EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
FOR THE QUEST DIAGNOSTICS RC COVID-19 +FLU RT-PCR TEST USED WITH THE QUEST DIAGNOSTICS SELF-COLLECTION KIT FOR COVID-19 +FLU

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

INTENDED USE

The Quest Diagnostics RC COVID-19 +Flu RT-PCR is intended for the simultaneous qualitative detection and differentiation of nucleic acid from SARS-CoV-2, influenza A virus and/or influenza B virus in nasal swab specimens self-collected at home, using the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu by individuals suspected of respiratory viral infection consistent with COVID-19 when home collection is determined to be appropriate by a healthcare provider. Clinical signs and symptoms of respiratory viral infection due to SARS-CoV-2 and influenza can be similar. Specimens collected using the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu can be transported at ambient temperature for testing.

Testing is limited to laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests.

Results are 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. RNA from SARS-CoV-2, influenza A, and influenza B are generally detectable in nasal swabs during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2, influenza A virus, and/or influenza B virus 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. Specimens that are self-collected will not be tested with an internal control to confirm that the specimen was properly collected. Self-collected specimens from SARS-CoV-2, influenza A, and/or influenza B positive individuals may yield negative results if the specimen was not collected properly.

Testing with the Quest Diagnostics RC COVID-19 +Flu RT-PCR is intended for use by qualified and trained laboratory personnel specifically instructed and trained in the molecular testing and in vitro diagnostic procedures. The Quest Diagnostics RC COVID-19 +Flu RT-PCR and the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu are only for use under the Food and Drug Administration’s Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

1) Device Description:

The Quest Diagnostics RC COVID-19 +Flu RT-PCR for use with the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu enables the self-collection of a nasal swab specimen by an individual suspected of respiratory viral infection consistent with COVID-19 when home collection is determined to be appropriate by a healthcare provider. This specimen is then transported to a laboratory designated by Quest Diagnostics for SARS-CoV-2, influenza A and/or influenza B testing using the Quest Diagnostics RC COVID-19 +Flu RT-PCR assay. The Quest Diagnostics COVID-19 +Flu Self-Collection Kit includes the following materials:

Sample Collection and Shipping Instructions
Swab (foam or a wrapped polyester)
Specimen Transport Tube
Zip-lock bag (biohazard symbol) and desiccant
Test Requisition (pre-printed)
Shipping box
FedEx Bag with FedEx Label (pre-printed)
Priority label (optional)
Pre-printed tube label

The Quest Diagnostics Self-Collection Kit for COVID-19 +Flu was reviewed for adherence to the Department of Transportation's shipping requirements for hazardous materials. The kit was found to be acceptable and appropriate for shipping within the United States.

2) Test Principle:
The Quest Diagnostics RC COVID-19 +Flu RT-PCR is only used for patients suspected of respiratory viral infection consistent with COVID-19 when home collection is determined to be appropriate by a healthcare provider. Home self-collection is intended for individuals 18 years of age and older. After a healthcare provider qualifies a patient for testing using the self-collection kit, the healthcare provider will submit the order to Quest Diagnostics. Quest Diagnostics will then ship the self-collection kit to the patient.

Upon receipt of the kit, the patient will be directed to review the Instructions' READ FIRST FOR YOUR SAFETY section, which includes direction to watch a self-collection demo video available online. After collection, the patient ships the specimens to Quest Diagnostics via FedEx overnight shipping as per the self-collection instructions for use. Self-collected nasal swab specimens will be tested using the Quest Diagnostics RC COVID-19 +Flu RT-PCR which is performed using the FDA EUA-authorized Roche cobas SARS-CoV-2 & Influenza A/B molecular test, which is an automated RT-PCR based platform. The test report will then be electronically delivered to both the ordering healthcare provider and the participant.

