EMERGENCY USE AUTHORIZATION (EUA) SUMMARY

OraRisk COVID-19 RT-PCR

(Access Genetics, LLC)

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only

(The OraRisk COVID-19 RT-PCR test will be performed at the Access Genetics, LLC laboratory, located at 7400 Flying Cloud Drive, Eden Prairie, MN 55344, that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high complexity tests as described in the Standard Operating Procedures that were reviewed by the FDA under this EUA.)

INTENDED USE

The OraRisk COVID-19 RT-PCR test is a real-time (rt) reverse transcriptase (RT) polymerase chain reaction (PCR) intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in nasopharyngeal swab and anterior nasal (nasal) swab specimens collected in universal transport media, nasal swabs collected in saline oral rinse, and saline oral rinse specimens from individuals suspected of COVID-19 by their healthcare provider.

This test is also for use with anterior nasal (nasal) swab specimens that are collected using the binx health At-home Nasal Swab COVID-19 Sample Collection Kit when used consistent with its authorization.

Testing is limited to Access Genetics, LLC laboratory, located at 7400 Flying Cloud Drive, Eden Prairie, MN 55344, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high complexity tests.

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

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information. Negative results for SARS-CoV-2 RNA from saline oral rinse should be confirmed by testing of an alternative specimen type if clinically indicated.

The OraRisk COVID-19 RT-PCR test is intended for use by qualified clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and *in vitro* diagnostic procedures. The OraRisk COVID-19 RT-PCR test is only for use under the Food and Drug Administration's Emergency Use.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The OraRisk COVID-19 RT-PCR test is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test. The SARS-CoV-2 primer and probe set(s) is designed to detect RNA from the SARS-CoV-2 in upper respiratory specimens and oral rinse from individuals suspected of COVID-19 by their healthcare provider. The test measures the presence or absence of RNA encoding the RdRp (polymerase) of the SARS-CoV-2. For detection of RdRp the Smart Logix Coronavirus 2019 assay authorized on April 3, 2020 is used in the OraRisk COVID-19 RT-PCR test. The test also co-extracts and amplifies sequences from the human RNase P gene detected by a differently labeled fluorophore.

RNA is isolated from claimed specimens and then reverse transcribed to cDNA and subsequently amplified using the LightCycler 480 II instrument with Sequence Detection Software version 1.5.1.62. During the amplification process, the probe anneals to a specific target sequence located between the forward and reverse primers. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades the bound probe, causing the reporter dye (FAM and CAL Fluor Red 610) to separate from the quencher dye (BHQ), generating a fluorescent signal. Fluorescence intensity is monitored at each PCR cycle by the LightCycler 480 II instrument.

SAMPLE COLLECTION

- Nasopharyngeal Swab are collected in 3 mL Universal Transport Media (UTM)
- Nasal Swabs can be collected in 3 mL Universal Transport Media (UTM) or in 5 mL Saline Oral Rinse
- Saline Oral Rinse collection involves the intake of 5 mL sterile saline with the instruction to swish and gargle it for 30 seconds followed by expectoration into the attached funneled tube. Saline Oral Rinse is shipped by couriers 3 time daily and is processed the same day.
- Dry anterior nasal (nasal) swab collected using the binx health At-Home Nasal Swab COVID-19 Sample Collection Kit when used consistent with its authorization (EUA202509) and processed via rehydration of the swab in 700µL of saline upon receipt and assay as per protocols described herein.

INSTRUMENTS USED WITH TEST

For extraction of viral RNA, the PerkinElmer Chemagic MSM I automated specimen processing system (PerkinElmer, Waltham, MA) is used with the CMG-1033-S kit.

For thermocycling and detection of amplified DNA products the LightCycler 480 II qPCR System running the LightCycler 480 Software version 1.5.1.62 (Roche Molecular System) is used.

