510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K253882

B Applicant

CorDx, Inc.

C Proprietary and Established Names

CorDx Tyfast COVID-19 Ag Rapid Test Rx

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QVF	Class II	21 CFR 866.3982 - Simple Point-Of-Care Device To Directly Detect Sars-Cov-2 Viral Targets From Clinical Specimens In Near-Patient Settings	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for the CorDx Tyfast COVID-19 Ag Rapid Test Rx.

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):

See Indications for Use below.

B Indication(s) for Use:

The CorDx Tyfast COVID-19 Ag Rapid Test Rx is a visually read lateral flow immunoassay intended for the rapid, qualitative detection of SARS-CoV-2 nucleocapsid protein antigen directly in anterior nasal swab specimens from individuals with signs and symptoms of upper respiratory tract infection. The test is intended for use as an aid in the diagnosis of SARS-CoV-2 infections (COVID-19) in symptomatic individuals when either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the CorDx Tyfast COVID-19 Ag Rapid Test Rx and followed up with a molecular test.

A negative test result is presumptive and does not preclude SARS-CoV-2 infection; it is recommended these results be confirmed by a molecular SARS-CoV-2 assay.

Positive results do not rule out co-infection with other respiratory pathogens and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Performance characteristics for SARS-CoV-2 were established from September 2023 to December 2023, when SARS-CoV-2 Omicron was dominant. When other SARS-CoV-2 virus variants are emerging, performance characteristics may vary.

Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IVD - For In Vitro Diagnostic Use

C Special Instrument Requirements:

Not applicable

IV Device/System Characteristics:

A Device Description:

The CorDx Tyfast COVID-19 Ag Rapid Test Rx is a visually read, rapid immunochromatographic assay that uses monoclonal antibodies to detect SARS-CoV-2 nucleocapsid protein antigen in anterior nasal swab specimens from individuals with signs and symptoms of upper respiratory tract infection. This device is intended for prescription use only by healthcare professionals. 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.

Test Kit Component:

CorDx Tyfast COVID-19 Ag Rapid Test Rx is available in three (3) different configurations. See Table 1 below for the contents of the CorDx Tyfast COVID-19 Ag Rapid Test Rx Kit in each configuration.

Table 1. Materials Provided with the Commercial Test Kit

Reagent/Materials	Test Kit Components		
	2 tests/kit	10 tests/kit	25 tests/kit
Test cassette	2	10	25

Swab	2	10	25
Tube with sample processing solution	2	10	25
Tube holder (back of box)	2	2	2
Instructions for use	/*	/*	/*
Quick reference guide	1	1	1
Positive control swab	/	/	/**
Negative control swab	/	/	/**

* ***A link for full Instruction for use is provided as QR code in QRG.***

/** ***External controls are not included with the test kits. The 25 test kit configuration is available in two versions, each assigned a distinct reference number, allowing end users to select their preferred option at the time of purchase — either with or without one pair of optional external controls.***

External Control Kit Component:

The CorDx Tyfast COVID-19 Ag Control Swab Kit is a ready-to-use external control kit for use with the CorDx Tyfast COVID-19 Ag Rapid Test Rx. See Table 2 below for the contents of the CorDx Tyfast COVID-19 Ag Control Swab Kit.

Table 2. Materials Provided in the Commercial Control Kit

Reagent/Material	Quantity	Description
Positive Control Swab	10	The positive control swab contains SARS-CoV-2 antigen (non-infectious recombinant antigen)
Negative Control Swab	10	The negative control swab contains negative sample matrix (nasal cavity wash)
Package Insert	1	Instructions for use

B Principle of Operation:

Upon introduction of the sample extract into the sample well, the sample reconsitutes the conjugates dried onto the reagent pad and migrate them along the membrane. 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 Rx may give three possible outcomes, a positive, negative, or an invalid result that would require retesting with a new device.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Nano-Check COVID-19 Antigen Test

B Predicate 510(k) Number(s):

K231187

C Comparison with Predicate(s):

