EMERGENCY USE AUTHORIZATION (EUA) SUMMARY

SelfCheck cobas SARS-CoV-2 + Flu Assay for use with the SelfCheck Nasal Swabbing Kit

The Cleveland Clinic Foundation

For In vitro Diagnostic Use
For use under Emergency Use Authorization (EUA) only
For prescription use only
For use with anterior nasal swabs self-collected by individuals 18 Years of Age or Older

(The SelfCheck cobas SARS-CoV-2 + Flu Assay will be performed at the Cleveland Clinic Robert J. Tomsich Pathology and Laboratory Medicine Institute located at 9500 Euclid Ave/LL2, Cleveland, OH 44195, 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. The Laboratory Standard Operating Procedures were reviewed by the FDA under this EUA.)

INTENDED USE

The SelfCheck cobas SARS-CoV-2 + Flu Assay is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test intended for the simultaneous qualitative detection and differentiation of SARS-CoV-2, influenza A virus, and/or influenza B virus RNA in anterior nasal swab specimens that are self-collected at home using the SelfCheck Nasal Swabbing Kit, by individuals (18 years of age or older) who are suspected of respiratory viral infection consistent with COVID-19 by a healthcare provider based on either a telemedicine visit or an in-person visit with a healthcare provider. Samples collected using the SelfCheck Nasal Swabbing Kit are transported at ambient temperature for testing at a laboratory. The SelfCheck cobas SARS-CoV-2 + Flu Assay is intended for use as an aid in the differential diagnosis of SARS-CoV-2, influenza A, and influenza B in humans and is not intended to detect influenza C. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar.

Testing is limited to the Cleveland Clinic Robert J. Tomsich Pathology and Laboratory Medicine Institute, located at 9500 Euclid Ave/LL2, Cleveland, OH 44195, 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.

RNA from SARS-CoV-2, influenza A, and influenza B is generally detectable in anterior nasal swab specimens during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, influenza A, and/or influenza B 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 SARS-CoV-2 results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2, influenza A, and/or influenza B 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 SelfCheck cobas SARS-CoV-2 + Flu Assay is intended for use by qualified laboratory personnel specifically instructed and trained in the molecular testing and in vitro diagnostic procedures. The SelfCheck cobas SARS-CoV-2 + Flu Assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

SelfCheck cobas SARS-CoV-2 + Flu Assay uses an EUA authorized molecular test, cobas SARS-CoV-2 & Influenza A/B (EUA202635), for the qualitative detection of nucleic acid from SARS-CoV-2, influenza A, and influenza B in anterior nasal swab specimens self-collected at home using the SelfCheck Nasal Swabbing Kit.

1) cobas SARS-CoV-2 & Influenza A/B

cobas SARS-CoV-2 & Influenza A/B is a qualitative test for use on the cobas 6800/8800 Systems for the detection of the 2019 novel coronavirus (SARS-CoV-2), influenza A, and influenza B RNA in both nasal and nasopharyngeal swab samples. cobas SARS-CoV-2 & Influenza A/B is based on fully automated sample preparation (nucleic acid extraction and purification) followed by PCR amplification and detection. The RNA Internal Control, used to monitor the entire sample preparation and PCR amplification process, is introduced into each sample during sample processing. In addition, the test utilizes external controls (low titer positive control and a negative control).

Selective amplification of SARS-CoV-2 target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for ORF1a/b non-structural region that is unique to SARS-CoV-2. Additionally, a conserved region in the structural protein envelope E-gene was chosen for pan-Sarbecovirus detection. The pan-Sarbecovirus detection set will also detect SARS-CoV-2 virus. For influenza A and influenza B viruses, selective amplification of target nucleic acid from the sample is achieved by the use of target-specific forward and reverse primers for the matrix proteins 1 and 2 (M1/M2) for influenza A and the nuclear export protein (NEP) / nonstructural protein 1(NS1) genes for influenza B, respectively. Selective amplification of RNA Internal Control is achieved by the use of non-competitive sequence specific forward and reverse primers which have no homology with the coronavirus or influenza genomes. Amplified target is detected by cleavage of fluorescently labeled oligonucleotide probe. A thermostable DNA polymerase enzyme is used for amplification. Fluorescence intensity is monitored at each PCR cycle by the cobas 6800/8800 Systems. The data are analyzed and interpreted using the cobas 6800/8800 software and cobas SARS-CoV-2 & Influenza A/B analysis package.