EQUIPMENT, REAGENTS AND MATERIALS

The following equipment/reagents/materials are required to run this test:

1. Swab and universal transport media for nasal swab collection, or
2. iClean (for nasopharyngeal swabs; Hcy, Huachenyang Technology, LTD, China; #CY-96000T) and universal transport media
3. Optional: Access Genetics Convenience Kit for nasal swab in oral rinse collection (PathTec, Midland, GA; #BM-000674; sterilized) consisting of:
   a. Swab for Specimen Collection (e.g., Dacron swab, Puritan Medical Products Company, LLC, Guilford, ME; #25-3406-H)
   b. Sarstedt tube filled with 5mL of sterile saline, Inc, Newton, NC; #86.290.104)
4. RNA Extraction Reagents (PerkinElmer; CMG-1033-S)
5. AccuPlex SARS-CoV-2 Reference Material Kit (Sercare #0505126)
6. SARS-CoV-2 Assay Kit (Co-Diagnostics, Inc., Salt Lake City, UT; #Covid K-001)
7. PCR reaction plate (Roche Lightcycler Multiwell Plate, Clear; #05102413001)

COLLECTION KIT USED WITH THIS TEST

The OraRisk COVID-19 RT-PCR test can be used with anterior nasal swabs (Copan Swab,159C Polyester) that are collected using the binx health At-Home Nasal Swab COVID-19 Sample Collection Kit which is manufactured by Binx Health.

INSPECTION OF SPECIMENS RECEIVED:
Applies to specimens received from patients using home collection kit

Specimens collected using the binx health At-Home Nasal Swab COVID-19 Sample Collection Kit should be checked for the following criteria before entering the work flow, and must otherwise meet receiving requirements imposed by Access Genetics, LLC laboratory:

• **Labeling** – Improperly/inadequately labeled specimens that cannot be resolved are rejected

• **Expired shipping time** – If a specimen is received ≥ 56 hours from the collection date/time, the specimen is rejected.

• **Improper return of sample packaging** - sample not returned in supplied packing materials; sample not in correct collection/transport tube; sample integrity appears compromised

• **Missing Information** - customer did not adequately annotate specimen as to date and time of specimen collection

CONTROLS TO BE USED WITH THE COVID-19 RT-PCR

- **Internal Control:** Each sample that contains nucleic acid (positive control, negative control, LOD control, and patient samples) must demonstrate the presence of the internal control (IC) amplicon. The IC is created from PCR

amplification of a locus within the RNase P human gene and monitors adequate amounts and quality of RNA in the sample and correct sample processing.

- **No template control (NTC)**: A no template control is comprised of normal saline. This control is carried through all aspects of sample processing including the extraction and monitors for reagent contamination. It should be negative for amplification of SARS-CoV-2 (FAM) and RNase P (IC- CAL Fluor Red 610).
- **Negative Extraction Control**: The RNase P containing control pseudovirus provided in the AccuPlex SARS-CoV-2 Reference Material Kit (Sercare #0505126) is used as a Negative Extraction Control. The pseudovirus is combined with saline and is included in each extraction run with a concentration of 30 copies/µL. This control is subjected to all processing steps including heat inactivation, RNA extraction, reverse transcription and PCR.
- **LOD Extraction Control**: Pseudovirus containing SARS-CoV-2 target sequence (Sercare #0505126) is assayed with each extraction run of the test. Briefly, this reagent is diluted to the Limit of Detection (LoD) of the OraRisk COVID-19 RT-PCR test in a diluent of saline. This control is subjected to all processing steps including RNA extraction, RT-PCR set up, and thermocycling.
- **Positive PCR Control**: The positive PCR control consist of a proprietary blend of SARS-CoV-2 synthetic templates provided by the LogixSmart test kit and is included in the PCR only with each batch of samples. The positive control is used to verify that the PCR run is performing as intended. The positive control contains targets for RdRP and RP. The positive control is used once on every PCR plate.

INTERPRETATION OF RESULTS

All test controls should be examined prior to interpretation of patient results. If the controls are not valid, the patient results cannot be interpreted. Result interpretation for patient samples was established based on a cutoff of 40 Ct for SARS-CoV-2 target.