Device & Predicate Device(s):	K231187	K253318
Device Trade Name	Nano-Check COVID-19 Antigen Test	CorDx Tyfast COVID-19 Ag Rapid Test Rx
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Nano-Check COVID-19 Antigen Test is a lateral flow immunochromatographic assay for the rapid, qualitative detection of SARS-CoV-2 nucleoprotein protein antigens directly in anterior nasal swab specimens from individuals with signs and symptoms of upper respiratory infection (i.e., symptomatic) when testing is started within 4 days of symptom onset. The test is intended for use as an aid in the diagnosis of SARS-CoV-2 infections (COVID-19) in symptomatic individuals when either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the Nano-Check COVID-19 Antigen Test and followed up with a molecular test. The test does not differentiate between SARS-CoV or SARS-CoV-2. A negative test result is presumptive, and it is recommended these results be confirmed by a molecular SARS-CoV-2 assay. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Performance characteristics for SARS-CoV-2 were established during the 2022-2023 SARS-CoV-2 pandemic when SARS-CoV-2 Omicron was the predominant SARS-	The CorDx Tyfast COVID-19 Ag Rapid Test Rx is a visually read lateral flow immunoassay intended for the rapid, qualitative detection of SARS-CoV-2 nucleocapsid protein antigen directly in anterior nasal swab specimens from individuals with signs and symptoms of upper respiratory tract infection. The test is intended for use as an aid in the diagnosis of SARS-CoV-2 infections (COVID-19) in symptomatic individuals when either: tested at least twice over three days with at least 48 hours between tests; or when tested once, and negative by the CorDx Tyfast COVID-19 Ag Rapid Test Rx and followed up with a molecular test. A negative test result is presumptive and does not preclude SARS-CoV-2 infection; it is recommended these results be confirmed by a molecular SARS-CoV-2 assay. Positive results do not rule out co-infection with other respiratory pathogens and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Performance characteristics for SARS-CoV-2 were established from September 2023 to December 2023, when SARS-CoV-2 Omicron was dominant. When other SARS-CoV-2 virus variants are emerging, performance characteristics may vary.

	CoV-2 variant in circulation. When other SARS-CoV-2 virus variants are emerging, performance characteristics may vary.	
Regulation Number	21 CFR 866.3982	Same
Regulatory Class	Class II	Same
Product Code	QVF	Same
Target population	Individuals with signs and symptoms respiratory tract infection	Same
Sample type	Anterior nasal swab specimens	Same
Analyte	SARS-CoV-2 nucleocapsid protein	Same
Test type	Lateral flow immunoassay	Same
Test result	Qualitative (positive, negative, invalid)	Same
Detection format	Test cassette, visually read	Same
General Device Characteristic Differences		
Reading time	15 - 30 minutes	10-30 minutes

VI Standards/Guidance Documents Referenced:

Document	Title	Publisher	Applicable study
21 CFR 866.3982	Simple Point-Of-Care Device to Directly Detect Sars-Cov-2 Viral Target From Clinical Specimens In Near-Patient Setting	FDA	All
11135:2014	Sterilization of health care products - Ethylene oxide - Requirements for development, validation and routine control of a sterilization process for medical devices	ISO	Sterility
10993-7	Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals	ISO	Sterility
10993-1	Biological Evaluation of Medical Devices – Part 1: Evaluation and testing within a risk management process	ISO	Biocompatibility
10993-5	Biological Evaluation of Medical Devices - Tests for in vitro cytotoxicity	ISO	Biocompatibility

Document	Title	Publisher	Applicable study
10993-10	Biological Evaluation of Medical Devices –Tests for irritation and skin sensitization	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. Precision/Reproducibility:

a. Multi-Lot Precision Study:

A precision study was conducted to assess variability across days, operators, and device lots. Over ten (10) consecutive days, two (2) operators tested three (3) device lots in triplicates. Testing utilized three analyte concenterations: two distinct concentrations of contrived UV-inactivated SARS-CoV-2 into negative pooled nasal wash matrix (PNWM) and one unspiked PNWM sample as presented below. The matrix used was supported by a matrix equivalency study and found to be equivalent to negative clinical nasal swab matrix. A total of 60 results were obtained per concentration per device lot.