Components of the cobas SARS-CoV-2 & Influenza A/B:
Reagents, materials and other consumables required for use on the cobas 6800/8800 Systems are as follows and are further described in the instructions for use of the authorized cobas SARS-CoV-2 & Influenza A/B assay.

- cobas SARS-CoV-2 & Influenza A/B Kit (384 test cassette P/N 09233474190)
- cobas SARS-CoV-2 & Influenza A/B Control Kit (P/N 09233482190)
- cobas Buffer Negative Control Kit (P/N 07002238190)
- cobas omni reagents for sample preparation
- Materials and consumables for use on cobas 6800/8800 Systems as described in the instructions for use of the authorized cobas SARS-CoV-2 & Influenza A/B assay.

Table 1: Reagent storage (when reagent is not on the system)

Reagent	Storage temperature
cobas SARS-CoV-2 & Influenza A/B – 384	2–8°C
cobas SARS-CoV-2 & Influenza A/B Control Kit	2–8°C
cobas Buffer Negative Control Kit	2–8°C
cobas omni Lysis Reagent	2–8°C
cobas omni MGP Reagent	2–8°C
cobas omni Sample Diluent	2–8°C
cobas omni Wash Reagent	15–30°C

2) SelfCheck Nasal Swabbing Kit

a) Product Overview:

The SelfCheck Nasal Swabbing Kit provided to the patient consists of a nylon, flocked nasal swab, pre-labeled 3 mL saline in a screw-capped collection tube, biohazard bag with absorbent sheet, padded envelope, test order requisition and SelfCheck collection and return instructions.

The SelfCheck Nasal Swabbing Kit consists of the following components:

Table 2: Content of the SelfCheck Nasal Swabbing Kit

Name	Description	Quantity	Material Supplier
Instructions	Instruction sheet, 8.5 x 11 in, full color, double-sided print, ¼ folded, customer art, text, logo	1	Various
Nasal Swab	Swab sampling, sterile, 152 mm length, nylon floss (flocked) tip; shaft: ABS (acrylonitrile butadiene styrene); item #8202-3	1	Jiangsu Hanheng Medical Technology (ASP)
Saline tube	0.85% sterile saline, 3 ml screw-capped tube; #4S0085; patient label is added at time of pickup	1	TEKNova

Name	Description	Quantity	Material Supplier
Absorbent sheet	Sheet desiccant 6 x 6 in	1	Consolidated packaging
Reclosable bag	Bag, reclosable, 2MIL 6 x 9 in MGRL2P0609	1	Minigrip
Biohazard bag	Sample transport bag, 6 x 9 in; 2 MIL Clear	1	Cardinal Health
Padded envelope	Gold Self-seal padded mailer #0 - 6 x 10 in S-1412 with return label	1	Uline
Test Order Requisition	8 ½ x 11 in paper with orders printed from EPIC HIS	1	Cleveland Clinic providers

b) Description of Sample Collection Steps:

The IFU for sample collection and shipping to the laboratory includes the following steps:

The patient should wash hands prior to opening the kit and removing the contents. The patient will verify name and date of birth on the pre-labeled tube. The cap is removed from the collection tube and set aside. The swab is removed from the wrapper. The tip of the swab is placed into the nares and the inside of one nostril is swabbed using a circular motion and light pressure. Sample from the other nostril is similarly collected using the same swab.

After a nasal swab sample(s) is collected, the swab is placed into the pre-labeled tube with 3 ml normal saline and the shaft is broken by bending at the breakpoint. The cap is screwed onto the tube tightly to prevent leakage. Upon contacting the saline, the collected nasal swab samples will remain stable for up to 56 hours prior to testing.

For device return, the patient places the tube in a biohazard bag and puts the test order and biohazard bag into a return envelope. On the day of collection, the patient brings the sealed envelope to a Cleveland Clinic drop box located inside a designated Cleveland Clinic location, e.g., a Cleveland Clinic Pharmacy, Express Care or other designated facility. Drop-boxes are locked and samples can only be accessed by Cleveland Clinic designated personnel. Samples will be picked-up by Cleveland Clinic or contracted couriers on established routes and transported in cars at ambient temperature to the Robert J. Tomsich Pathology and Laboratory Medicine facility. Couriers use electronic scanning to track time of pickup and delivery. Samples will not be received through the U.S. mail or by a shipping service.