a. Control Result Interpretation

Table 1: Expected Performance of Controls

Control Name	Ct Value		Interpretation	Action
	COVID (RdRp) FAM	**RNase P (Internal Control) CAL Fluor Red 610**		
Positive PCR control (SeraCare)	**25.8-26.6**	**<38**	**Pass**	PCR is valid
	None	<38	Fail	Run is invalid and needs to be repeated
No template control (NTC)	**None**	**None**	**Pass**	Run is valid
	>0	>0	Fail	Run is invalid. Investigate contamination and repeat run
Negative Extraction control	**None**	**<38**	**Pass**	Run is valid
	>0	<38	Fail	Run is invalid. Investigate

				contamination and repeat run
	None	>38	Fail	Investigate failed RT-PCR
LoD Extraction Control	**35.2- 38.3**	**<38**	**Pass**	Run is reported
	>38.3	<38	Fail	Low sensitivity run, repeat

If any of the above controls do not exhibit the expected performance as described, the assay may have been improperly set up and/or executed improperly, or reagent or equipment malfunction could have occurred. Invalidate the run and re-test.

b. Examination and Interpretation of Patient Specimen Results:

Assessment of clinical specimen test results should only be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted, and testing needs to be repeated after a root cause is identified and eliminated.

Table 2: Interpretation of Sample Results

COVID-19 FAM	RNase-P Red-610	Test Result	Interpretation (reported)	Action
-	**-**	Invalid	None	Do not report result. Repeat extraction and PCR assay. If no internal control is detected in the repeat test, re-sampling is required
-	+	SARS-CoV-2 RNA Not Detected	The submitted sample is negative (absence of the RNA) from SARS-CoV-2, the virus that causes the disease called COVID-19.	Report results to healthcare provider. Consider test for other viruses that cause similar symptoms
Ct≤40	+	SARS-CoV-2 RNA Detected	The submitted sample is positive (presence of the RNA) from SARS-CoV-2, the virus that causes the disease called COVID-19.	Report results to healthcare provider and appropriate public health authorities
<50 Ct>40	+	Inconclusive	Initially inconclusive results are not reported. If repeat inconclusive it is reported as "repeat inconclusive. Absence or presence of SARS CoV-2 RNA could not be established. Additional testing on a new specimen is required"	Repeat extraction and PCR assay. If repeat test has COVID FAM <40 report as *SARS-CoV-2 Detected* and report results to healthcare provider and appropriate public health authorities If the result is repeatedly inconclusive. additional testing is required with a new sample and/or a different test.

PERFORMANCE EVALUATION

1) *Limit of Detection (LoD) -Analytical Sensitivity:*

a. Tentative LoD Study: Nasal swab combined with saline oral rinse
To establish the limit of detection (LOD) for the OraRisk COVID-19 RT-PCR test, a tentative LoD study was performed. A dilution series was performed with the SeraCare SARS-CoV-2 RNA based pseudovirus diluted into a pool of nasal swab in oral rinse previously tested negative for infection with the SARS-CoV-2 virus.

b. Confirmation of the LoD: Nasal swab combined with saline oral rinse
Confirmation of the LoD for the nasal swab combined with a saline oral rinse was performed by testing a various number of replicates of the SARS-CoV-2 RNA based pseudovirus diluted into clinical matrix (i.e., nasal swabs combined with saline oral rinse) at slightly above (1.5x LoD), and slightly below (0.5x LoD and 0.75x LoD) the tentative LoD. Testing was performed according to the Laboratory SOP; all replicates were individual extraction replicates. Data are summarized in the table below and support a final LoD of 15 copies/mL for Nasal Swab in oral rinse for this test.

Table 3: Confirmatory LoD Study in Nasal Swab in Oral Rinse Matrix

SARS-CoV-2 RNA (copies/mL)	Number Tested	Positive	Ct Value			
			SARS-CoV-2		RNase P IC	
			Mean	SD	Mean	SD
10	40	30 (75%)	37.8	0.80	24.1	1.20
15	**20**	**19 (95%)**	**37.1**	**0.79**	**23.8**	**1.05**
20	**60**	**57 (95%)**	**36.7**	**0.56**	**25.2**	**0.40**
30	20	20 (100%)	36.3	0.90	24.8	0.37

c. Confirmation of the LoD: Nasopharyngeal (NP) Swab
An identical study design as described above was used, testing a narrow range of virus concentrations, each condition in 20 individual extraction replicates using nasopharyngeal swab in 5 mL of saline (no oral rinse). The data are summarized in the table below and support a final LOD for this test in Nasopharyngeal swab specimens of 15 copies/mL.