The Quest Diagnostics Self-Collection Kit for COVID-19 +Flu will include instructions, a pre-printed test requisition form, nasal swab, transport tube containing appropriate fluid (i.e., 0.9% saline), pre-printed tube label, zip-lock bag (with biohazard symbol) containing a desiccant,

shipping box, and FedEx UN3373 shipping bag with pre-printed FedEx Shipping Label attached. Instructions are included in the kit to direct the home users how to appropriately collect the nasal swab specimen, place the specimen into the transport tube, properly package the specimen, and mail the specimen back to the laboratory using the pre-labeled FedEx return bag. Each Quest Diagnostics COVID-19 +Flu Self-Collection Kit is intended to be returned via FedEx service at ambient conditions on the same day of collection.

Specimens received at the laboratory designated by Quest Diagnostics will undergo review for integrity of packaging, adequacy of sample, verification of patient information, and acceptable time window between specimen collection and receipt at the laboratory prior to acceptance for testing.

Laboratories designated by Quest Diagnostics are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests using an FDA authorized NAAT test per the Instructions for Use.

3) Medical Oversight and Process to be Used:
Medical oversight of the process is provided by the healthcare provider who is ordering the test. Quest Diagnostics will only distribute self-collection kits to patients suspected of respiratory viral infection consistent with COVID-19 when home collection is determined to be appropriate by a healthcare provider.

PATIENT INCLUSION/EXCLUSION CRITERIA

Inclusion of patients suspected of respiratory viral infection consistent with COVID-19 when home collection is determined to be appropriate by a healthcare provider.

INSPECTION OF SPECIMENS

Quest Diagnostics submitted an SOP for Receipt and accessioning of COVID-19 +Flu Self-Collection Kits at Quest Diagnostics Laboratory. This protocol is summarized below.

Applies to specimens received from individuals using the home collection kit:
Specimens received through the self-collection kit will be checked for the following criteria before entering the workflow:

- Proper return of sample packaging: confirm that sample is present, test requisition is present, the sample tube is not broken, sample is not leaking,
- Verification of Patient Information: ensure the patient information on the sample container matches the information on test requisition
- Sample Acceptability: ensure sufficient sample volume, acceptable sample temperature, sample was received within 2 days from patient shipping date, and sample was received within acceptable stability window after collection

4) Test results and interpretation

CONTROLS TO BE USED WITH QUEST DIAGNOSTICS RC SARS-COV-2 ASSAY
Quest Diagnostics will use the controls included in the Roche cobas SARS-CoV-2 & Influenza A/B Assay, which includes an internal control, positive control and negative control. These controls will be used in accordance with the package insert.

Roche stipulates a separate required but not provided control kit that includes the positive controls and negative controls, and the controls are ready-to-use. The instrument assesses the validity of the run and will not run patient samples until valid control results are achieved.

INTERPRETATION OF RESULTS
All test controls must 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.

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 Quest Diagnostics RC COVID-19 +Flu RT-PCR will use the result interpretation displayed in the table below:

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
Positive	Negative	Negative	Negative	Influenza A RNA Detected
Positive	Negative	Negative	Positive	Influenza A and Influenza B RNA Detected

Target 1 Influenza A	Target 2 SARS-CoV-2	Target 3 Pan-Sarbecovirus	Target 4 Influenza B	Interpretation
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.

Target 1 Influenza A	Target 2 SARS-CoV-2	Target 3 Pan-Sarbecovirus	Target 4 Influenza B	Interpretation
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 a result is invalid, then the assay will be repeated if adequate specimen is available. If on repeat the specimen is still invalid, then Quest Diagnostics will offer the patient the opportunity to collect a second specimen at no additional cost and/or a refund of their purchase minus the ordering provider's fee. All results are delivered electronically to the healthcare provider and the participant.

Collection Device Stability:
Quest Diagnostics will evaluate stability of its specimen collection media and container/closure systems in real time (25%, 50%, 75%, 100% and 125% of shelf life) and may use accelerated stability analysis to supplement the real time studies. Stability inspection of transport media would include: pH, bioburden, precipitation, leakage, and integrity of the container/closure system.