An instructional video for sample collection, answers to frequently asked questions and a list of Cleveland Clinic Pharmacy and Express Care Clinics, including hours of operation, is available at www.clevelandclinic.org/selfcheck. Help is also available at 216.344.0300.

c) Medical Oversight and Process:

The SelfCheck Nasal Swabbing Kit will be distributed by Cardinal Health, Inc. A contract between Cardinal Health, Inc. and the Cleveland Clinic Foundation, ensures that the SelfCheck Nasal Swabbing

Kit product will only be distributed to the Cleveland Clinic Pharmacies, Express Cares, outpatient laboratory/phlebotomy stations and designated providers via the Cleveland Clinic electronic supply ordering system.

Outpatients will be evaluated for use of the SelfCheck Nasal Swabbing Kit by qualified providers either at an in-person or telemedicine visit. Licensed providers follow CDC guidelines for molecular testing. Only patients ≥18 years of age with an order for the test either placed in the EPIC electronic hospital information system (HIS) or on a Cleveland Clinic requisition may receive the kit. Patients may pick-up the kit at a designated Cleveland Clinic location, e.g., a Cleveland Clinic pharmacy, Express Care, or from an authorized provider. Locations may be found at www.clevelandclinc.org/selfcheck or by calling 216-444-0300. A test order requisition and sample label will be generated by the Cleveland Clinic authorized location that gives the patient the kit. The sample label will be placed on the tube. The test order requisition and labeled sample tube will be placed inside the kit before the patient is given the kit.

d) Accessioning of Nasal Swab Samples at Cleveland Clinic:

Samples collected with the SelfCheck Nasal Swabbing Kit are checked for the following criteria upon receipt at Cleveland Clinic prior to processing as outlined in the SelfCheck Nasal Swabbing Kit accessioning standard operating procedure (SOP):

- Identifiers and Orders: The name and date of birth on the sample label and paper requisition must match. The identifiers on the sample and requisition are verified in comparison to orders.
- Sample acceptability: The source, collection swab type and transport media are verified. (See rejection criteria below.)
- Transport time: The collection date and time on the sample and received date and time are recorded electronically in the Laboratory information System. Samples exceeding the established sample stability window are rejected.

Rejection criteria for the SelfCheck Nasal Swabbing Kit:

- Patient <18 years old
- Patient order/sample identification discrepancy
- Improper swab submitted (only the swab provided with the kit is accepted; wood, calcium alginate and gel swabs are rejected)
- Improper media used (only the saline provided in the kit is acceptable)
- Improper source (anything other than nasal)
- Broken or leaking sample container
- Sample outside of established stability (56 hours ambient)

If a test is rejected, the order will be cancelled, and the ordering provider will be contacted.

Note: The sample will not be rejected if collection date and time are missing on the requisition. The patient will be contacted to provide the information. The sample will be tested and result reported only after collection date/time information is confirmed to be within the established stability window.

INSTRUMENT REQUIREMENTS

The cobas 6800/8800 software and cobas SARS-CoV-2 & Influenza A/B analysis package must be installed on the instrument(s). The Instrument Gateway (IG) server will be provided with the system.

Table 3: Instrumentation

Equipment	**P/N**
cobas 6800 System (Moveable Platform)	05524245001 and 06379672001
cobas 6800 System (Fixed Platform)	05524245001 and 06379664001
cobas 8800 System	05412722001
Sample Supply Module	06301037001
Instrument Gateway	06349595001

CONTROLS TO BE USED WITH THE SELFCHECK COBAS SARS-COV-2 + FLU ASSAY

cobas SARS-CoV-2 & Influenza A/B used in the SelfCheck cobas SARS-CoV-2 + Flu Assay includes the following controls:

- Negative Control: The cobas Buffer Negative Control (no template control) is included with each batch of samples to monitor reagent and system contamination.

- Positive Control: The SARS-CoV-2 & Influenza A/B Positive Control is composed of non-infectious plasmid DNAs (microbial) containing SARS-CoV-2 sequence, pan-Sarbecovirus sequence, influenza A sequence and influenza B sequence. The positive control is included with each batch of samples to monitor for failures of RT-PCR reagents and reaction conditions.

- RNA Internal Control (RNA IC): Non-infectious RNA in MS2 bacteriophage is added to patient samples to monitor the entire sample preparation and PCR amplification process.

