EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay
Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only
Updated December 18, 2020

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay will be performed at the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard located at 320 Charles Street, Cambridge, Massachusetts 02141, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, as described in the laboratory procedure that was reviewed by the FDA under this EUA.

INTENDED USE

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay (Version 1 and Version 2) is intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (such as nasopharyngeal, oropharyngeal, nasal, and mid-turbinate swabs, nasopharyngeal wash/aspirate or nasal aspirate specimens) and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their health care provider. Your product (Version 2) is also for the qualitative detection of nucleic acid from SARS-CoV-2 in dry nasal swabs from individuals suspected of COVID-19 by their healthcare provider.

In addition, the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay (Version 2) is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in dry nasal swab specimens self-collected unsupervised using the CRSP Self-Swab kit, by individuals (18 years of age and older) suspected of COVID-19 by their healthcare provider and when determined to be appropriate by the healthcare provider. The kit is provided to individuals by the healthcare provider and the specimens collected using the CRSP Self-Swab kit will be dropped off at the designated location and transported via courier for testing at the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard.

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay (Version 2) is also authorized for use with the Color COVID-19 Self-Swab Collection Kit for individuals (18 years of age and older) to self-collect nasal swab specimens unsupervised at home or in a healthcare setting when determined by a healthcare provider to be appropriate based on results of a COVID-19 medical questionnaire.

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay (Version 2) is also authorized for use with binx health At-home Nasal Swab COVID-19 Sample Collection Kit for individuals (18 years of age and older) for self-collection of nasal swab specimens at home (which includes in a community based setting), when determined by a healthcare provider to be appropriate based on the results of an online COVID-19 questionnaire.

All testing is limited to the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard, located at 320 Charles Street, Cambridge, MA 02141 which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets requirements to perform high complexity tests.

Results are for the detection and identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in upper 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.

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay 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 CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay is a reverse transcriptase real-time polymerase chain reaction (rRT-PCR) assay for the qualitative detection of SARS-CoV-2 specific RNA. This test uses primer/probe sets developed by the CDC that target two viral gene targets in the Nucleocapsid gene of SARS-CoV-2, N1 and N2, and an internal control gene, RNase P (RP) for Assay Version 1 or N2 and RP for Assay Version 2.

The test consists of four processes in a single assay: 1) nucleic acid extraction, 2) reverse transcription of target RNA to cDNA, 3) PCR amplification of target and internal control DNA, and 4) simultaneous detection of PCR amplicons by fluorescent dye labelled probes.

There are two assay versions:

Assay Version 1 uses CDC developed SARS-CoV-2 nucleocapsid N1, N2, and human RP primers and probes. The respiratory specimen types are transported in VTM or sterile saline. Assay Version 1 was validated for use with the Applied Biosystems Viia7 thermocycler or the Applied Biosystems QuantStudio 7 Flex each with QuantStudio software version 1.3.

Assay Version 2 uses CDC SARS-CoV-2 nucleocapsid N2, and human RP primers and probes. This assay is intended to be used with dry anterior nares swabs. Assay Version 2 is validated for use with the Applied Biosystems QuantStudio 7 Flex thermocycler with QuantStudio software version 1.3.

Table 1. Summary of Similarities and Differences Between the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 and Version 2.

	V1	**V2**
Transport medium	VTM or 0.9% sterile saline	None ("dry swab")
Swab reconstitution for "dry swabs"	N/A	1mL Norgen Biotek preservative
Liquid handler for initial sample handling	N/A	Hamilton STARlet
Extraction method	ThermoFisher MagMAX Viral RNA Isolation Kit	ThermoFisher MagMAX Viral RNA Isolation Kit
Extraction format	96-well	384-well
Liquid handler for extraction	Agilent Bravo	Agilent Bravo
Extraction sample input volume	50µl into extraction	37.5µl into extraction
Extraction output volume	50µl	15µl
Liquid handler for RT-PCR plate set-up	Formulatrix Tempest and Agilent Bravo	Formulatrix Tempest and Agilent Bravo
RT-PCR template volume	5µl	5µl
RT-PCR total reaction volume	15µl	10µl
RT-PCR plate format	384-well	384-well
Thermocycler	Viia7 or QuantStudio 7 Flex	QuantStudio 7 Flex
Thermocycler software version	QuantStudio software version 1.3	QuantStudio software version 1.3

