported by data generated by the National Institutes for Health (NIH) and the University of Massachusetts Chan Medical School (in collaboration with the FDA) demonstrating that repeat testing over multiple days improves test performance and increases the likelihood that a COVID-19 antigen test will accurately detect an infection. These results have informed the FDA's general understanding that repeat testing after a negative result from a COVID-19 antigen test reduces the risk of a false negative result. Please refer to the following studies for additional details:

- Finding a Needle in the Haystack: Design and Implementation of a Digital Site-less Clinical Study of Serial Rapid Antigen Testing to Identify Asymptomatic SARS-CoV-2 Infection - https://www.medrxiv.org/content/10.1101/2022.08.04.22278274v1
- Performance of Screening for SARS-CoV-2 using Rapid Antigen Tests to Detect Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infection: findings from the Test Us at Home prospective cohort study - https://www.medrxiv.org/content/10.1101/2022.08.05.22278466v1

3. Variant Monitoring Plan:

The sponsor established a variant monitoring plan for the Tyfast COVID-19 Ag Rapid Test to ensure the continued performance of the test device with future SARS-CoV-2 variants. Specifically, CorDx plans the continuous surveillance of emerging SARS-CoV-2 Variants of Interest (VOI), particularly those exceeding a 1% frequency threshold through monitoring weekly updates on VOI prevalence and cross-referencing with CDC and CovMT data to identify any variants posing a public health risk above 5%.

If clinically significant variants are identified with mutations in the nucleocapsid protein, the impact on device performance will be assessed through wet testing. In the absence of mutations in the nucleocapsid protein, it will be concluded that the test's clinical performance remains unaffected. Clinical or appropriate contrived samples from identified VOIs will be obtained for wet testing, where available, in partnerships with Axteria BioMed Consulting Inc. and Cleardx Labs, Inc.

Testing will follow the protocol established through the validation of the test. The impact on the test's analytical sensitivity will be determined, and if significant changes are detected these will be reported to FDA and all stakeholders. Additionally, the Instructions for Use (IFU) will be revised to reflect the performance metrics with these variants.

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.