EMERGENCY USE AUTHORIZATION (EUA) SUMMARY OF THE KPMAS COVID-19 TEST USED WITH THE KPMAS COVID-19 HOME COLLECTION KIT

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

INTENDED USE

The KPMAS COVID-19 Test is intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasal swab specimens self-collected by KPMAS Health Plan members observed at home via telemedicine, using the KPMAS COVID-19 Home Collection Kit. Specimens are collected from individuals who are suspected of COVID-19 by their healthcare provider and from any individual, including from individuals without symptoms or other reasons to suspect COVID-19. Specimens collected using the KPMAS COVID-19 Home Collection Kit can be transported at ambient temperature for testing.

Testing is limited to the KPMAS Regional laboratory, Rockville, MD, 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 identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in nasal swabs 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.

Testing with the KPMAS COVID-19 Test is intended for use by qualified and trained laboratory personnel specifically instructed and trained in the molecular testing and in vitro diagnostic procedures. The KPMAS COVID-19 Test is only for use under the Food and Drug Administration's Emergency Use Authorization.

DEVICE DESCRIPTION AND TEST PRINCIPLE

1) ***Device Description:***

The KPMAS COVID-19 Home Collection Kit enables the self-collection of a nasal swab sample by an individual when observed at home via telemedicine, that is then transported to KPMAS Regional laboratory or laboratories designated by the KPMAS, for RT-PCR testing for SARS-CoV-2 with the KPMAS COVID-19 Test, when determined by treating physician based on the CDC and KPMAS COVID-19 testing guidelines. The KPMAS COVID-19 Home Collection Kit includes the following materials:

Sample collection and shipping instructions
Biohazard bag (95kPa) containing
Specimen label with patient's name, date of birth, and medical record number
Nasal (polyester) swab
Saline collection tube
Absorbent sheet
Medium alcohol prep pad
Shipping box
FedEx UN3373 Pak (pre-paid, pre-labeled with return address)
Clean table mat

The KPMAS COVID-19 Home Collection Kit is kitted by KPMAS.
Kit components, manufacturer and suppliers are listed in the table below.

Kit components used to collect clinical specimen

Name	Description	Quantity	Material Supplier
Nasal Swab	polyester nasal swab (Puritan® or Copan Q® swab)	1	BD Fisher Scientific
Saline in tube (aliquoted in house)*	0.9% saline (Braun®) in 15mL Conical Tube (Falcon®)	1	Cardinal Health Fisher Scientific
Saline in tube (pre-packaged from manufacturer)*	0.8.5% saline (BD BBL™ saline)	1	Becton Dickinson and Company

*Only one saline in tube will be packaged. Initially the product aliquoted in house will be used until the pre-packaged product is available.

The home collection kit was reviewed by the Department of Transportation for adherence to shipping requirements for hazardous materials. The kit was found to be acceptable and appropriate for shipping within the United States.

2) ***Test Principle:***

The KPMAS COVID-19 Home Collection Kit will be dispensed to the KPMAS Health Plan patients meeting the inclusion criteria set by the CDC and KPMAS. The kit will be either picked up by the patient or mailed to the patient's home address. To provide guidance and ensure proper self-collection of the nasal swab, a video visit will be scheduled for each patient and the nasal swab self-collection will be observed and documented in the patient's electronic medical chart. Self-collected COVID-19 nasal swab sample will be shipped to the KPMAS Regional Laboratory, Rockville, MD overnight via FedEx for testing. The KPMAS COVID-19 Test t will be performed using the FDA EUA authorized Cobas® SARS-CoV-2 test kits in the Roche Cobas 6800 instrument, which is an automated RT-PCR based platform. Test result will be reviewed by the ordering physician and then released into the patient's electronic medical chart, so it can be viewed by the patient at kp.org or via KP mobile app. Positive patients will be also contacted by the patient's medical provider or care coordinator to discuss the result in a timely manner.

The KPMAS COVID-19 Home Collection Kit is comprised of a nasal swab, sample tube containing 0.9% saline (3 mL), alcohol pad, clean table mat, 2D Barcode label (with patient's name, date of birth, and medical record number), biohazard bag, small shipping box, and pre- labeled FedEx UN3373 Pak. Instructions are included in the kit to direct the home users on how to appropriately collect the nasal swab specimen, place specimen into the saline transport tube, properly package the specimen, and how to mail the specimen back to the laboratory using the pre-labeled FedEx return envelope. Of note, included patient instructions indicate that the test must be performed during a scheduled telemedicine visit and not any other time. Each KPMAS COVID-19 Home Collection Kit is intended to be returned via FedEx service at ambient conditions on the same day or the day following sample collection in accordance with the standards as put forth by the CDC and WHO for the transport of suspected COVID-19 samples.