INSTRUMENTS USED WITH TEST

The CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay is to be used with the following instrumentation:

- Specimen Lysis/RNA Extraction/Realtime PCR Reagent Preparation: Agilent Bravo Liquid Handling Platform (running VWorks (Build 11.4.0.1233)) for automated extraction and/or RT-PCR plate set-up, and Formulatrix Tempest and Agilent Bravo Liquid Handling Platform also for RT-PCR plate set-up.
- RT-PCR Platforms: Applied Biosystems QuantStudio 7 Flex Real-Time PCR System (QuantStudio Software V1.3), Applied Biosystems ViiA7 (QuantStudio Software V1.3).

Table 2. REAGENTS AND MATERIALS

Item	Vendor	Vendor Catalog Number
4X TaqPath, 1-Step RT-qPCR Master Mix, GC (2,000 rxns/kit)	Thermo Fisher Scientific	A15300
2019-nCoV CDC EUA Primer/Probe Kit (500 rxns/box)	IDT	10006606
Tip, 1000ul Fltr, Conductive(480/PK)	Hamilton Robotics, Inc.	235905
Tip, 70ul, St. Fltr,Cond,Bravo(3840/PK)	AGILENT TECHNOLOGIES INC	19133-142
Plate, 384W, DW, V-Bottom(60/CA)	VWR International, LLC	82051-320
Plate, 384w Twintec Clear 40ul(25/BX)	VWR International, LLC	12000-658
Plate, 96w Twintec Clear (25/BX)	VWR International, LLC	47744-116
Plate, 384w Clear, FB, NS (100/CA)	VWR International, LLC	82051-298
AB-3720 Thermo foil pierce-able seal	Thermo Fisher Scientific	AB-3720
Ethanol, 100%, (24pints/CA)	VWR International, LLC	89125-170
Thermo Viral RNA Isolation Kit	Thermo Fisher Scientific	AMB18365
Isopropanol, 99% (4x4L/case)	VWR International, LLC	TXMK303216BRI
Wipe, RNase Zap Ambion (100/PK)	Thermo Fisher Scientific	AM9786
DNA ZAP!, Degradation Solution(250ml/BT)	Life Technologies, Inc.	AM9890
Disinfectant, Germicidal (625ml/BT)	WW GRAINGER CO	3VDL4
Ethanol, 70% USP 140Proof (32oz/BT)	VWR International, LLC	76212-358
Kit,2019-nCoV_N_Positive Control(1/bx)	Integrated DNA Technologies, Inc.	10006625
Tube, 50ml orange cap (25/PK)	VWR International, LLC	21008-775
Super rags (250/case)	BLUE THUNDER TECHNOLOGIES, INC.	WI-1318Q.250
Bags, Heavy weight, 8"x12" (100/pack)	VWR International, LLC	11215-280
Tip, 2ml St. Fltr LTS(480/CA)	Mettler-Toledo Rainin LLC	17002923
Pipette, 25ml, Serological, St(200/CA)	VWR International, LLC	53392-198
Tip, pipette1000ul LTS Rainin (768/Ca)	Mettler-Toledo Rainin LLC	30389212
AB-3720 Thermo foil pierceable seal	Thermo Fisher Scientific	AB-3720
Kit, 2019-nCoV CDC EUA(500Rxn/BX)	Integrated DNA Technologies, Inc.	10006606
TaqPath,1Step RTqPCR MtrMx,CG(2000rx/KT)	Life Technologies, Inc.	A15300
Water, Sterile,Nuclease-Free (1000ml/BT)	VWR International, LLC	10220-384
DNA ZAP!, Degradation Solution(250ml/BT)	Life Technologies, Inc.	AM9890
Wipe, RNase Zap Ambion (100/PK)	Life Technologies, Inc.	AM9786

CONTROLS TO BE USED WITH THE CRSP SARS-CoV-2 REAL-TIME REVERSE TRANSCRIPTASE (RT)-PCR DIAGNOSTIC ASSAY

- A “no template” (negative) control (NTC) is used for every run and is needed to confirm that there is no contamination for the assay.