PERFORMANCE EVALUATION

1) Quest Diagnostics Self-Collection Kit for COVID-19 +Flu Sample Stability Studies:
A specimen stability study was conducted to confirm that signal degradation at high and low temperatures would not occur during shipping. Contrived samples for this study were prepared by spiking a SARS-CoV-2 remnant positive patient sample (or influenza A or B culture) into pooled remnant negative patient samples at concentrations targeting 2X LoD and 10X LoD. The SARS-CoV-2 remnant patient samples used for this study included upper respiratory swabs in sterile normal saline (0.9% NaCl). For each transport media, a total of 20 replicates at 2X LoD and 10 replicates at 10X LoD were tested for each analyte.

This study simulated shipping conditions by cycling the samples through the following temperature excursion:

Summer Excursion

Storage Temperature	Time at Storage Temp (hours)	Total Time (hours)	Mean Ct Values							
			SCoV2		Pan SARS		Flu A		Flu B	
			2x	10x	2x	10x	2x	10x	2x	10x
N/A	0	0	34.11	32.59	33.47	32.12	31.15	29.57	31.23	28.73
40°C	8	8	34.06	33.02	33.47	32.34	31.62	30.31	31.83	29.84
22°C	4	12	34.20	32.71	33.47	32.19	31.41	29.89	31.80	29.02
40°C	2	14	34.04	32.66	33.48	31.99	31.33	29.88	31.38	28.96
30°C	36	50	34.03	32.77	33.37	32.03	31.24	29.90	31.48	29.07
40°C	6	56	34.08	32.73	33.36	32.02	31.40	29.92	31.65	29.41

Winter Excursion

Storage Temperature	Time at Storage Temp (hours)	Total Time (hours)	Mean Ct Values							
			SCoV2		Pan SARS		Flu A		Flu B	
			2x	10x	2x	10x	2x	10x	2x	10x
N/A	0	0	34.26	32.88	33.67	32.23	31.60	29.60	31.53	28.91
-10°C	8	8	34.52	32.92	33.91	32.29	31.71	29.55	31.65	29.02
18°C	4	12	34.30	32.85	33.70	32.23	31.60	29.50	31.53	29.25
-10°C	2	14	34.41	32.97	33.90	32.26	31.79	29.69	31.59	29.13
10°C	36	50	34.49	32.92	33.54	32.08	31.39	29.81	31.59	29.15
-10°C	6	56	34.43	33.23	33.67	32.50	31.43	30.18	31.95	29.95

Samples were tested at each timepoint with the Quest Diagnostics RC COVID-19 +Flu RT-PCR assay. The Ct values at each timepoint were compared to the Ct values at time zero. All samples remained positive at 56 hours after cycling in and out of high and low temperatures. Additionally, Ct values remained within 3.0 Ct between time 0 and 56 hours, indicating acceptable specimen stability under simulated shipping conditions.

2) Human Usability Studies for the Quest Diagnostics Self-Collection Kit for COVID-19:

The Instructions for Use for the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu are the same as those for the Quest Diagnostics Self-Collection Kit for COVID-19. Therefore, the study demonstrating usability of the Quest Diagnostics Self-Collection Kit for COVID-19 is applicable to the usability of the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu. The usability study performed for Quest Diagnostics Self-Collection Kit for COVID-19 is described and summarized in the paragraphs below.

A usability study was conducted to confirm that patients could follow the instructions included in the Quest Diagnostics Self-Collection Kit for COVID-19 to appropriately collect, package, and ship a self-collected nasal specimen to a Quest Diagnostics laboratory for testing. The study was completed in an actual home-use environment.

After providing informed consent, participants were mailed a Quest Diagnostics Self-Collection Kit for COVID-19, which included the instructions for use, test requisition form, foam nasal swab, specimen transport tube containing transport media, biohazard bag containing desiccant, transport box, pre-printed FedEx label and shipping bag. The participants proceeded to collect a nasal specimen unobserved in their home environment and then shipped the specimens back to a laboratory designated by Quest Diagnostics via FedEx following the instructions on the kit. Participants were also asked to fill out a questionnaire that assessed their ability to understand the different steps in the instructions for use.