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. Results are reported as Positive, Presumptive Positive, Negative, or Invalid (Table 4). Presumptive positive SARS-CoV-2 results are considered positive and are only retested if it is necessary to differentiate between SARS-CoV-2 and other SARS Coronaviruses.

Table 4: cobas SARS-CoV-2 & Influenza A/B results interpretation

Target 1 Influenza A*	**Target 2 SARS- CoV-2**	**Target 3 Pan-Sarbecovirus**	**Target 4 Influenza B***	**Interpretation**
Negative	Negative	Negative	Negative	No target RNA Detected
Negative	Negative	Negative	Positive	Influenza B RNA Detected

Target 1 Influenza A*	**Target 2 SARS- CoV-2**	**Target 3 Pan-Sarbecovirus**	**Target 4 Influenza B***	**Interpretation**
Positive	Negative	Negative	Negative	Influenza A RNA Detected
Positive	Negative	Negative	Positive	Influenza A and Influenza B RNA Detected
Negative	Negative	Positive	Negative	Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS- CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Negative	Negative	Positive	Positive	Presumptive Positive for SARS-CoV-2 RNA and Influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Positive	Negative	Positive	Negative	Influenza A RNA Detected and Presumptive Positive for SARS-CoV-2 RNA. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Positive	Negative	Positive	Positive	Influenza A RNA Detected, Presumptive Positive for SARS-CoV-2 RNA, and Influenza B RNA Detected. A negative SARS-CoV-2 result and a positive pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the SARS-CoV-2 target region in the oligo binding site, 3) infection with some other Sarbecovirus (e.g., SARS-CoV or some other Sarbecovirus previously unknown to infect humans), or 4) other factors. For samples with a Presumptive Positive result, additional confirmatory testing may be conducted, if it is necessary to differentiate between SARS-CoV-2 and SARS-CoV-1 or other Sarbecovirus currently unknown to infect humans, for epidemiological purposes or clinical management.
Negative	Positive	Negative	Negative	SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan- Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.

Target 1 Influenza A*	Target 2 SARS- CoV-2	Target 3 Pan-Sarbecovirus	Target 4 Influenza B*	Interpretation
Negative	Positive	Negative	Positive	SARS-CoV-2 RNA and Influenza B RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Positive	Positive	Negative	Negative	Influenza A RNA and SARS-CoV-2 RNA Detected. A positive SARS-CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Positive	Positive	Negative	Positive	Influenza A RNA, SARS-CoV-2 RNA, and Influenza B RNA Detected. A positive SARS- CoV-2 result and a negative pan-Sarbecovirus results is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the pan-Sarbecovirus target region, or 3) other factors.
Negative	Positive	Positive	Negative	SARS-CoV-2 RNA Detected
Negative	Positive	Positive	Positive	SARS-CoV-2 RNA and Influenza B RNA Detected
Positive	Positive	Positive	Negative	Influenza A RNA and SARS-CoV-2 RNA Detected
Positive	Positive	Positive	Positive	Influenza A RNA, SARS-CoV-2 RNA, and Influenza B RNA Detected

If any individual target result is invalid, the presence or absence of that individual target cannot be determined. Other initial valid target results can be interpreted as described in the table.

* Results (positive and negative) for influenza should be interpreted with caution. If an influenza result is inconsistent with clinical presentation and/or other clinical and epidemiological information, FDA-cleared Influenza NAATs are available for confirmation if clinically indicated.

PERFORMANCE EVALUATION

1) cobas SARS-CoV-2 & Influenza A/B Assay Analytical and Clinical Performance Evaluation

The SelfCheck cobas SARS-CoV-2 + Flu Assay is based on the cobas SARS-CoV-2 & Influenza A/B assay run on the cobas 6800/8800 Systems per Roche's Instructions for Use (IFU) without modifications. The analytical and clinical performance of the cobas SARS-CoV-2 & Influenza A/B assay has been demonstrated by Roche Molecular Systems, Inc. in an Emergency Use Authorization (EUA202635). Roche has granted Cleveland Clinic right of reference to data using cobas SARS-CoV-2 & Influenza A/B assay in support of the SelfCheck cobas SARS-CoV-2 + Flu Assay. The details of the performance of the cobas SARS-CoV-2 & Influenza A/B assay can be found here: https://www.fda.gov/media/141887/download

2) SelfCheck Nasal Swabbing Kit Sample Stability Studies:

A sample stability study was conducted to confirm that signal degradation at high and low temperatures would not occur during shipping of the SelfCheck Nasal Swabbing Kit when tested with the SelfCheck cobas SARS-CoV-2 + Flu Assay. Contrived samples were prepared by spiking positive patient samples (SARS-CoV-2 or influenza A or B) into pooled remnant negative nasal swab samples at concentrations targeting 2x LoD and 10x LoD. A total of 20 replicates at 2x LoD and 10 replicates at 10x LoD were tested for each analyte at time zero and at each time point described in the summer and winter profiles below.