1. Negative Sample
2. Low Positive Sample at 2x LoD
3. Positive Sample at 4x LoD

50 µL of each sample was applied to dry nasal swabs, and after blinding and randomizing, samples were processed per the IFU of the candidate device. All replicates prepared at each concentration demonstrated 100% agreement with the expected results. The results from precision study are summarized below.

Table 3. Precision Study Summary Results

Sample	# of positive result/# of total tested (% positive rate)			Total sample count (% positive rate)
	Lot 1	Lot 2	Lot 3	
True negative	0/60 (0.0%)	0/60 (0.0%)	0/60 (0.0%)	0/180 (0.0%)

Low positive (2x LoD)	60/60 (100.0%)	60/60 (100.0%)	60/60 (100.0%)	180/180 (100.0%)
Moderate positive (4x LoD)	60/60 (100.0%)	60/60 (100.0%)	60/60 (100.0%)	180/180 (100.0%)

b. Multi-Site Reproducibility Study:

A reproducibility study was conducted to evaluate the performance of the candidate device across multiple sites, operators, days, and test lots. The study was performed at three (3) CLIA-waived clinical sites. Six (6) untrained operators tested a total of 360 blinded, contrived anterior nasal swab samples over five (5) non-consecutive days using three (3) investigational test lots. Samples were prepared by spiking pooled human pooled nasal swab matrix (PNSM) using the heat-inactivated SARS-CoV-2-omicron variant (LoD established at 9.9 X 10^3 $TCID_{50}$/mL) at four concentration levels — true negative, high negative (0.1× LoD), low positive (1× LoD), and moderate positive (3.5× LoD) — with each operator testing samples in triplicate per panel.

Each diluted sample (50 µL) was directly applied onto the sample collection swab head. True negative swab samples were prepared by applying 50 µL of negative PNSM directly onto the sample collection swab head.

Overall, the six untrained operators correctly interpreted 355 of 360 tests (98.6%; 95% CI: 96.8%–99.4%), demonstrating comparable performance between operator groups. All analyte concentration levels met the pre-specified reproducibility acceptance criteria. The results for the untrained operator are shown below in Table 4.

Table 4. Reproducibility Study Summary Results

Sample	# of positive result/# of total tested (% positive rate)			Total sample count (% positive rate)
	Site 1	Site 2	Site 3	
True negative	0/30 (0.0%)	0/30 (0.0%)	0/30 (0.0%)	0/90 (0.0%)
High negative (0.1x LoD)	1/30 (3.3%)	0/30 (0.0%)	1/30 (3.3%)	2/90 (2.2%)
Low positive (1x LoD)	30/30 (100.0%)	29/30 (96.7%)	28/30 (93.3%)	87/90 (96.7%)
Moderate positive (3.5x LoD)	30/30 (100.0%)	30/30 (100.0%)	30/30 (100.0%)	90/90 (100.0%)

2. Linearity:

Not applicable. This is a qualitative assay with binary, visually read results.

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 matrix. The organisms were evaluated for their ability to cross-react or interfere with the antibodies of the test by adding 50 µl of each sample directly to the test swab and then processing the sample swabs per the instructions for use. The study was performed with three (3) replicates per

microorganism. Microbial interference testing was performed in the same manner but in the presence of UV-inactivated SARS-CoV-2 (USA-WA1/2020) co-spiked into the samples at 3x LoD.

