Updated November 27, 2020

EMERGENCY USE AUTHORIZATION (EUA) SUMMARY
FOR THE QUEST DIAGNOSTICS RC SARS-COV-2 ASSAY
For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only

INTENDED USE

The Quest Diagnostics RC SARS-CoV-2 Assay is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasal swab specimens self-collected at home, using the Quest Diagnostics Self-Collection Kit for COVID-19, or other authorized home-collection kit, by individuals suspected of COVID-19 when home collection is determined to be appropriate by a healthcare provider. Specimens collected using the Quest Diagnostics Self-Collection Kit for COVID-19 can be transported at ambient temperature for testing.

This assay is also intended for the qualitative detection of nucleic acids from SARS-CoV-2 in pooled samples containing up to six individual upper respiratory swab specimens (nasopharyngeal, mid-turbinate, anterior nares or oropharyngeal swabs) that were collected in individual vials containing transport media from individuals suspected of COVID-19 by their healthcare provider or with nasal swab specimens self-collected at home, using the Quest Diagnostics Self-Collection Kit for COVID-19, or other authorized home-collection kit, by individuals suspected of COVID-19 when home collection is determined to be appropriate by a healthcare provider.

Negative results from pooled samples should be treated as presumptive and, if inconsistent with clinical signs and symptoms or necessary for patient management, pooled samples should be tested individually. Specimens included in pools with a positive, presumptive positive, or invalid result must be tested individually prior to reporting a result. Specimens with low SARS-CoV-2 RNA concentrations may not be detected in sample pools due to the decreased sensitivity of pooled testing.

Testing is limited to laboratories designated by Quest Diagnostics that are certified under CLIA, 42 U.S.C. §263a, and meet 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 upper respiratory swab 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 SARS-Cov-2 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. 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 positive individuals may yield negative results if the specimen was not collected properly.

Testing with the Quest Diagnostics RC SARS-CoV-2 Assay 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 SARS-CoV-2 Assay and the Quest Diagnostics Self-Collection Kit for COVID-19 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 SARS-CoV-2 Assay for use with the Quest Diagnostics Self-Collection kit for COVID-19 enables the self-collection of a nasal swab specimen by an individual qualified by their healthcare provider as needing SARS-CoV-2 testing. This specimen is then transported to a laboratory designated by Quest Diagnostics for SARS-CoV-2 testing using the Quest Diagnostics RC SARS-CoV-2 Assay. The Quest Diagnostics COVID-19 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 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 SARS-CoV-2 Assay is only used for patients who have been previously qualified by their healthcare provider as needing SARS-CoV-2 testing based on the provider's medical judgement regarding symptoms, exposure, and risk factors. 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. The patient then 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 SARS-CoV-2 Assay which is performed using the FDA EUA-authorized Roche cobas SARS-CoV-2 molecular test on the cobas 6800/8800 Systems, 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 includes instructions, a pre-printed test requisition form, nasal swab, transport tube containing appropriate fluid (i.e., VCM, 0.9% saline, or PBS), 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 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.

In sample pooling, specimens are identified from populations based on positivity rate (for example, by county, zip code or by client). The positivity rate will be used to determine the pool size that provides the maximum testing efficiency. The assay is validated for up to six sample pooling, however, in practice, the pool size will not exceed four samples. If the pool is positive or inconclusive or invalid, then each of the constituent samples is re-tested as a separate individual specimen. If the pool is negative, then each constituent sample is reported as negative.

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 who were previously qualified for SARS-CoV-2 testing by a healthcare provider based on symptoms, exposure, and risk factors.

PATIENT INCLUSION/EXCLUSION CRITERIA

Only patients who are suspected of COVID-19 by a healthcare provider are eligible to receive the Quest Diagnostics COVID-19 self-collection kit.

INSPECTION OF SPECIMENS AND VERIFICATION OF OBSERVED SELF-COLLECTION

Quest Diagnostics has submitted an SOP for Receipt and accessioning of COVID-19 self-collection kits at Quest Diagnostics Laboratory. This protocol is summarized below.

Applies to specimens received from patients 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) ***Procedure, Test results and interpretation***

Procedure

Quest Diagnostics will perform the procedure as described in the manufacturer's instructions, except for sample pooling:

- When performing pooling, laboratories will monitor sample pooling in accordance with Roche cobas SARS-Cov-2 assay Protocol for Monitoring of Sample Pooling Testing Strategies.

In preparing sample pools combine and mix equal amounts of each specimen (e.g., for 4 specimens, combine 200 µL) for a total pool sample volume of 0.8 mL in the cobas omni secondary tube. Following the addition of the last specimen, mix by pipetting the pool up and down in the cobas omni secondary tube.

CONTROLS TO BE USED WITH QUEST DIAGNOSTICS RC SARS-COV-2 ASSAY

Controls used with the Quest Diagnostics RC SARS-CoV-2 Assay preformed using the Roche cobas SARS-CoV-2 Assay include an internal control, positive control, and negative control, and are used in accordance with the package insert.

The Roche assay requires a separate control kit that is not provided in the assay kit. The control kit 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 results are achieved.

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.