Table 4: Confirmatory LoD Study in NP Swabs

SARS-CoV-2 RNA (copies/mL)	Number Tested	Positive	Ct Value			
			SARS-CoV-2		RNase P IC	
			Mean	SD	Mean	SD
5	20	8 (40%)	38.7	0.82	28.9	0.27
15	**20**	**19 (95%)**	**38.5**	**0.63**	**28.7**	**0.24**
20	20	20 (100%)	38.1	0.70	29.0	0.29

d. Confirmation of the LoD: Saline Oral Rinse

An identical study design as described above was used, testing a narrow range of virus concentrations, each condition in 20 individual extraction replicates using 5 mL of saline oral rinse only (no added nasal or NP swab). The data are summarized in the table below and support a final LOD for this test in oral rinse specimens of 20 copies/mL.

Table 5: Confirmatory LoD Study in Saline Oral Rinse

SARS-CoV-2 RNA (copies/mL)	Number Tested	Positive	Ct Value			
			SARS-CoV-2		RNase P IC	
			Mean	SD	Mean	SD
5	20	11	38.5	0.82	25.5	0.20
15	20	17	38.1	0.68	25.5	0.14
20	**20**	**20**	**37.3**	**0.95**	**25.5**	**0.13**
30	20	20	36.8	0.46	25.6	0.11

e. Confirmation of LoD: Anterior Nasal Swabs in VTM Re-examined Using Chemically Inactivated SARS-CoV-2 Virus

This study was performed to assess LoD of the Copan polyester swabs applied to bilateral, anterior nasal vestibule collections procured in viral transport media (VTM). These studies differ from previous LoD studies in two ways. First, an inactivated form of the SARS-CoV-2 (Virapur, Microbiologics, Inc., St. Cloud, MN) replaces the previously used control reagent, a pseudovirus containing the RNA genome of the SARS-CoV-2 (AccuPlex SARS-CoV-2 Reference Material Kit (Seracare #0505126). Second, the technique to apply the viral material involved pipetting a small volume of the reagent directly onto the fibers of the swab after collection of the nasal secretions, followed by placement of the inoculated swab into 3 mL viral transport media._Following this, each swab in VTM was subjected to heat inactivation, as per protocol. Subsequently, 300 µL of the VTM sample was subjected to RNA extraction and assaying by rt-PCR identically as per the protocol described in this application. The data are summarized in the table below and support a final LoD for this sample type of 30 viral copies/mL .

Table 6: Confirmatory LoD Study in Anterior Nasal Swabs in VTM

SARS-CoV-2 RNA (copies/mL)	Number Tested	Positive	Ct Value			
			SARS-CoV-2		RNase P IC	
			Mean	SD	Mean	SD
20	20	16	38.5	0.30	26.3	1.60
30	**20**	**19**	**38.5**	**0.24**	**27.8**	**1.70**
60	20	20	38.2	0.73	27.1	1.57
90	20	20	37.4	0.67	27.0	2.53

f. Confirmation of the LoD: Dry Anterior Nasal Swabs Collected Using Binx Health At-Home Nasal Swab COVID-19 Sample Collection Kit

A study was performed using the Copan polyester swab that is a component of the binx health At-Home Nasal Swab COVID-19 Sample Collection Kit (EUA202509). Briefly, individual persons used the Copan polyester swabs to collect the left and right anterior nares, as per the sample collection kit instructions. Each swab was then inoculated with a narrow range of SARS-CoV-2 virus concentrations (Virapur, Microbiologics, Inc., St. Cloud, MN) using the process of pipetting the concentrated virus solution directed onto the polyester fibers. The swabs were then dried within their protective sheath for 12 hours. Following this, each swab was rehydrated for 30 minutes in 700 µL of saline by submerging the tip in that volume in a 5 mL plastic vial. Subsequently, each rehydrated swab in saline was subjected to heat inactivation, as per protocol. Next, 300 µL of the saline sample was subjected to RNA extraction and assaying by rt-PCR as per protocol. The data are summarized in the table below and support a final LoD for this sample type of 60 copies/mL .

