CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW250025

II. Parent Document Number

K253882

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

CorDx, Inc.

V. Proprietary and Established Names

CorDx Tyfast COVID-19 Ag Rapid Test Rx

VI. Measurand (analyte)

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

VII. Sample Type(s)

Anterior Nasal Sample

VIII. Type of Test

Qualitative lateral flow immunoassay

IX. Test System Description

A Overview

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.

To initiate testing, a sterile swab provided with the test kit is used to collect anterior nasal swab samples from both nostrils of the patient. The patient sample is then placed in the provided reagent tube pre-filled with sample processing solution. The swab is rotated to elute, lyse, and

homogenize the sample material. Three (3) drops of extracted sample are then applied to the test cassette sample well. Upon sample application, colored conjugates dried onto the conjugate pad are dissolved and migrate along with the sample. If SARS-CoV-2 nucleocapsid protein antigen is present in the sample, a complex will form between the anti-SARS-CoV-2 conjugate and the viral antigen, and will be captured by the specific anti-SARS-CoV-2 monoclonal antibody coated on the test line region (T), resulting in the presence of a visible colored line. As a procedural control, a colored line will always appear in the control line region (C) when excess colored conjugates are carried along the test strip by the sample and captured by the immobilized goat anti-mouse IgG antibodies in the control region. Test results are read visually between 10-30minutes without the use of an instrument.

External quality controls are required to be run with the test and are sold separately. Positive and negative control swabs should be processed according to the instructions for use upon receiving a new lot or shipment of test kits or for each untrained operator. The control swabs are intended to be used as quality control samples representative of positive and negative test samples to demonstrate that the reagents are functional, and the assay procedure is performed correctly.

B Test System Components

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

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

The CorDx Tyfast COVID-19 Ag Rapid Test Rx is designed to be simple and easy to use incorporating the following key features:

- The test is self-contained and only requires sample incubation in the extraction reagent prior to sample application.
- The test uses direct unprocessed anterior nasal swab specimens.
- The test needs only basic, non-technique-dependent specimen manipulation and reagent handling to obtain accurate results.
- The reagent is pre-measured and provided in sealed, single-use vials.
- The test does not require any operator intervention during the analysis step.
- The test does not require technical or specialized training for troubleshooting or interpretation of multiple or complex error codes.
- The test does not require any electronic or mechanical maintenance beyond simple tasks.
- The test produces results that do not require operator calibration, interpretation, or calculation.
- The test produces results easy to determine, such as "positive", "negative", or "invalid".

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

A comprehensive risk analysis was conducted in accordance with ISO14971 which included identification and addressing of potential risks or error sources, analyzing potential causes, effects and the existing measures or mitigation factors related to the CorDx Tyfast COVID-19 Ag Rapid Test Rx. The elements considered included operator error, environmental factors, specimen and reagent handling, storage, and external controls.

Potential sources of errors that could adversely affect system performance were identified and mitigated first through system design verification and validation studies and then through additional precautions and warnings in the labeling. The identified risks which could result in erroneous test results were evaluated in flex studies that stressed the functional limits of the test system (see Item 3 below).

2. Fail-Safe and Failure Alert Mechanisms:

The CorDx Tyfast COVID-19 Ag Rapid Test Rx was designed to include numerous features and fail-safe mechanisms built into the system to prevent erroneous results.

Design Features

- Each test cassette is individually pouched in foil with desiccant to maintain the integrity of the test device.
- The foil pouch of the test cassette and extraction buffer are printed with the lot number and expiration date to ensure clarity and appropriate use.
- Nasal samples are directly added into the tube with sample processing solution, and the extracted antigen is then applied directly to the test cassette, eliminating additional specimen-transfer steps.
- The leak-proof dropper tip of the tube with sample processing solution helps prevent sample loss and contamination.
- The ergonomic flexibility of the tube with sample processing solution enables the swab specimen to be squeezed.
- The test cassette is printed with "COVID-19 Ag" to confirm the assay type being tested and to further ensure clarity and accuracy.
- Each test cassette bears clear marking next to the result window to facilitate clear and accurate result interpretation: the control line is denoted as "C", and the COVID-19 antigen line is denoted as "T".
- Each test cassette features a three-drop icon beneath its sample-loading port to ensure the correct amount of sample is added.
- Each positive and negative external control swabs are supplied separately in the External Control Swab kit are clearly marked on the labeling with control swab name, lot number, and expiration date to ensure clarity and appropriate use.

Fail-safe Features

- ***Internal Procedural Control:***

  Each device includes a built-in "C" line that confirms proper sample flow, adequate volume, and overall assay integrity. A visible pink-red band must appear in the "C" region within 10 minutes. If the "C" line does not appear, the result is invalid. It is recommended to review the instructions again and repeat the test with a new sample and a new cassette.