Specimens received at the KPMAS Regional Laboratory for testing will undergo review for integrity of packaging, adequacy of sample volume, legible patient labeling, and time between specimen collection and delivery to the KPMAS Regional Laboratory (less than 48 hours) prior to accessioning and acceptance for testing. See *Accessioning SOP* for details.

KPMAS Regional Laboratory is a High Complexity certified laboratory (Clinical Laboratory Improvement Amendments of 1988(CLIA), 42 U.S.C. §263a 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 KPMAS healthcare teams. An electronic order for home collection kit will be placed in the patient's electronic medical chart, if the patient is eligible for COVID-19 testing based on the guidelines set by the KPMAS and CDC. The kit will be prepared by KPMAS and either mailed to the patient's home address or picked up by the patient at a designated facility location. In addition, a 15-minute telemedicine appointment will be scheduled with the patient. During the telemedicine encounter, a physician or a trained healthcare provider will guide and observe the patient through the nasal swab collection process. This is to ensure optimal collection of the sample, since RNaseP internal control is not present in the Roche assay used at the KPMAS Regional Laboratory. A summary of this telemedicine encounter will be documented in the patient's electronic medical chart with a statement that indicates the collection was visualized and adequately collected.

The Clinical Directors of various specialties will examine quality metrics, address workflow issues, and enhance all process elements needing improvements, as necessary. Physicians and healthcare providers will be routinely trained on all aspects of care programs to ensure delivery of quality care to our patients. The Chief Medical Officer of KPMAS ultimately oversees all aspects of the care program and conducts routine checks on all facets of patient care support.

PATIENT INCLUSION/EXCLUSION CRITERIA

Applies to patients using KPMAS COVID-19 Home Collection kit.
These criteria are based on current CDC (criteria below in use as of 06/01/2020) and KPMAS testing guidelines.

Exclusion:

- Patients outside of KPMAS Health Plan or affiliated health care systems
- Individuals with severe symptoms (will be directed to seek immediate care)

Inclusion:

- Patients with "mild" symptoms
- Individuals with known exposure, sick contact, or living in area of Community Spread, with no symptoms
- Patients with scheduled imaging study or inpatient/outpatient procedure, with no symptoms or known exposure

INSPECTION OF SPECIMENS AND VERIFICATION OF OBSERVED SELF-COLLECTION

KPMAS has submitted a SOP for Receipt and accessioning of COVID-19 home test kits as KPMA Rockville Regional Lab. This protocol is summarized below.

Applies to specimens received from patients using the home collection kit: Specimens received through the KPMAS COVID-19 Home Collection Kit will be checked for the following criteria before entering the workflow:

- **Improper return of sample packaging -** sample not returned in supplied packing materials; sample not returned in biohazard bag; sample not in correct collection/transport tube
- **Missing order -** patient erroneously received the kit
- **QNS –** insufficient specimen volume (< 0.6 mL) for processing due to leakage or spill
- **Missing Information -** patient did not write date and time of specimen collection
- **Invalid Date -** date of collection that is written on specimen is either in the future or exceeded expiration (> 48 hours post-collection)
- **Missing Specimen Label**
- **Missing Telemedicine Encounter Note –** patient self-collected sample without observation by a trained healthcare provider
- **Improper/inadequate Sample Collection** - Telemedicine Encounter Note states improper/inadequate self-collection of a nasal sample

4) ***Test results and interpretation***

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

1) A negative control is needed to eliminate the possibility of sample contamination on the assay run and is used on every assay run of 94 samples. Roche cobas® SARS-CoV-2 Negative Control kit will be used.

2) A positive control is needed to verify that the assay run is performing as intended and is used on every assay run of 94 samples. Roche cobas® SARS-CoV-2 Positive Control kit will be used. The positive control does not detect the presence of human clinical sample as this target is not included in the positive control.

3) The Internal Control is included in cobas® SARS-CoV-2 reagents to help identify the specimens containing substances that may interfere with nucleic acid isolation and PCR amplification. The internal control does not detect the presence of human clinical sample.

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.

Target 1	Target 2	Result	Interpretation
+	+	Positive	Result for SARS-CoV-2 RNA is Detected
+	Invalid	Positive	Result for SARS-CoV-2 RNA is Detected
Invalid	+	Positive	Result for SARS-CoV-2 RNA is Detected
+	-	Presumptive 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.
-	+	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	Result for SARS-CoV-2 RNA is Not Detected
Invalid	Invalid	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.
-	Invalid	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.
Invalid	-	Invalid	Sample should be retested. If the result is still invalid, a new specimen should be obtained.