Table 7: Confirmatory LoD Study in Dry Anterior Nasal Swabs Rehydrated in 0.7mL Saline

SARS-CoV-2 RNA (copies/mL)	Multiple of the LoD of swab in VTM	Number Tested	Positive	Ct Value			
				SARS-CoV-2		RNase P IC	
				Mean	SD	Mean	SD
30	1x	20	1	38.5	N/A	26.8	3.18
60	**2x**	**20**	**19**	**38.2**	**0.69**	**25.1**	**1.91**
120	4x	20	20	38.1	0.54	25.5	1.72

g. Matrix Equivalency Study: Dry Anterior Nasal Swabs Collected Using Binx Health At-Home Nasal Swab COVID-19 Sample Collection Kit vs. Anterior Nasal Swabs in VTM

In this analytical matrix equivalency study, laboratory personnel, previously tested negative for COVID-19, were used to collect multiple Copan swabs from the anterior nares following the instructions provided in the binx health At Home Nasal Swab COVID-19 Sample Collection Kit. The cohort of swabs were accessioned, each swab was assigned a unique identifier number. Following this, 40 swabs in the cohort were inoculated with a solution containing chemically inactivated SARS-CoV-2 virus, (Virapur, Microbiologics, Inc. St. Cloud, MN) at varying concentrations to deliver the equivalent of (1x, 2x, 5x and 0x of the LoD determined for the anterior nasal swabs in VTM). The remaining 40 swabs in the cohort were collected in the identical manner and placed in 3 mL of viral transport media. The dry swab cohort was dried in their plastic sheath for 12 hours. Following this, the dry swabs were placed in a 5 mL plastic vials and rehydrated in 700 µL of saline for 30 minutes. Subsequently, the rehydrated swab samples

were processed as per protocol, beginning with a 45 minute heat inactivation step. The swab in VTM cohort samples were processed directly as per protocol, beginning with a 45 minute heat inactivation step. Each of the subsequent steps were identical for testing both cohorts using the OraRisk COVID-19 RT-PCR test.

The detectability of testing dry anterior nasal swabs (ANS) rehydrated in 0.7 mL saline was observed to be equivalent to that of testing anterior nasal swabs in 3 mL VTM at 2x LoD.

Table 8: Matrix Equivalency Study Results (Dry Anterior Nasal Swabs Collected Using Binx Health At-Home Nasal Swab COVID-19 Sample Collection Kit vs. Anterior Nasal Swabs in VTM)

xLoD	Concentration (Copies/mL)	ANS in VTM	ANS Rehydrated in Saline
		# of Replicates Detected/Total Replicates Tested	# of Replicates Detected/Total Replicates Tested
1x LoD	30	10/10	1/10
2x LoD	**60**	**20/20**	**19/20**
5x LoD	150	5/5	5/5
0x LoD	0	0/5	0/5

The matrix equivalency study results are supportive of using the binx health At Home Collection Kit to collect dry anterior nasal swab samples to be tested with the OraRisk COVID-19 RT-PCR test, following the specific rehydration protocol in 0.7 mL saline.

2) Analytical Inclusivity/Specificity:

a. Inclusivity

The sponsor uses a proprietary product for which primers and probe sequences are not available to the laboratory, namely the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit. The manufacturer of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit (Co-Diagnostics) has granted right-to-reference to Access Genetics, LLC to leverage their inclusivity data.

Previous in silico analysis performed by Co-Diagnostics since initial design in Feb-2020 observed that none of the mutations related to the lineages B.1.1.7 (Alpha) (Public Health England, 2020) (Rambaut, et al., 2020), B.1.351 (Beta), B.1.427 (Epsilon), B.1.429 (Epsilon), and P.1 (Gamma) had any predicted impact in the performance of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit. Co-Diagnostics has conducted monthly BLASTn queries of a subsampling from the Nextstrain database to monitor the homology of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit CoPrimers. The most recent in silico analysis performed in June 2021 found that variants of concern lineages B.1.1.7 (Alpha) (GISAID, 2020), B.1.351 (Beta), B.1.427 (Epsilon), B.1.429 (Epsilon), and P.1 (Gamma) still do not