- A positive template control (COVID-19_N_Postive, IDT, #10006625) targeting the SARS-CoV-2 N-gene (N1 and N2) is used for every run and is needed to confirm that the assay is completed by the intended design.

- An internal control primer/probe set, targeting the human RNase P gene, is used for every patient sample to confirm appropriate specimen collection and to monitor the integrity of nucleic acid extraction and RT-PCR reactions.

- A human specimen (HSC) extraction control is included in each run to test for failure in lysis and extraction and potential contamination during extraction.

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 (Refer to **Table 3** for a summary of expected control results).

1. ***COVID-19 RT-PCR Test controls – Positive, Negative, Extraction, and Internal*:**

   Controls should produce the results outlined in **Table 3**, below.

Table 3. Expected Control Results for the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1*

Control Location	N1	N2	RP	Result Interpretation	Action
NTC well	-	-	-	Plate passes NTC QC	Plate sent for review and reporting
NTC well	Any target positive			Plate Fails NTC QC	Plate reworked from RNA extraction
HSC well	-	-	+	Plate passes Extraction QC	Plate sent for review and reporting
HSC well	Any target positive		+/-	Plate fails Extraction QC	Plate reworked from RNA extraction
HSC well	-	-	-	Plate fails Extraction QC	Plate reworked from RNA extraction
nCoVPC	+	+	-	Plate passes Assay QC	Plate sent for review and reporting
nCoVPC	If ≤1 target is positive		-	Plate fails Assay QC	Plate reworked from RNA extraction

*Note: The results of the assay are reported according to the following categories where a + indicates a Ct of<40 and a - indicates a Ct of>40 or undetermined.

Table 4. Expected Control Results for the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 2.*

Control	N2	RP	Result Interpretation	Action
NTC wells (2 RP and 2 N2)	Both wells '-'	Both wells '-'	Plate passes NTC QC	Plate sent for review and reporting
NTC wells	Any well positive		Plate fails NTC QC	Plate reworked from RNA extraction
HSC+nCoVPC wells (2 RP and 2 N2)	≥1 out of 2 wells are '+'	≥1 out of 2 wells are '+'	Plate passes Extraction and Assay QC	Plate sent for review and reporting
HSC+nCoVPC wells (2 RP and 2 N2)	Both wells '-'	≥1 out of 2 wells are '+'	Plate fails Extraction and Assay QC	Plate reworked from RNA extraction
HSC+nCoVPC wells (2 RP and 2 N2)	≥1 out of 2 wells are '+'	Both wells '-'	Plate fails Extraction and Assay QC	Plate reworked from RNA extraction
HSC+nCoVPC wells (2 RP and 2 N2)	Both wells '-'	Both wells '-'	Plate fails Extraction and Assay QC	Plate reworked from RNA extraction

*Note: The results of the assay are reported according to the following categories where a + indicates a Ct of<40 and a - indicates a Ct of>40 or undetermined.

2. ***Examination and Interpretation of Patient Specimen Results***:
   Assessment of clinical specimen test results should 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. Please see **Tables 5 and 6** for guidance on patient specimen result interpretation and reporting of results.

Table 5. CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1*

2019 nCoV_N1	2019 nCoV_N2	RP	Result Interpretation
+	+	±	SARS-CoV-2 detected
If at least one target is positive		±	Inconclusive
-	-	+	SARS-CoV-2 not detected
-	-	-	Invalid Result

*Note: The results of the assay are reported according to the following categories where a + indicates a Ct of<40 and a - indicates a Ct of>40 or undetermined.

Table 6. CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 2*

2019 nCoV_N2	RP	Result Interpretation
+	+	SARS-CoV-2 detected
-	+	SARS-CoV-2 not detected
±	-	Invalid Result

*Note: The results of the assay are reported according to the following categories where a + indicates a Ct of<40 and a - indicates a Ct of>40 or undetermined.