In the case of positive or presumptive positive results:

- Call or secure electronic communication will be made by care coordinator or physician via Kp.org promptly from the time of receiving the test results
- Outreach communications include: result of the test, counseling on the disease and next steps based on immediate symptoms including isolation vs in-person or emergency care, and the opportunity to have a telehealth consult with a physician or trained healthcare provider
- Results are reported by KPMAS to all public health agencies as required

In the case of negative results:

- Call or secure electronic communication will be made by care coordinator or physician via Kp.org promptly from the time of receiving the test results
- Results are reported by KPMAS to all public health agencies as required

In the case of invalid result:

- Patient will be asked to re-collect specimen with the new home collection kit or visit one of the designated drive-through sites for sample collection by a trained healthcare provider, if clinically indicated.

All individuals will have the opportunity to follow up with physicians or trained healthcare providers with regards to what to watch for, specific symptoms, self-quarantine questions as appropriate, and when to seek care with necessary parameters provided.

5) ***Laboratories:***

Table 2. List of Laboratories where the KPMAS COVID-19 Home Collection Kit will be sent and the EUA for SARS-CoV-2 testing run at that laboratory.

Laboratory	**EUA Assay**	**Lab Testing Capacity**
KPMAS Regional Laboratory, Rockville, MD	Cobas® SARS-CoV-2 test kits on the Roche Cobas6800 instrument	8,000 samples/week

1) Collection Device Stability:

The proposed study designs are for evaluation of the stability of KPMAS COVID-19 Home Collection Kit inclusive of nasal swab and saline in individual sterile containers (aliquoted in house). Two stability evaluations of collection kit components will be performed in parallel using an accelerated design of materials stored at 30℃ and a real-time design of materials stored at room temperature (15-30℃). For the accelerated stability study, evaluations will be made at baseline and after 2 weeks, 4 weeks, 8 weeks and 12 weeks at 30℃. For the real-time stability

study, evaluations will be performed at baseline, 6 weeks, 4 months, 8 months, and 14 months. For all stability evaluations, testing will include assessment of 5 spiked samples at 2xLoD (low positives) and 5 spiked samples at 10x LoD (high positives) and 5 negative specimens (clinical matrix). Additionally, evaluations at each timepoint will also include one (1) external positive and one (1) negative control. At least three lots of sterile individual components will be included in the study as permitted by supply. Individual pre-packaged components must be tested within the permitted printed date of expiration at time of assessment.

Acceptance Criteria for the evaluations will be as follows: Low Positive Samples should demonstrate ≥95% agreement with expected results. High Positive Samples must have 100% agreement with expected results. Negative Samples must demonstrate 100% agreement with expected results. Shelf life stability will be determined based on regression analysis. Any %change (%shift) from time zero (baseline) will be calculated between the target claim and the zero-time as (Ttest-Tbaseline)/ Tbaseline*100 with 95%CI using the regression equation obtained from plotting the mean values. Stability will be defined as the next to last tested point that was within +/- 10% of time zero.

PERFORMANCE EVALUATION

1) KPMAS COVID-19 Home Collection Kit Sample Stability Studies:

The stability study of the nasal swab sample transported in saline has been conducted by the Quantigen Biosciences, with support from The Gates Foundation and UnitedHealth Group.

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.

Briefly, nasal swabs were dipped in one of two concentrations (2XLoD and 10XLoD) of SARS- CoV-2 positive patient sample pools. Swabs were then placed into 1 mL of saline and incubated at 40℃ for 12 hours, followed by 32℃ for 18 or 42 hours, respectively. Samples were tested using an EUA authorized assay at time 0, 30, and 54 hours post-incubation

Average Ct Values for Each time point for both sample dilutions.

Swab	Time Point	N	MS2	N Gene	ORF1ab	S Gene
2xLoD swab in Saline	0h	5	23.74	32.23	30.03	31.80
10xLoD swab in Saline	0h	5	23.27	29.46	27.58	28.67
2xLoD swab in Saline	30h	20	26.00	32.69	31.33	34.59
10xLoD swab in Saline	30h	10	26.19	29.54	28.37	28.69
2xLoD swab in Saline	54h	20	25.70	32.03	31.09	32.10
10xLoD swab in Saline	54h	10	26.11	28.73	27.25	25.09

All positive samples were still positive after 50 hours and the average Ct values for the N gene and ORF1ab gene did not change more than 3Ct. While the S gene, in some cases, did change more than 3Ct this did not change the final result as only 2 out of 3 genes need to be positive to call the sample positive. This data supports stability of the sample over the time course and is broadly applicable to other authorized COVID-19 diagnostic tests using nucleic acid amplification technology.

Results from this study demonstrated that positive nasal swab sample in saline transport medium is stable with over-night or 48-hour shipping and the findings support the stability of the KPMAS COVID-19 Home Collection Kit.

2) Human Usability Studies for the KPMAS COVID-19 Home Collection Kit:

The usability of KPMAS COVID-19 Home Collection Kit was tested with 30 individuals with no symptoms or no known exposure. The participants were of varying ages (16-83), ethnicity, and education levels. The participants had no prior experience with self-collection or medical/laboratory training background.