The Quest Diagnostics RC SARS-CoV-2 Assay will follow the result interpretation displayed in the tables below:

Specimen Result Interpretation for Unpooled Specimens

Target 1	Target 2	Result	Interpretation
Positive	Positive	Positive	Result for SARS-CoV-2 RNA is Detected
Positive	Negative	Positive	Result for SARS-CoV-2 RNA is Detected. A positive Target 1 result and a negative Target 2 result is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the Target 2, target region, or 3) other factors.
Negative	Positive	Presumptive Positive	Result for SARS-CoV-2 RNA is Presumptive Positive. A negative Target 1 result and a positive Target 2 result is suggestive of 1) a sample at concentrations near or below the limit of detection of the test, 2) a mutation in the Target 1 target region in the oligo binding sites, or 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	Negative	Result for SARS-CoV-2 RNA is Not Detected
Positive	Invalid	Positive	Result for SARS-CoV-2 RNA is Detected
Invalid	Positive	Presumptive Positive	Result for SARS-CoV-2 is Presumptive Positive. 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	Invalid	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	Negative	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	Invalid	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.

If a result for a self-collected specimen (that is unobserved by a healthcare provider) 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.

Specimen Result Interpretation for Pooled Specimens

Target 1	Target 2	Result	Interpretation
Positive	Positive	**POOLED POSITIVE – DO NOT REPORT**	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Positive	Negative	**POOLED POSITIVE – DO NOT REPORT**	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Negative	Positive	**POOLED POSITIVE – DO NOT REPORT**	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Negative	Negative	Negative	Result for SARS-CoV-2 RNA is Not Detected
Positive	Invalid	**POOLED POSITIVE – DO NOT REPORT**	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Invalid	Positive	**POOLED POSITIVE – DO NOT REPORT**	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Negative	Invalid	Invalid	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Invalid	Negative	Invalid	Repeat each constituent specimen in the pool as a separate unpooled specimen.
Invalid	Invalid	Invalid	Repeat each constituent specimen in the pool as a separate unpooled specimen.

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 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 into pooled negative patient samples at concentrations targeting 2X LoD and 10X LoD. The remnant patient samples used for this study included upper respiratory swabs in sterile normal saline (0.9% NaCl). A total of 20 replicates at 2X LoD and 10 replicates at 10X LoD were tested.

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)**
40°C	8	8
22°C	4	12
40°C	2	14
30°C	36	50
40°C	6	56

Winter Excursion

Storage Temperature	Time at Storage Temp (hours)	Total Time (hours)
-10°C	8	8
18°C	4	12
-10°C	2	14
10°C	36	50
-10°C	6	56

Samples were tested at each timepoint with the Quest Diagnostics EUA assay, Quest SARS-CoV-2 rRT-PCR. The Ct values at each timepoint were compared to the Ct values at time zero. All samples for both transport media remained positive at 56 hours after cycling in and out of high and low temperatures. Additionally, Ct values remained less than 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:

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 were 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 SARS-CoV-2 Assay Analytical and Clinical Performance Evaluation:***

The Quest Diagnostics RC SARS-CoV-2 Assay is performed on the Roche cobas SARS-CoV-2 Assay on the cobas 6800/8800 systems using nasal swabs collected with the Quest Diagnostics Self-Collection Kit for COVID-19. The analytical and clinical performance of the Roche cobas SARS-CoV-2 Assay has been demonstrated by Roche in the Emergency Use Authorization submission authorized on 03/12/2020. The EUA was re-authorized to allow testing of up to and including 6-sample pools on 10/15/2020. The details of the performance of the authorized Roche cobas SARS-CoV-2 test can be found here: https://www.fda.gov/media/136049/download. Roche granted Right of Reference to Quest Diagnostics for Roche's authorized Roche cobas SARS-CoV-2 test.

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

Quest Diagnostics selected 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 also appears to be un-necessary.

5) ***Quest Diagnostics RC SARS-CoV-2 Assay Pooling Performance Evaluation:***

The Quest Diagnostics RC SARS-CoV-2 Assay is performed on the Roche cobas SARS-CoV-2 Assay on the cobas 6800/8800 systems using nasal swabs collected with the Quest Diagnostics Self-Collection Kit for COVID-19. Roche demonstrated in their Emergency Use Authorization submission originally authorized on 03/12/2020 and reissued on 10/15/2020, detection of nucleic acids from SARS-CoV-2 in pooled samples containing up to and including six individual samples from clinician-instructed self-collected nasal swab specimens (collected on site), or clinician-collected nasal, nasopharyngeal, and oropharyngeal swab specimens. The details of the

performance of the authorized Roche cobas SARS-CoV-2 test can be found here: https://www.fda.gov/media/136049/download. Roche granted Right of Reference to Quest Diagnostics for Roche's authorized Roche cobas SARS-CoV-2 test.

Based on data demonstrating similar performance for the detection of SARS-CoV-2 RNA between HCP collected nasopharyngeal samples and unsupervised, self-collected nasal swab samples and the RNase P study demonstrating that nearly all participants were able to self-collect an adequate nasal swab specimen without observation, and the sample pooling validation Conducted by Roche to assess the risk of reduced sensitivity due to the dilution effect, no additional validation studies were needed to support the pooling of home collected samples when tested with Quest Diagnostics RC SARS-CoV-2 Assay.

Warnings:

- This test has not been FDA cleared or approved;
- This test 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 test has been authorized only for the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens; and
- This test 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 authorization is terminated or revoked sooner.
- Some positive samples may not be detected when diluted and tested in pools. SARS-CoV-2 RNA concentration is reduced when a positive sample is pooled with other samples, and the reduction corresponds inversely to the pool size. For example, if there is only one positive sample in a pool of 6, the concentration in the original sample would need to be 6 times the assay limit of detection in order for the concentration in the pool to be at the limit of detection.

Contact Information, Laboratory Service Ordering, and Support

Quest Diagnostics Infectious Disease, Inc. 33608 Ortega Highway, Bldg. B-West Wing San Juan Capistrano, CA 92675

U.S.A.

+1.949.728.4000