PERFORMANCE EVALUATION

Analytical Sensitivity – Limit of Detection (LoD):

The LoD for Assay Version 1 SARS-CoV-2 detection was determined using dilutions of patient nasopharyngeal samples previously determined to be positive by the Massachusetts State Public Health Laboratory (MSPHL) CDC EUA assay. The SARS CoV-2 copy number in each patient sample was estimated using a relative standard curve generated by diluting SARS-CoV-2 synthetic RNA of a known concentration from Twist Biosciences (Cat no. MN908947.3, SKU: 102024). Each patient sample was diluted in VTM, independently extracted, and analyzed on the Applied Biosystems Viia7 thermocycler. Twenty of twenty replicates were detected at 4.0 x 10^3 copies/mL dilution (**Table 7**).

Table 7. CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 LoD Confirmation Study.

Concentration	# Positive Replicates/# Total Replicates
4.0 x 10^3 copies/mL	20/20

A bridging study was also conducted to determine LoD of both Version 1 and Version 2 of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay using the same spike-in material and factoring in pre-analytical steps. Spun polyester swabs (Fisher Scientific, NC1817884) were dipped in a negative clinical matrix and allowed to dry.

A high viral load positive clinical specimen was diluted in a range finding experiment to evaluate conversion of spiked-in molecules to detectable molecules. The positive clinical specimen had previously been run in the V1 assay with N1 and N2 Cts of 14.4 and 14.7, respectively, translating to ~322,000 genome copies/µl of media. This diluted patient sample material was then pipetted onto the swabs prepared as above.

Swabs being used in the V1 assay were placed in to 3mL of VTM. Swabs being used in V2 assay were placed into dry tubes. Swabs were processed through the dry swab reconstitution (V2 only), extraction, and detection protocols. 20 replicates at 2-fold above and 2-fold below the initially identified viral load level were also tested. LoD was determined as the level at which 19/20 replicates were successfully called positive. LoD was confirmed at 4.8 x 10^3 copies/mL for Assay Version 1 and 1.6 x 10^3 copies/mL for Assay Version 2 (**Table 8**).

Table 8. LoD confirmation Summary for Nasal Swabs Using the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 or Version 2 Workflows.

Assay Version	Spike-in Concentration	#positive replicates/ #total replicates	% Positive	Avg N Ct (V1) or N2 Ct (V2)	Std Dev Ct
V1	4.8 x 10^3 copies/mL	20/20	100%	33.1	1.0
	2.4 x 10^3 copies/mL	17/20	85%	34.1	2.0
	1.2 x 10^3 copies/mL	14/20	70%	34.4	2.0
V2	1.6 x 10^3 copies/mL	20/20	100%	32.5	0.9
	0.8 x 10^3 copies/mL	17/20	85%	33.5	1.3
	0.4 x 10^3 copies/ml	12/20	60%	33.6	1.4

Analytical Sensitivity – Inclusivity:
The sequences for the N1 and N2 primers/probes used in this assay are identical to the primer/probe sequences used in the FDA emergency use authorized CDC 2019-Novel Coronavirus (2019-nCoV) Diagnostic Panel. CDC has provided a right of reference to their Inclusivity Study data, which is available at https://www.fda.gov/media/134922/download.

Analytical Specificity – Cross-Reactivity:
In-silico Cross-Reactivity Assessment
The sequences for the N1 and N2 primers/probes used in this assay are identical to the primer/probe sequences used in the FDA emergency use authorized CDC 2019-Novel Coronavirus (2019-nCoV) Diagnostic Panel. CDC has provided a right of reference to their Cross-Reactivity Study data, which is available at https://www.fda.gov/media/134922/download.

Clinical Evaluation:
Performance of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 was evaluated using the Applied Biosystems Viia7 thermocycler and residual specimens collected from individual patients. Thirteen positive oropharyngeal (OP) swabs, 10 positive nasopharyngeal (NP) swabs, 10 positive NP/OP swabs, and 40 negative NP swabs were all previously tested by Massachusetts State Public Health Laboratory (MSPHL) using the CDC EUA authorized SARS-CoV-2 test. The results from the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-

PCR Diagnostic Assay Version 1 had 100% agreement with the expected results for the 73 samples compared to the EUA authorized SARS-CoV-2 comparator (**Table 9**).