- ***External Quality Controls:***

  Positive control swabs (containing non-infectious recombinant SARS-CoV-2 antigen) and negative control swabs are provided supplied in a separate External Control Kit. The manufacturer recommends the positive and negative external controls be run with each new kit lot, shipment received, and with each new untrained operator.

  Both positive and negative control swabs are ready to use and are tested using the same procedure as patient samples. Each control swab should produce the expected positive or negative result to validate the test kit performance. The controls monitor the entire assay and serve to detect product defects or reagent deterioration between the manufacturer's lot release date and the date of use. The controls also monitor operator performance and identify any procedural errors.

  External control swabs are extracted and processed according to the test instructions for use. When the positive control is tested, lines appear at the C (Control) as well as T (test) positions. When the negative control is tested, a line appears at the C position

only. Each control swab is individually packaged in a foil pouch and the pouch is printed with information such as control swab type and the expiration date. Users are instructed not to use expired external controls. Upon confirmation of the expected results, the kit is ready for use with patient specimens. If external controls do not perform as expected, users are instructed to not use the test results and to repeat the tests or to contact the manufacturer.

3. Flex Studies:

To assess the robustness and risk of false results of the test, the sponsor conducted a series of flex studies. For all these studies, the following study design was shared: Two (2) samples, a negative and a positive sample were contrived in negative pooled nasal wash material (PNWM). The positive sample was spiked with UV-inactivated SARS-CoV-2 virus at 2x LoD to generate a low positive sample (the bubbles in sample chamber flex study used heat-inactivated virus contrived in pooled nasal swab matrix (PNSM) and all other flex studies used UV-inactivated virus). 50 µL of each respective samples was added directly to the tip of the swab and the sample was processed per the test's IFU. Operators were blinded to the test parameters/conditions and sample identity. The studies included lots of three (3) devices. Three (3) operators tested up to 3 replicates per lot (except for the bubble study in which 5 replicates per device lot were used) for all conditions. The summary of results is presented in Table 3 below.

Table 3. Summary Results of Flex Studies

Conditions Tested		Results for Positive (2x LoD) Samples (n/N[1])	Results for Negative Samples (n/N[1])
Effect of Pre-Extraction Delay on Test Swab Samples Stored Without Buffer	**Control: No Delay**	3/3	0/3
	Delay for 5 minutes	3/3	0/3
	Delay for 10 minutes	3/3	0/3
	Delay for 30 minutes	3/3	0/3
	Delay for 60 minutes	3/3	0/3
Effect of Delay in Extracted specimen left in the extraction tubes	**Control: No Delay**	3/3	0/3
	Delay for 5 minutes	3/3	0/3
	Delay for 10 minutes	3/3	0/3
	Delay for 30 minutes	3/3	0/3
	Delay for 60 minutes	3/3	0/3
Swab Rotation Times Flex Study	**0 Rotations**	9/9	0/9
	2 Rotations	9/9	0/9
	5 Rotations	9/9	0/9
	Control: 10 Rotations	9/9	0/9
	15 Rotations	9/9	0/9
	20 Rotations	9/9	0/9
	No Squeezing	15/15	0/15

Conditions Tested		Results for Positive (2x LoD) Samples (n/N[1])	Results for Negative Samples (n/N[1])
Swab Squeezing Flex Study	**Squeezing**	15/15	0/15
Extracted Specimen Volume Flex Study	**1 drop**	4/9 (5 invalids)	0/9 (4 invalids)
	2 drops	9/9	0/9
	IFU: 3 drops	9/9	0/9
	4 drops	9/9	0/9
	5 drops	9/9	0/9
	6 drops	9/9	0/9
Reading Time Flex Study	**0 minutes**	0/3 (3 invalids)	0/3 (3 invalids)
	3 minutes	1/3	0/3
	6 minutes	7/18	0/18
	7 minutes	11/15	0/15
	8 minutes	15/15	0/15
	9 minutes	15/15	0/15
	IFU: 10 minutes	18/18	0/18
	IFU: 15 minutes	3/3	0/3
	IFU: 30 minutes	3/3	0/3
	45 minutes	3/3	0/3
	60 minutes	3/3	0/3
Disturbance during Development Flex Study	**Drop the test cassette from the operating table to the floor, pick up immediately and place back to the operation table**	3/3	0/3
	Move it to another surface during sample flow	3/3	0/3
	Place it vertically along the short side (sample well at the top)	3/3	0/3
	Place it vertically along the short side (sample well at the bottom)	3/3	0/3