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

Table 5. Cross Reactivity and Microbial Interference Testing Results

Microorganism	Concentration Tested	Test Results			
		Cross Reactivity		Microbial Interference	
		n/N[1]	Result Agreement (%)[2]	n/N[1]	Result Agreement (%)[2]
Human coronavirus 229E	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Human coronavirus OC43	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Human coronavirus NL63	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
MERS-coronavirus	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
SARS-coronavirus (Gamma-irradiated virus in Vero E6 cells in DMEM)	$1x10^5$ PFU/mL	0/3	100%	N/A	N/A
SARS-coronavirus (Gamma-irradiated virus in PBS)	$1x10^7$ PFU/mL	0/3	100%	3/3	100%
Human Adenovirus 1	$1x10^6$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Human Metapneumovirus	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Parainfluenza virus – Type 1	$1x10^7$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Parainfluenza virus – Type 2	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Parainfluenza virus – Type 3	$1x10^7$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Parainfluenza virus – Type 4A	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Influenza A/Perth/16/09 (H3N2)	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Influenza A/California/07/09 (H1N1)	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Influenza B/Brisbane/60/08 (Victoria)	For Cross-reactivity: $4.7 x10^4$ $TCID_{50}$/mL For Interference: $2.3 x10^4$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Influenza B/Wisconsin/01/10 (Yamagata)	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Enterovirus	$1x10^6$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Respiratory syncytial virus	$1x10^6$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Rhinovirus Type 1A	$1x10^5$ $TCID_{50}$/mL	0/3	100%	3/3	100%
Haemophilus influenzae type b	$1x10^7$CFU/mL	0/3	100%	3/3	100%
Streptococcus pneumoniae	$1x10^7$CFU/mL	0/3	100%	3/3	100%
Streptococcus pyogenes	$1x10^7$CFU/mL	0/3	100%	3/3	100%
Candida albicans	$1x10^7$CFU/mL	0/3	100%	3/3	100%

Pooled human nasal wash	NA	0/3	100%	3/3	100%
Bordetella pertussis	$1x10^7$ CFU/mL	0/3	100%	3/3	100%
Mycoplasma pneumoniae	$1x10^7$ CCU/mL	0/3	100%	3/3	100%
Chlamydia pneumoniae	$1x10^7$ IFU/mL	0/3	100%	3/3	100%
Legionella pneumophila Philadelphia	$1x10^7$ CFU/mL	0/3	100%	3/3	100%
Staphylococcus aureus	$1x10^7$ CFU/mL	0/3	100%	3/3	100%
Staphylococcus epidermidis	$1x10^7$ CFU/mL	0/3	100%	3/3	100%

[1] # of positive results/# of replicates.
[2] Agreement with the expected result.
[3] Tested at lower than recommended concentration.

An *in silico* analysis was performed for human coronavirus HKU1, and the lower respiratory pathogens *Mycobacterium tuberculosis* (mTB), 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 76.0% of available sequences, and cross-reactivity/interference cannot be ruled out.

b. Endogenous/Exogenous Substances Interference:

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

Both studies had a similar study design using three (3) device lots and triplicate measurements of samples contrived in PNWM. Samples were contrived by individually adding the substances listed in the table below and tested with and without UV-inactivated virus spiked into the sample. 50 µL of each contrived sample was applied to the head of a swab and processed per the IFU/QRI of the test. No false results were observed (Table 6).

Table 6. Endogenous/Exogenous Interfering Substances Testing Results

Potentially Interfering Substances	Concentration Tested	Test Results			
		No analyte		With Analyte	
		n/N[1]	Result Agreement (%)[2]	n/N[1]	Result Agreement (%)[2]
No other substance	N/A	0/6*	100%	6/6*	100%
Whole Blood	4%	0/3	100%	3/3	100%
Mucin	0.5%	0/3	100%	3/3	100%
Chloraseptic (Menthol/ Benzocaine)	3 mg/mL	0/3	100%	3/3	100%
	1.5 mg/mL	0/3	100%	3/3	100%
Naso GEL (NeilMed)	5% v/v	0/3	100%	3/3	100%
CVS Basal Drops (Phenylephrine)	15% v/v	0/3	100%	3/3	100%
Afrin (Oxymetazoline)	15% v/v	0/3	100%	3/3	100%
CVS Nasal Spray (Cromolyn)	15% v/v	0/3	100%	3/3	100%