Table 9. Summary of Clinical Performance of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 Compared to MSPHL CDC EUA Assay.

NP, OP, and NP/OP Specimens		**EUA Comparator Assay**		
		Positive	**Negative**	**Total**
CRSP SARS-CoV-2 Assay V1	**Positive**	33	0	33
	Negative	0	40	40
	Total	33	40	73
Positive Agreement		100% (33/33), 95% CI: (89.6, 100%)		
Negative Agreement		100% (40/40), 95% CI: (91.2, 100%)		

Performance of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay was also evaluated using the Applied Biosystems QuantStudio 7 Flex (QuantStudio software version 1.3) comparing paired nasopharyngeal (NP) specimens collected in VTM (Assay Version 1) and anterior nares swab specimens transported "dry" in a sterile tube, with no transport medium (Assay Version 2). Results are summarized in **Table 10** below. A scatterplot of the paired sample N2 target data is shown in **Figure 1** below. The majority of discordant samples were at, or below, the apparent LoD of the respective assay versions.

Table 10. Summary of Clinical Performance Paired NP Swabs in VTM (Assay Version 1) vs. Anterior Nares Swabs, "dry" (Assay Version 2).

		CRSP SARS-CoV-2 Assay Version 1 (NP Swab in VTM)		
		Positive	**Negative**	**Total**
CRSP SARS-CoV-2 Assay Version 2 (Dry Anterior Nares Swab)	**Positive**	69	14	83
	Negative	16	154	170
	Total	85	168	253
Positive Agreement		83.3%, 95% CI: (73.7, 89.7%)		
Negative Agreement		90.6%, 95% CI: (85.3, 94.1%)		

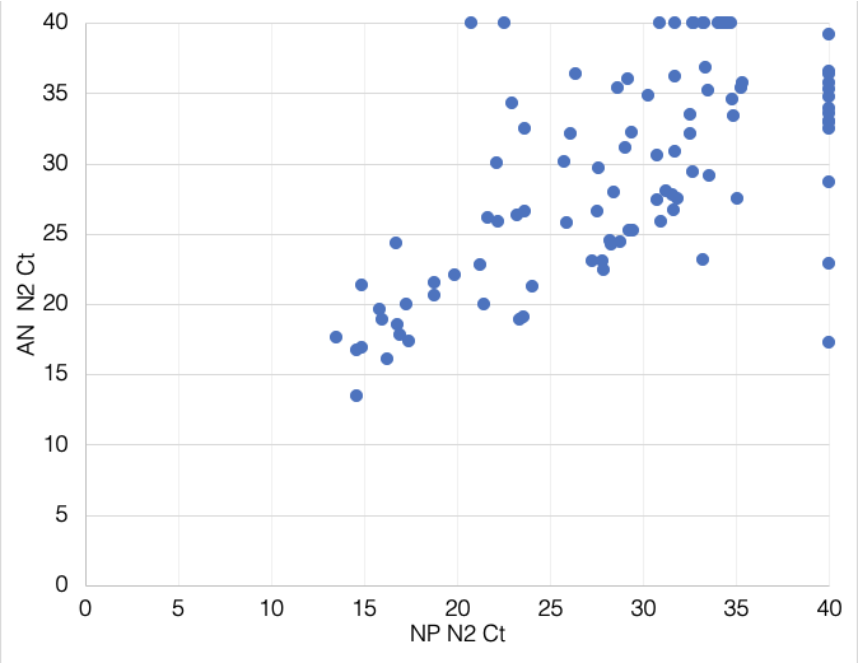

Figure 1. Scatterplot of Ct values for paired NP swabs in VTM (Assay Version 1, N2 target) vs. "dry" AN swabs (Assay Version 2, N2 target).

To better understand, and support, assay performance for "dry" anterior nares swabs using assay version 2, an additional clinical study was conducted. Anterior nares swab samples were consecutively collected from individuals and analyzed using the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay compared to another EUA authorized assay at a different laboratory. The results are summarized in **Table 11** below.

Table 11. Summary of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 2, Dry Anterior Nares Swab Specimens, Compared to an EUA Authorized Assay at a Different Laboratory.