A total of 47 individuals consented to participate in the study. These participants included individuals representing varying education levels and age ranges. Of the 47 individuals, 42 returned the kit and questionnaire within the study window. Of these 42, 95.2% (40/42) returned a specimen that was acceptable for testing according to pre-determined acceptance criteria. The returned specimens were also tested with a PCR assay detecting the internal house-keeping gene RNase P. All specimens yielded strong RNase P signals, indicating successful sampling of human biological material.

3) Quest Diagnostics RC COVID-19 +Flu RT-PCR Analytical and Clinical Performance Evaluation:

The Quest Diagnostics RC COVID-19 +Flu RT-PCR is performed using the Roche cobas SARS-CoV-2 & Influenza A/B test on the cobas 6800/8800 systems, testing nasal swabs collected with the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu. The analytical and clinical performance of the Roche cobas SARS-CoV-2 & Influenza A/B Assay has been demonstrated by Roche in the Emergency Use Authorization submission authorized on 10/28/2020. The details of the performance of the authorized Roche cobas SARS-CoV-2 & Influenza A/B test can be found here: https://www.fda.gov/media/141887/download. Roche granted Right of Reference to Quest Diagnostics for Roche's authorized cobas SARS-CoV-2 & Influenza A/B test. While it has been determined, based on data generated in studies evaluating specimen adequacy (e.g., by evaluating RNase P), that unobserved self-collected nasal swab (NS) samples using the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu will likely contain similar levels of human cellular genetic materials as HCP-collected NS samples, performance of testing self-collected NS samples using the Quest Diagnostics

Self-Collection Kit for COVID-19 +Flu and the Quest Diagnostics RC COVID-19 +Flu RT EUA test has not been specifically evaluated.

4) Not including RNase P Control for Unobserved Self-Collection – RNase P Negative Rate in Health Program Population (n = 37,084)

   Quest Diagnostics evaluated all nasal swab specimens (n = 37,084) that were self-collected using the Quest Diagnostics Self-Collection Kit for COVID-19 without observation under a health program sponsored by an employer or school of higher education. All specimens were tested with the Quest SARS-CoV-2 rRT-PCR and RNase P RT-PCR. Of the 37,084 specimens, 12,303 were from females and 24,781 were males. Of the 12,303 females, almost 100% (12,302/12,303 95% CI 99.95-100%) had an acceptable Ct value for the RNase P marker, and 0.008% (1/12,303) had an unacceptable Ct value (>35) for the RNase P marker. Of the 24,781 males, almost 100% (24,776/24,781, 95% CI 99.95-100%) had an acceptable Ct value for the RNase P marker and 0.020% (5/24,781) had an unacceptable Ct value (>35) for the RNase P marker. These data demonstrate that nearly all participants were able to self-collect an adequate nasal swab specimen without observation for SARS-CoV-2 testing. Therefore, the requirement to observe patients using the Quest Diagnostics Self-Collection Kit for COVID-19 to collect nasal specimens appears to be un-necessary.

Warnings:

- This product has not been FDA cleared or approved but has been authorized by FDA under an EUA for use by laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests;
- This product has been authorized only for the detection of nucleic acid from SARS-CoV-2, influenza A and influenza B, not for any other viruses or pathogens
- 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.
- While it has been determined, based on reviewing studies evaluating specimen adequacy (e.g., by evaluating RNase P), that unobserved self-collected NS samples using the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu will likely contain similar levels of human cellular genetic materials as HCP-collected NS samples, performance of testing self-collected NS samples using the Quest Diagnostics Self-Collection Kit for COVID-19 +Flu and the Quest Diagnostics RC COVID-19 +Flu RT EUA test has not been specifically evaluated;
- 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.