expect to impact the performance of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit, as none of the mutations on the lineages in the Variants of Concern occur in a region targeted by the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit. The lineage B.1.167.2 (Delta) (PANGO lineages, 2021) contains a single point mutation within the binding site of one of the two CoPrimers. However, the single mismatch caused by this mutation is not expected to prevent the primer to bind to the SARS-CoV-2 genome. Although the Co-Diagnostics risk analysis did not indicate that loss of sensitivity was likely with the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit, the impact of the single point mutation was analyzed for Tm impact. The impact on Tm was determined to be modest, and the affected portion of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit CoPrimer retained a predicted annealing temperature above that used in the validated thermocycling protocol. Therefore, the predicted Tm impact analysis corroborated with the previous risk determination that sensitivity with the Delta lineage was unlikely to be affected. As a final analysis, synthetic RNAs were obtained with the Wild Type sequence and with the single point mutation present in the Delta lineage. The wet testing analysis confirmed that both RNAs exhibited estimated and confirmed Limits of Detection (LoD) within the 3-fold limit set as the acceptance criterion, further corroborating that the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit is expected to retain full sensitivity for the Delta lineage.

b. Cross-reactivity

The sponsor uses a proprietary product for which primers and probe sequences are not available to the laboratory, namely the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit. The manufacturer of the Logix Smart Coronavirus Disease 2019 (COVID-19) Kit has granted right-to-reference to Access Genetics, LLC. Accordingly, a cross reactivity study was not repeated.

3) Clinical Evaluation:

Validation of Nasal and Nasopharyngeal Swabs

Four different clinical studies were performed testing clinical samples in comparison to nucleocapsid gene (N1/N2) based EUA authorized RT-PCR comparator tests by two different laboratories. Both comparators are using a Ct cutoff of 40.0, with Cts ≤40 being scored positive. The investigational tests were processed, and the results interpreted per laboratory SOP using a cutoff of Ct 40 including the heat-inactivation step.

A total of 77 samples were collected from patients with signs and symptoms of an acute respiratory illness (30 nasopharyngeal swab specimens in VTM and 46 nasal swabs in VTM or saline oral rinse).

Test results for nasopharyngeal swab samples collected in VTM are summarized in the table below.

Table 9: Clinical Performance in Nasopharyngeal Swab Specimens

NP swab in VTM		EUA Authorized Comparator (N1/N2)			Total
		Positive	Inconclusive	Negative	
OraRisk COVID-19 Test	Positive	15	0	0	15
	Negative	0	0	15	15
Total		**15**	**0**	**15**	**30**

Performance for nasopharyngeal swabs in VTM is calculated as:
Positive Percent Agreement (PPA): 15/15 = 100% (95% CI: 79.6% - 100%)
Negative Percent Agreement (NPA): 15/15 = 100% (95% CI: 79.6% - 100%)

Test results for nasal swab samples collected in VTM or saline oral rinse are summarized in the Table below. The table combines nasal swabs in VTM and in saline oral rinse because the LoDs of the OraRisk COVID-19 RT-PCR test in swabs in VTM and in saline oral rinse are comparable (within 3x LoD; please refer to the LoD study above).

Table 10: Clinical Performance in Nasal Swab Specimens (in VTM or Oral Rinse)

Nasal swab in VTM or Saline Oral Rinse		EUA Authorized Comparator (N1/N2)			Total
		Positive	Inconclusive	Negative	
OraRisk COVID-19 Test	Positive	22	1*	1**	24
	Negative	0	0	22	22
Total		**22**	**1**	**23**	**46**

*One sample detected as positive by the investigational device was detected by the comparator test only in N2 target channel (with Ct >39). Since no amplification was detected in second N1 target channel of the comparator test, this sample was inconclusive by the comparator, which would typically reflex to re-testing. Retesting could not be performed for this sample. The sample was excluded from the analysis because with one positive and one negative target detection, it is considered to be neither Positive nor Negative.
**One sample was detected as positive by the investigational test from Access Genetics. This sample had a Ct values of 38.7, indicative of a low positive result; this sample was not detected by the comparator test.

Performance for Nasal swabs is calculated as:
Positive Percent Agreement (PPA): 22/22 = 100% (95% CI: 85.1% - 100%)
Negative Percent Agreement (NPA): 22/23 = 95.7% (95% CI: 79.0% - 100%)

Validation of Saline Oral Rinse

Oral Rinse only, without the insertion of a nasal swab was validated through a paired sample study comparing nasal swab combined with saline oral rinse to saline oral

rinse alone. Samples were collected from symptomatic and asymptomatic individuals suspected of COVID-19.