		EUA Authorized Comparator (Dry Anterior Nares Swab)		
		Positive	**Negative**	**Total**
CRSP SARS-CoV-2 Assay Version 2 (Dry Anterior Nares Swab)	**Positive**	32	1	33
	Negative	1	85	86
	Total	33	86	119
Positive Agreement		97.0%, 95% CI: (84.7, 99.5%)		
Negative Agreement		98.8%, 95% CI: (93.7, 99.8%)		

SUMMARY OF THE EVALUATION OF THE CRSP SELF-SWAB KIT OR COLOR COVID-19 SELF-SWAB KIT OR BINX HEALTH AT-HOME NASAL SWAB COVID-19 SAMPLE COLLECTION KIT

SPECIAL CONDITIONS FOR USE FOR CRSP SELF-SWAB KIT STATEMENTS:
For Emergency Use Authorization (EUA) only.
For prescription use only.
For in vitro diagnostic use only.
For professional use only.
For use by people 18 years of age or older.

CRSP SELF-SWAB KIT DESCRIPTION AND TEST PRINCIPLE

This kit is intended to be used to facilitate testing to support safe return to campuses and other settings (e.g. offices) where other risk mitigations such as social distancing may not be possible. At risk populations will be identified by their universities or employers. The ordering physician determines who should be tested and CRSP Self-Swab Kit is not available as a direct-to-consumer test. If appropriate, physician-ordered testing is indicated and the individual is directed to collect a sample with CRSP Self-Swab Kit. Since the intended populations are co-located in a given setting the kits can be centrally issued (and collected) instead of being mailed.

CRSP Self-Swab Kit is to be used with authorized the CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay.

The CRSP Self-Swab Kit consists of a swab and a collection tube. The individual using the CRSP Self-Swab Kit to collect a nasal swab specimen performs sample collection according to the Collection Instructions.

For device transport, the individual must drop off the collected swab in the tube at a designated, staffed drop-off location (e.g. on campus) where the tube is registered and placed into a rack for packaging and transport to the laboratory. Subjects are directed to swab on the same day that they drop off the tube. All tubes collected on any given day are transported to the laboratory at the end of that day.

REAGENTS AND MATERIALS FOR CRSP SELF-SWAB KIT

Kit components:

Name	Description	Quantity	Material Supplier
Polyester Nasal Swab (NC1817884)	3-inch, sterile, individually wrapped, polyester nasal swab	1	Fisher Scientific
BD Vacutainer (BD 366408)	Sterile plastic tubes that are empty	1	Fisher Scientific
Bag	Resealable plastic bag containing kit components	1	
Instructions	Instruction sheet	1	

MEDICAL OVERSIGHT AND PROCESS TO BE USED FOR COLLECTION WITH CRSP SELF-SWAB KIT

The ordering physician determines who should be tested. Only negative results are available to the patients via the online interface. Positive and invalid test results are returned to the ordering healthcare provider who must call patients with those results. Sites cannot change this workflow.

Laboratory Accessioning Criteria:

- Collection time: Collection time on the tube label should be <56 hours prior to the current time.
  - If collection time is >56 hours from time of the start of testing, sample is rejected and moved to the quarantine rack for a supervisor to register as invalid in the system.
- Tube contains one swab.
  - If zero or more than one swab is in the tube, quarantine sample and bring to the attention of the General Supervisor on duty.
- The existing single swab in tube is oriented correctly - with cotton tip facing down (away from cap).
- Check to see if 'solid biological contents' are in tube.
  - Swab may be 'dry' or 'moist' without issue, but solids can cause issues with automation downstream. Mark any tubes with significant contents with a blue dot on the label to warn others downstream of potential errors on automation instrumentation.
  - If content appears that is will cause failure downstream if allowed to proceed, quarantine sample and bring to attention of the General Supervisor on duty.
- Label on tube exists and is intact and legible.
  - If label on tube does not exist, or is illegible or defaced, especially regarding Patient Name and/or Date of Birth, quarantine sample and bring to attention of the General Supervisor on duty
  - If label is placed on tube quite low or quite skewed, mark top of label with a red dot to warn others downstream of potential scanning error on automation instrumentation.