Table 5: Summer temperature excursion

Temperature	Cycle Period	Cycle Period Hours	Total Time Hours
40°C	1	8	8
22°C	2	4	12
40°C	3	2	14
30°C	4	36	50
40°C	5	6	56

Table 6: Winter temperature excursion

Temperature	Cycle Period	Cycle Period Hours	Total Time Hours
-10°C	1	8	8
18°C	2	4	12
-10°C	3	2	14
10°C	4	36	50
-10°C	5	6	56

Samples were tested at each time point with the cobas SARS-CoV-2 + Flu Assay. All samples remained positive following both summer and winter temperature exposure and Ct values remained within 3.0 Ct between time 0 and 56 hours, indicating acceptable sample stability under simulated shipping conditions. In addition, 10 negative samples tested at each time point, to monitor for false positives, remained negative throughout.

Summary results of the sample stability studies using the SelfCheck cobas SARS-CoV-2 + Flu Assay are below:

Table 7: Summary results for Summer Profile

Storage Temp	Storage Temp Time (hours)	Total Time (hours)	Mean Ct Values							
			SCoV-2		Pan SARS		Flu A		Flu B	
			2X	10X	2X	10X	2X	10X	2X	10X
N/A	0	0	34.42	32.99	34.15	32.51	31.54	29.49	33.17	31.59
40°C	8	8	34.51	33.00	34.01	32.43	31.67	29.54	33.31	31.68
22°C	4	12	34.28	32.91	33.86	32.29	31.62	29.54	33.28	31.66
40°C	2	14	34.25	32.82	33.97	32.37	31.60	29.52	33.33	31.73
30°C	36	50	34.43	33.18	33.70	32.60	31.48	30.00	33.00	31.82

40°C	6	56	34.41	33.25	33.79	32.31	31.49	30.18	32.93	31.92

Table 8: Summary results for Winter Profile

Storage Temp	Storage Temp Time (hours)	Total Time (hours)	Mean Ct Values							
			SCoV-2		Pan SARS		Flu A		Flu B	
			2X	10X	2X	10X	2X	10X	2X	10X
N/A	0	0	34.87	33.49	34.43	33.14	31.49	29.40	33.14	31.30
-10°C	8	8	35.11	33.58	34.60	33.20	31.70	29.65	33.40	31.66
18°C	4	12	35.33	33.63	34.64	33.21	31.83	29.70	33.53	31.72
-10°C	2	14	35.37	33.77	34.71	33.28	31.91	29.68	33.61	31.78
10°C	36	50	35.04	33.63	34.38	33.31	31.93	29.90	33.60	31.90
-10°C	6	56	34.93	33.61	34.43	33.19	31.99	30.12	33.47	32.10

These data support the use of the SelfCheck Nasal Swabbing Kit for transport and storage of self-collected nasal swab samples in saline at room temperature for up to 56 hours from the time of collection.

3) Human Usability Study:

A Human Usability Study of the SelfCheck COVID-19 Swabbing Kit (identical to the SelfCheck Nasal Swabbing Kit) was conducted with the Cleveland Clinic SARS-CoV-2 Assay (https://www.fda.gov/media/140788/download) using identical kit components and SelfCheck instructions as described above. The study was conducted at a Cleveland Clinic Express Care site to simulate the at-home environment and the participants were observed directly by a health care worker during the sample collection and packing process. The goal was to assess user comprehension of the SelfCheck Nasal Swabbing Kit for both collection and packaging of the nasal samples for transport.