Paired positive samples were collected from 121 patients. A total of 56 patients previously tested positive for COVID-19 by the OraRisk COVID-19 RT-PCR test and the individuals were re-sampled and re-tested within 2 days of the initial positive test. In addition, paired sample collection of nasal swab in oral rinse versus saline oral rinse alone was performed in a long-term care facility on 65 persons (staff and residents). The result of the OraRisk COVID-19 RT-PCR test on Nasal swab in oral rinse was used as a comparator test. All samples were tested based on the laboratory SOP authorized for the OraRisk COVID-19 RT-PCR test.

The table below summarizes the results of the paired samples, nasal swab in saline oral rinse versus saline oral rinse alone and Positive Percent Agreement (PPA) and Negative Percent Agreement (NPA) are calculated below.

Table 11: Clinical Performance in Saline Oral Rinse

		OraRisk COVID-19 Test *Nasal Swab in Saline Oral Rinse*			**Total**
		Positive	**Inconclusive**	**Negative**	
OraRisk COVID-19 Test *Saline Oral Rinse*	**Positive**	56	0	0	56
	Negative	0	0	65	65
Total		**56**	**0**	**65**	**121**

In summary, the performance of the oral rinse sample as compared to the EUA authorized nasal swab in saline oral rinse is calculated below:

PPA: 56/56 = 100% (95% CI: 93.6% - 100%)
NPA: 65/65 = 100% (95% CI: 94.5% - 100%)

WARNINGS:

- For *in vitro* diagnostic use.
- Rx only.
- For use under Emergency Use Authorization (EUA) only.
- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by the authorized laboratory.
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of *in vitro* diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Handle all specimens as if infectious using safe laboratory procedures. Refer to Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens

Associated with 2019-nCoV https://www.cdc.gov/coronavirus/2019-nCoV/lab-biosafety-guidelines.html.

- Use personal protective equipment such as (but not limited to) gloves, eye protection, and lab coats when handling kit reagents while performing this assay and handling materials including samples, reagents, pipettes, and other equipment and reagents.
- Amplification technologies such as PCR are sensitive to accidental introduction of PCR product from previous amplifications reactions. Incorrect results could occur if either the clinical specimen or the real-time reagents used in the amplification step become contaminated by accidental introduction of amplification product (amplicon). Workflow in the laboratory should proceed in a unidirectional manner.
- Dispose of unused kit reagents and human specimens according to local, state, and federal regulations.

LMITATIONS:

- This procedure is optimized for PCR reactivity to detect SARS-CoV-2 RNA samples extracted from Oral Rinse, Nasal Swab Collections in either Oral Rinse or Universal Media Transport, and Nasopharyngeal swab samples collected in UTM.
- The presence of unidentified inhibitors of PCR may not be removed during the extraction procedure and samples with measurable quantities of RNA may not produce a detectable PCR product.
- False negative results can be generated when:
  - Specimens have a target copy number below the assay's limits of detection may not yield sufficient target RNA for detection of any or all of the target organisms.
  - Samples contain severely degraded template RNA due to erroneous handling and/or storage. RNA degradation to fragment sizes smaller than the expected PCR amplicon size prohibits amplification of the regions defined by the respective primer sets.
  - There is inadequate specimen collection technique, or inappropriate specimen storage or shipping conditions.
- False positive results can be generated when:
  - Specimens are contaminated during handling when being accessioned
  - Contamination due to carry over with volumetric transfers to extraction process plate or during PCR setup.
- Testing of nasal swabs, nasal swabs combined with saline oral rinse, and saline oral rinse only specimens is limited to patients with signs and symptoms of COVID-19.
- Testing using the authorized binx health At-home Nasal Swab COVID-19 Sample Collection Kit with the OraRisk COVID-19 RT-PCR test requires adherence to and no modification of the "Medical Oversight and Process to be Used", the "Inspection of Specimens", and the "Interpretation of Results" aspects of the binx health At-home Nasal Swab COVID-19 Sample Collection Kit EUA.
- The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.