This study took place in a simulated environment. The entire workflow was performed by each individual participant using the kit, including sample self-collection and packing of the sample in the pre-labeled FedEX UN7337 Pak. Each participant was asked to read and follow the provided instructions for sample collection and packaging. A physician was also present in the same room to observe the participant and provide guidance in order to simulate a telemedicine encounter. Each participant was asked to complete a questionnaire regarding the ease of use of the kit and sample collection as well as understanding the consequences if steps were not performed correctly. All sample packages were dropped off at a FedEX pick up location nearest to the study site.

Upon receipt of the samples in the laboratory, samples were tested on an EUA authorized assay, BD MAX, that includes internal human sample control (RNaseP) to determine adequacy of sample collected by participants. The acceptance criteria are:

- 100% of samples delivered to the laboratory within 24 hours of specimen drop off,
- Ct values of RNaseP less than 40 for at least 95% of self-collected samples (specimen adequacy), and
- confirmation of usability/ease of the kit by at least 95% of participants.

Results:

- 100% of participants confirmed the ease of use of the kit, method of self-collection, and clarity of provided instructions. In addition, 100% of participants demonstrated understanding of the consequences of not following steps and collecting inadequate sample.
- 100% of samples were successfully delivered to the KPMAS Regional Laboratory in less

than 24 hours without specimen leakage or damage via FedEx overnight services.
- 100% of samples demonstrated Ct values of RNaseP less than 35 (mean: 26.0, median: 26.1, range: 21.5-34.7).

At launch of the KPMAS COVID-19 Home Collection Kit, the laboratory leadership team will implement a usability assessment to identify and characterize user success and error rates by comparing the rate of invalid results of self-collected samples against samples collected by healthcare provider. This will be a prospective assessment of error rate and overall success for samples received at the laboratory to identify potential areas for improvement in user instructions and experience. KPMAS will use the acceptance criteria of 10% for error rate type and 90% success as thresholds for implementing corrective actions (e.g. modifications to user instructions). Corrective action will be undertaken in the event a specific error rate type exceeds the criterion or if the success rate falls below the user success acceptance criteria.

3) ***Roche cobas® SARS-CoV-2 assay Analytical and Clinical Performance Evaluation:***
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 details of the performance of the authorized Roche cobas® SARS-CoV-2 assay can be found here: https://www.fda.gov/media/136049/download. Roche granted Right of Reference to KPMAS for Roche's authorized Roche cobas® SARS-CoV-2 assay.

4) Asymptomatic Testing Claim: Clinical Concordance Validation for Asymptomatic Positive and Negative Samples
A post-authorization study was performed at KPMAS Regional Laboratory to evaluate assay performance of nasal swab specimens collected from asymptomatic individuals. Presence or absence of symptoms was asked and visually verified by the healthcare provider observing the specimen collection. This information was documented in the patient's electronic medical chart. Bilateral anterior nares specimen was collected using a flocked or polyester swab and transported in a collection tube containing 3 mL of physiologic (0.9%) saline at 2-9ºC. All samples were tested on the cobas 6800 instrument in accordance with the manufacturer's guidelines. Twenty consecutively collected asymptomatic samples that tested positive or presumptive positive and 100 consecutively collected asymptomatic samples that tested negative in the cobas 6800 instrument were re-tested using another EUA authorized molecular assay.

As shown in Table 3, 19 of 20 asymptomatic positive or presumptive positive specimens in cobas 6800 also resulted positive in the comparator platform. Specimen P8, which tested positive in cobas 6800 but resulted negative in the comparator assay, demonstrated high Ct values at 35.26 (ORF1ab) and 37.62 (E-gene) (Table 3).

As shown in Table 3, 100 of 100 asymptomatic specimens that tested negative in cobas 6800 also resulted negative in the comparator platform (data reviewed, line data now shown).

Positive Percent Agreement 19/19 = 100% (95% Confidence Interval; 83.19% - 100.00%)
Negative Percent Agreement 100/101 = 99.01% (95% Confidence Interval; 94.60% - 99.80%)

Table 3: Comparison of asymptomatic clinical samples in two EUA authorized assays

Asymptomatic Nasal Swab Specimens		**EUA Authorized Assay**	
		Positive	Negative
cobas® 6800	Positive	19	1
	Negative	0	100

Sample ID	**cobas® 6800**		**EUA Authorized Assay**	
	ORF1ab Ct	**E-gene Ct**	**E-gene Ct**	**N2 Ct**
Average Ct (±Stdev)	27.91 (±5.93)	29.95 (±6.70)	28.33 (±7.33)	32.40 (±7.73)

Warnings:

- This test has not been FDA cleared or approved;
- This test has been authorized by FDA under an EUA for use by the KPMAS Regional laboratory, Rockville, MD which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform high complexity tests;
- 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.