CONTROLS TO BE USED WITH THE CRSP SELF-SWAB KIT

1) Patient Samples are tested with CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay which is authorized under EUA200147 with applicable controls.

2) The CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay includes an RNAse P (RP) probe to test for the presence of sufficient human sample in the swab specimen.

CRSP SELF-SWAB KIT VALIDATION

CRSP Self-Swab Kit Sample Stability

The CRSP Self-Swab Kit uses polyester nasal swabs transported in dry tubes. As such CRSP is referencing the stability studies conducted by Quantigen Biosciences. Quantigen Biosciences has granted a right of reference to any sponsor wishing to pursue an EUA to leverage their COVID-19 swab stability data as part of that sponsor's EUA request. Quantigen Biosciences sample stability study for dry swabs supports 56-hour sample stability.

Human Usability Study for CRSP Self-Swab Kit

CRSP performed two usability studies for unsupervised collection using the CRSP Self-Swab Kit and dropping the sample off for transport to the CRSP CLIA-certified lab for testing. The Collection Instructions were updated based on the first study results and prior to conducting the second study. Actual-use testing was performed with 30 participants. The site observers observed the participant using the collection kit at a simulated kit swab/drop-off site. Cognitive debriefing interviews were conducted following the actual-use testing to gather users' perspectives on each critical task or use scenario and answers to survey questions were collected. Results of the usability testing were analyzed qualitatively to determine if the design of the kit and/or kit instructions need to be modified to reduce the use-related risks to acceptable levels.

Successful sample collection was measured by the presence of human RNase P in the sample. All samples were acceptable for testing and no samples failed processing due to particulate matter. The RNase P was detected in all samples (30/30).

The usability study results support the use of Collection Instructions with CRSP Self-Swab Kit.

SAMPLE COLLECTION KITS

- The CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay can be used with the CRSP Self-Swab Kit manufactured by CRSP.
- The CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay can be used with the Color COVID-19 Self-Swab Collection Kit. Color Genomics, Inc. granted the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard a right of reference to the data supporting use of this authorized home collection kit.
- The CRSP SARS-CoV-2 RT-PCR Diagnostic Version 2 Assay can be used with the binx health At-home Nasal Swab Covid-19 Sample Collection Kit. binx health, Inc. granted the Clinical Research Sequencing Platform (CRSP), LLC at the Broad Institute of MIT and Harvard a right of reference to the data supporting use of this authorized home collection kit.

ADDITIONAL REQUIREMENTS

Upon authorization, within 30 days CRSP will submit to the FDA a summary of any testing performed with CRSP Self-Swab Kit, the Color COVID-19 Self-Swab Collection Kit, and the binx health At-home Nasal Swab Covid-19 Sample Collection Kit including how many kits were prescribed and distributed for unsupervised collection, how many kits were returned, how many specimens had to be rejected during accession and the main reasons for rejection, and the positivity rate of the collection device

LIMITATIONS

- The use of this assay as an *in vitro* diagnostic under the FDA Emergency Use Authorization (EUA) is limited to Clinical Research Sequencing Platform, LLC at the Broad Institute of MIT and Harvard, Cambridge, MA which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, and meets requirements to perform high complexity tests. Use of this assay is limited to personnel who are trained in the procedure. Failure to follow these instructions may result in erroneous results.
- The performance of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1 was established using nasopharyngeal (NP), oropharyngeal (OP), and combined nasopharyngeal/oropharyngeal (NP/OP) swabs in viral transport media (VTM) or 0.9% sterile saline Nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal aspirates, and bronchoalveolar lavage specimens are also considered acceptable specimen types for use with the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 1, but the performance has not been established with these specimens.
- The performance of the CRSP SARS-CoV-2 Real-time Reverse Transcriptase (RT)-PCR Diagnostic Assay Version 2 was established using "dry" anterior nares swabs in a sterile tube (with no transport medium)
- Samples must be collected, transported, and stored using appropriate procedures and conditions. Improper collection, transport, or storage of specimens may hinder the ability of the assay to detect the target sequences.

WARNINGS:

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by authorized laboratories;
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
- 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, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.