Conditions Tested		Results for Positive (2x LoD) Samples (n/N[1])	Results for Negative Samples (n/N[1])
	Place it vertically along the long side	3/3	0/3
	Place it horizontally	3/3	0/3
Lighting Flex Study	**Fluorescent environment**	9/9	0/9
	Incandescent environment	9/9	0/9
	Natural day light (outside)	9/9	0/9
	Dim lighting environment (100 Lux)	9/9	0/9
	Natural lighting environment (300 Lux)	9/9	0/9
	Strong lighting environment (500 Lux)	9/9	0/9
Temperature and Humidity Flex Study	**Low temperature (6.8°C) and low humidity (12% RH)**	9/9	0/9
	Normal temperature (22.4°C) and normal humidity (45% RH)	9/9	0/9
	High temperature (40.1°C) and high humidity (97% RH)	9/9	0/9
Bubbles in Sample Chamber Flex Study	**Lot 1**	5/5	0/5
	Lo2	5/5	0/5
	Lot 3	5/5	0/5

[1] # of positive results/# of replicates.

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

1. Comparison study:

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 4. 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)**		

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

2. Device Performance with Analyte Concentrations Near the Cutoff:

The precision and reproducibility studies were conducted separately.

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 5. Precision Study Summary Results

Sample	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 TCID50/mL) at four concentration levels — true negative, high negative (0.1x LoD), low positive (1x LoD), and moderate positive (3.5x 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 (6) 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 6.

Table 6. 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%)

3. Operator questionnaire:

A total of 104 untrained operators participated in a human factors assessment designed to evaluate comprehension of product labeling, test procedure, and result interpretation. Participants were provided with the Quick Reference Guidance (QRG) and test materials and instructed to perform the test without prior training. The assessment comprised 16 questions covering key aspects of test use, including comprehension of overall instructions, ease of following the test procedure and result interpretation, sample collection, expiration date awareness, identification of the intended use of the test, recognition and appropriate response to invalid or positive results, and knowledge of available support resources. Overall, results were acceptable and support the use of this device in a CLIA-waived environment by untrained operators.

D. Labeling for Waived Devices

The labeling submitted for the CorDx Tyfast COVID-19 Ag Rapid Test Rx consists of:

1. Quick Reference Instructions (QRG)
2. Instructions for Use (IFU)
3. Package Labeling – kit box labels

The following elements are appropriately present:

- The QRG and the IFU identify the test as CLIA waived.
- The IFU contains a statement that a Certificate of Waiver is required to perform the test in a waived setting.
- A statement clearly states the specimen type.
- A statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test.
- The IFU contains a statement that any modification to the test or the manufacturer’s instructions will result in the test being classified as high complexity. Step-by-step instructions for all control procedures, including frequencies and action to be taken if control results are out of range or invalid, or if other failure alert or fail-safe mechanisms are activated.
- The IFU and QRG provide instructions for conducting quality control procedures.
- A warning addressing color blindness when waived tests use color-coded reagents and/or endpoints.
- Telephone number to contact manufacturer for technical assistance or troubleshooting the test system which directs the user to call for assistance when the device or the control materials do not work as specified by the manufacturer.

- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

Benefit-Risk Considerations

After implementation of all risk control measures identified through the Design, Process, and Usability FMEA, the overall residual risks are acceptable and have been reduced to as low as reasonably practicable (ALARP) in accordance with ISO 14971. All hazards have been adequately mitigated through a combination of design features, fail-safe mechanisms, manufacturing controls, analytical verification, usability validation, and detailed labeling instructions. Importantly, no new risks were introduced as a result of implementing these risk controls, and additional controls did not create any unintended hazardous situations. Therefore, no further formal risk–benefit analysis is required.

Analytical performance studies demonstrated that the CorDx Tyfast COVID-19 Ag Rapid Test Rx reliably detects SARS-CoV-2 antigen and distinguishes it from other common respiratory pathogens, including seasonal coronaviruses. Clinical validation performed in simulated CLIA-waived environments showed that user-related errors were infrequent, and when they occurred, they did not lead to false positive results. The most meaningful potential residual risk— misinterpretation of weak or faint test lines by lay users—primarily results in false negative outcomes. This risk is substantially reduced through:

- clearly illustrated Quick Reference Guide (QRG)
- simplified workflow design
- intuitive labeling of the test cassette
- explicit interpretation examples including faint positives, and
- robust warnings and limitations within the Instructions for Use (IFU)

Furthermore, internal fail-safe mechanisms (e.g., mandatory control line, bias toward invalid results under stress conditions) ensure that device malfunction or major procedural errors result in INVALID outcomes rather than false negatives or false positives, supporting FDA's requirement for insignificant risk of erroneous result in CLIA-waived settings.

Overall, the benefits of using the CorDx Tyfast COVID-19 Ag Rapid Test Rx in the intended population and CLIA waived settings significantly outweigh the residual risks. When used according to the IFU, the device provides timely and clinically meaningful information that aids early detection of SARSCoV-2 infection, while maintaining a strong safety profile and a low likelihood of erroneous results.

Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.