Zicam	5% v/v	0/3	100%	3/3	100%
Homeopathic (Alkol)	10% v/v	0/3	100%	3/3	100%
Sore Throat Phenol Spray	15% v/v	0/3	100%	3/3	100%
Tobramycin	4µg/mL	0/3	100%	3/3	100%
Mupirocin	10 mg/mL	0/3	100%	3/3	100%
HealthA2Z Fluticasone Propionate Nasal Spray	15% v/v	0/3	100%	3/3	100%
Fluticasone Propionate	5% v/v	0/3	100%	3/3	100%
Tamiflu (Oseltamivir Phosphate)	5 mg/mL	0/3	100%	3/3	100%
Chloraseptic (Menthol/ Benzocaine)	3 mg/mL	0/3	100%	3/3	100%
Gericare Saline Nasal Spray (Sodium chloride with preservatives)	15% v/v	0/3	100%	3/3	100%
CVS Health Budesonide Allergy Nasal Spray (Budesonide)	15% v/v	0/3	100%	3/3	100%
Nasonex 24HR Allergy Nasal Spray (Mometasone)	15% v/v	0/3	100%	3/3	100%
Luffeel Nasal Spray (Luffa opperculata, Sulfur)	1.3% v/v	0/3	100%	3/3	100%
Boiron Galphimia glauca	15% v/v	0/3	100%	3/3	100%
Boiron Histaminum Hydrochloricum	15% v/v	0/3	100%	3/3	100%

[1] # of positive results/# of replicates.
[2] Agreement with the expected result.
*Conglomerate results from both independent studies.

4. Detection Limit and Assay Reportable Range:

a. Limit of Detection (LoD):

A limit of detection (LoD) study was conducted to determine the lowest detectable concentration of SARS-CoV-2 (USA-WA1/2020; UV-inactivated), at which at least 95% of all true positive replicates return a positive result. Testing was conducted on three (3) lots of test devices.

A preliminary LoD was first determined by testing serial 2-fold dilutions of virus stocks diluted in PNWM in Three (3) replicates per device lot for a total of 9 replicates per dilution. A 50 µL sample of each virus diluted in PNWM was pipetted onto the dry swab. The swab was then tested per the instructions for use. The preliminary LoD was confirmed by testing an additional twenty samples/lot at the preliminary LoD concentration as well as 2 and 4-fold above and below.

The final LoD was determined where all three (3) lots tested yielded at least 95% of the replicates (≥ 19/20) as positive. Data is presented in the table below.

Table 7. LoD Study Summary Results

Virus concentration		Positive results/total replicates	
$TCID_{50}$/mL	**$TCID_{50}$/Swab**	**Preliminary LoD**	**Confirmatory LoD**
5.0×10^4	2.5×10^3	9/9	60/60

Virus concentration		Positive results/total replicates	
2.5 x 10^4	1.25 x 10^3	9/9	60/60
1.25 x 10^4	**6.25 x 10^3**	9/9	**58/60**
6.25 x 10^3	3.1 x 10^3	2/9	28/60
3.1 x 10^3	1.6 X 10^2	0/9	0/60

b. ***NIBSC 21/368 –International Standard:***

The LoD of the candidate device was also determined by evaluating different dilutions of the International Standard for SARS-CoV-2 antigen (NIBSC code: 32/368) in PNSM. The International Standard for SARS-CoV-2 containing lyophilized SARS-CoV-2 antigen was reconstituted in ultra-pure water (for a final concentration of 20,000 IU/mL). The LoD was determined as the lowest virus concentration that was detected ≥95% of the time (i.e., concentration at which at least 19/20 replicates tested positive). Two (2) fold serial dilutions were made from the International Standard for SARS-CoV-2 antigen into PNSM. Three (3) replicates were tested on one device lot of the test device for each dilution to determine the preliminary LoD concentration of the device. For each replicate, 50 µL of virus dilution was applied to a swab which was tested according to the IFU. The lowest concentration with all concordant positive results was considered the preliminary LoD. The preliminary LoD was determined to be $5x10^2$ IU/ml.

The preliminary LoD concentration was tested with an additional 20 replicates to confirm the LoD. Concentrations above and below the preliminary LoD were also tested with 20 replicates to further refine the LoD. Samples were prepared as for the preliminary LoD study above. To confirm the LoD, at least 19 of 20 replicates should be positive per lot. The results are summarized in table below.