Briefly, 38 participants ≥18 years of age with varied education levels who placed an order for COVID-19 molecular testing were recruited in the study. The study participants read the instructions in the SelfCheck Nasal Swabbing Kit and used the instructions and materials to collect nasal samples under observation of a health care worker who has been trained on use of the kit and has experience in collection of swabs for COVID-19 testing. The health care worker did not provide assistance or answer questions during the usability study. After collection, the patient placed the swab in a tube with 3 ml of normal saline and packaged the sample for delivery to the lab as described in the kit instructions. A second sample was collected by the health care worker using a nasal swab and routine practices for COVID-19 testing. Upon the completion of the sample collection, both patients and the health care worker who observed the patient using the SelfCheck Nasal Swabbing Kit completed a questionnaire designed by the Cleveland Clinic to evaluate their experience and suggest enhancements. Based on answers from questionnaires, the Instructions for using the SelfCheck Nasal Swabbing Kit were modified slightly to provide clarification. Samples collected by patients were tested with the Cleveland Clinic SARS-CoV-2 Assay and results were compared to nasal swabs collected by the health care worker.

Thirty-seven out of 38 participants were able to successfully collect the nasal swab. All 37 samples were acceptable for SARS-CoV-2 molecular testing based on laboratory assessment. Adequate sampling was

determined by the presence of RNase P in all 37 samples and the amount of RNase P detected was similar to that detected with the health care worker -collected swab (average Δ Ct <0.2), indicating successful collection of human biological material that was extracted and amplified. All patients indicated that they would be comfortable using the SelfCheck Nasal Swabbing Kit at home.

Based on the usability study data and feedback, the SelfCheck Nasal Swabbing Kit instructions were understandable, the kit was easy to use, and samples were successfully self-collected, supporting adequate usability of the SelfCheck Nasal Swabbing Kit.

4) Omission of RNase P Testing for Unobserved Self-Collected Samples – RNase P Negative Rate in Consecutively Collected Samples (n = 6,185):

Cleveland Clinic tested anterior nasal swab samples (n = 6,185) that were consecutively self-collected using the SelfCheck COVID-19 Swabbing Kit (identical to the SelfCheck Nasal Swabbing Kit) without observation over a two-month period. All samples were tested with the Cleveland Clinic SARS-CoV-2 Assay. Of the 6,185 samples, almost 100% (6,180/6,185) had an acceptable Ct value (<40) for the RNase P marker and 0.08% (5/6,185) were undetected for the RNase P marker. These data demonstrate that nearly all patients were able to self-collect an adequate nasal swab sample without observation using the SelfCheck Nasal Swabbing Kit. Therefore, the requirement to run a separate RNase P assay to evaluate unobserved self-collection of adequate human sample appears to be un-necessary.

LIMITATIONS:

- Anterior nasal swab specimens are considered acceptable sample types for use with SelfCheck cobas SARS-CoV-2 + Flu Assay. Testing of anterior nasal swabs (self-collected, unsupervised) is limited to individuals (18 years of age or older) suspected of respiratory viral infection consistent with COVID-19 by a healthcare provider based on either a telemedicine visit or an in-person visit with a healthcare provider.
- Samples that are collected at home will not be tested with an internal control to confirm that the sample was properly collected. A false negative result may occur if a sample is improperly collected, transported or handled. False negative results may also occur if amplification inhibitors are present in the sample or if inadequate numbers of organisms are present in the sample.
- This test cannot rule out diseases caused by other bacterial or viral pathogens.
- Samples must be collected, transported, and stored using appropriate procedures and conditions. Improper collection, transport, or storage of samples may hinder the ability of the assay to detect the target sequences.
- Results from the SelfCheck cobas SARS-CoV-2 + Flu Assay should be used as an adjunct to clinical observations and other information available to the physician. The result is only for clinical reference, and the clinical management of patients should be considered in combination with their symptoms/signs, history, other laboratory tests and treatment responses.
- Although the detected target sequences of this test are in conserved regions of the SARS-CoV-2 and influenza A/B genomes, rare mutations may lead to negative results.

- Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for treatment or other patient management decisions. Optimum sample types and timing for peak viral levels during infections caused by SARS-CoV-2 have not been determined.
- Results (positive and negative) for influenza should be interpreted with caution. If an influenza result is inconsistent with clinical presentation and/or other clinical and epidemiological information, FDA-cleared influenza NAATs are available for confirmation if clinically indicated.
- The performance of this test was established based on the evaluation of a limited number of clinical samples. Clinical performance has not been established with 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.

WARNINGS:

- For in vitro diagnostic use under FDA Emergency Use Authorization only.
- For Prescription Use 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 and differentiation of nucleic acid from SARS-CoV-2, influenza A and/or influenza B, 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, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.