Table 8. Summary of LoD Study for International Standard

Preliminary LoD		Confirmatory LoD	
Dilution (IU/ml)	**Results**	**Dilution (IU/ml)**	**Results**
$4.0x10^3$	3/3	N/A	N/A
$2.0x10^3$	3/3	N/A	N/A
$1.0x10^3$	3/3	$1.5x10^3$	20/20
$5.0x10^2$	**3/3**	**$5.0x10^2$**	**20/20**
$2.5x10^2$	1/3	$1.7x10^2$	8/20
$1.3x10^2$	0/3	N/A	N/A
$6.3x10^1$	0/3	N/A	N/A
$3.1x10^1$	0/3	N/A	N/A

c. ***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: 4.6 x 10^6 $TCID_{50}$/ml). The virus was spiked into PNWM, and 50 µl 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 (3) device lots. Each of the 3 operators performed a single measurement for

each concentration per lot (Table 9). No high dose hook effect was observed in the study, up to the maximum concentration tested herein.

Table 9. High-Dose Hook Effect Study Results

Virus Concentration ($TCID_{50}$/mL)	#Positive/ #Total	% Positive
$4.6x10^6$ (365.6x LoD)	3/3	100.0%
$2.5x10^6$ (200.0x LoD)	3/3	100.0%
$1.3x10^6$ (100.0x LoD)	3/3	100.0%
$6.3x10^5$ (50.0x LoD)	3/3	100.0%
$1.3x10^5$ (10.0x LoD)	3/3	100.0%
$2.5x10^4$ (2.0x LoD)	3/3	100.0%

d. 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 negative nasal matrix and serial diluted 2-fold. Each dilution was tested with five (5) replicates by adding 50 µl contrived sample directly onto each test swab and processing the swab samples per the instructions for use. The number of positive replicates for the tested variants are shown in Table 10

Table 10. 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)
$1.0x10^5$	5/5	5/5	5/5	5/5	5/5	5/5	5/5
$5.0x10^4$	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
$1.3x10^4$	2/5	0/5	5/5	0/5	5/5	5/5	0/5
$6.3x10^3$	0/5	0/5	5/5	0/5	5/5	5/5	0/5
$3.1x10^3$	0/5	0/5	5/5	0/5	5/5	5/5	0/5
$1.6x10^3$	0/5	0/5	5/5	0/5	0/5	0/5	0/5
$7.8x10^2$	0/5	0/5	5/5	0/5	0/5	0/5	0/5
$3.9x10^2$	0/5	0/5	5/5	0/5	0/5	0/5	0/5
$1.9x10^2$	0/5	0/5	0/5	0/5	0/5	0/5	0/5

e. 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

i. *Internal Controls*:

The CorDx Tyfast COVID-19 Ag Rapid Test Rx contains a built-in internal procedural control. The anti-SARS-CoV-2 antibodies are conjugated with colloid gold nanoparticles leading to the coloration of the C line. 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.

ii. External Controls:

The external controls for CorDx Tyfast COVID-19 Ag Rapid Test Rx contains ten (10) positive external control swabs and ten (10) negative external control swab that allows for monitoring of the performance of the assay. The positive control swab contains non-infectious recombinant SARS-CoV-2 recombinant antigen, and the negative control swab contains negative nasal wash dried on the swab tip.

While no separate precision study was conducted for external controls, data from a 25-month real-time stability study provided insight into the precision of the external controls over an extended period. This assessment involved three (3) lots each of positive and negative control swabs stored at 2–30°C and tested in ten (10) replicates every three (3) months, following an initial baseline at month zero (0) of manufacturing. Throughout all testing intervals, 100% agreement with expected results was achieved for every external control lot, as detailed in the summary below.

Table 11. Summary of External Controls Precision/Real Time Stability Study Results

Time points (months)	Test Result/Total Tests						% Agreement to Expected Result
	# Negative Control Lot #			# Positive Control Lot #			
	1	2	3	1	2	3	
0	0/10	0/10	0/10	10/10	10/10	10/10	100%
3	0/10	0/10	0/10	10/10	10/10	10/10	100%
6	0/10	0/10	0/10	10/10	10/10	10/10	100%
9	0/10	0/10	0/10	10/10	10/10	10/10	100%
12	0/10	0/10	0/10	10/10	10/10	10/10	100%
15	0/10	0/10	0/10	10/10	10/10	10/10	100%
18	0/10	0/10	0/10	10/10	10/10	10/10	100%
21	0/10	0/10	0/10	10/10	10/10	10/10	100%
24	0/10	0/10	0/10	10/10	10/10	10/10	100%
25	0/10	0/10	0/10	10/10	10/10	10/10	100%
0	0/10	0/10	0/10	10/10	10/10	10/10	100%
3	0/10	0/10	0/10	10/10	10/10	10/10	100%
6	0/10	0/10	0/10	10/10	10/10	10/10	100%
9	0/10	0/10	0/10	10/10	10/10	10/10	100%
12	0/10	0/10	0/10	10/10	10/10	10/10	100%
15	0/10	0/10	0/10	10/10	10/10	10/10	100%
18	0/10	0/10	0/10	10/10	10/10	10/10	100%
21	0/10	0/10	0/10	10/10	10/10	10/10	100%

24	0/10	0/10	0/10	10/10	10/10	10/10	100%
25	0/10	0/10	0/10	10/10	10/10	10/10	100%

b. Stability

i. Specimen Stability:

Specimen stability was assessed using samples contrived in a PNSM either with or without 2x LoD of heat-inactivated SARS-CoV-2 virus. 50 µL of the prepared sample was added directly to the swab tip and processed per the instruction for use after storage at 30°C±2°C for 0 min, 30 min, 60 min, 90 min, 120 min, and 150 min. Measurements were made with three (3) device lots/three (3) operators, and five (5) replicates per condition per operator (n=15/condition). Results are shown in table below. No false results were observed in the study.

Table 12. Specimen Stability Summary Results

Time Point (minutes)	Positive Sample Results	Negative Sample Results
0	15/15	0/15
30	15/15	0/15
60	15/15	0/15
90	15/15	0/15
120	15/15	0/15
150	15/15	0/15

ii. Real Time Stability:

The stability of the CorDx Tyfast COVID-19 Ag Rapid Test Rx was determined for the intended storage conditions, 2-30 °C (36-86 °F). Within one month of manufacture, three (3) device lots were transferred to five (5) 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 (2) test samples, corresponding to 3.6x LoD and at 4.6x LoD, were tested at each time point. All study data were 100% concordant with expected results and thereby supportive of a 24 month shelf-life when stored at 2-30°C (36-86°F).

iii. Shipping Stability:

The effects of shipping on the integrity of the test device were evaluated with three (3) device lots that were manufactured within one month of the start of the study. 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. Assay Cut-Off:

Not applicable as this is a qualitative visually read assay without numeric data.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   See section C (clinical studies) below.

2. Matrix Comparison:

   The CorDx Tyfast COVID-19 Ag Rapid Test Rx is only intended for use with direct anterior nasal swab specimens. To support the use of pooled nasal wash matrix (PNWM) within analytical studies, a matrix equivalency study was conducted between pooled negative nasal swab matrix (PNSM) and the surrogate PNWM that was used in the analytical studies. The data demonstrated the equivalent performance of the test with both matrices.

C Clinical Studies:

A prospective clinical study was conducted to assess the performance of the candidate test 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 (4) CLIA-waived 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 and evaluated per the instruction for use by the lay users. 751 study subjects were enrolled in total, of which 693 subjects met the inclusion/exclusion criteria. The study included participants spanning a wide age range, with age groups represented including children and early adolescents (2–13 years), younger adults (14–21 years), working-age adults (22–64 years), and older adults (65 years and above). The clinical perfromance estimates as shown below.

Table 13. 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)**	

1. Clinical Sensitivity:

   Please refer to Section VI.C (Clinical Studies) above for the clinical validation.

2. Clinical Specificity:

   Please refer to Section VI.C (Clinical Studies) above for the clinical validation.

3. Serial Testing:

This clinical data set verifies the known lower sensitivity for samples collected on the day of symptom onset (i.e., Day 0) that was observed for test devices of similar technology and design across a multitude of clinical studies. As a mitigation, the Intended Use for this test device (and associated Instructions for Use) include recommendations for repeat testing (i.e., test at least twice over three days with at least 48 hours between tests). 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

4. Clinical Cut-Off:

The test is a qualitative test with a binary positive/negative signal and there is no clinical cut-off for the test.

D Expected Values/Reference Range:

A patient sample is expected to be negative for SARS-CoV-2.

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.
