Home Specimen Collection Molecular Diagnostic Template [1]

This template (the "template") provides the Food and Drug Administration's (FDA) current recommendations concerning what data and information should be submitted to FDA in support of a pre-EUA/EUA submission for prescription use only home collection devices used by an individual to collect certain clinical specimen(s) that are then sent to a clinical laboratory for testing with a molecular diagnostic for SARS-CoV-2 that is authorized for use with the home collection kit. This template does not cover non-prescription home collection devices or over the counter (OTC) tests for COVID-19 testing. This template is intended to help manufacturers provide appropriate validation data and other information to FDA, but alternative approaches can be used. It reflects FDA's current thinking on the topic, and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* means that something is suggested or recommended, but not required. For more information about EUAs in general, please see the FDA Guidance document: *Emergency Use Authorization of Medical Products and Related Authorities*.[2]

GENERAL INFORMATION ABOUT THIS TEMPLATE

- Text highlighted in yellow ***[Text]*** should be completed by the collection device developer (sponsor) as applicable to its specific device. Text in ***bold italic*** outlines FDA's additional recommendations for the sponsors' consideration when completing the suggested information in each section.

- This template is intended for home collection kits for anterior nares swab or saliva specimens; if you are considering other types of respiratory specimens (e.g., sputum, throat/tongue swabs, or nasal aspirates) or non-respiratory specimens (e.g., stool, etc.), please contact FDA at CDRH-EUA-Templates (CDRH-EUA-Templates@fda.hhs.gov) to discuss your validation strategy.

- Authorization of a home collection kit must be accompanied by authorization of one or more molecular assays that has been validated with specimens collected and transported with the subject home collection kit. This template includes FDA's current recommendations concerning the data and information that should be submitted to FDA in support of an EUA submission for a home collection kit. Please refer to the Molecular Diagnostic Template for Manufacturers or the Molecular Diagnostic Template for Laboratories for FDA's current recommendations concerning what data and information should be submitted to FDA in support of an accompanying molecular diagnostic for SARS-CoV-2, which may be submitted in the same EUA request as the home collection kit or in an accompanying EUA request.

[1] This template is part of the Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) - Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff.
[2] https://www.fda.gov/media/97321/download.

- There are three options for how to authorize a molecular assay with a home collection kit:
    - Within the same EUA at one time (i.e., when the same developer makes the home collection kit and molecular assay and seeks authorization at the same time for the assay and kit);
    - In one or more EUAs (i.e., when the developer of the home collection kit is different from the developer(s) of the molecular assay(s)); or
    - As an amendment to the EUA of a previously authorized assay to add home collection with the specific home collection kit.
- A home collection kit authorized under an EUA is only authorized for emergency use while the EUA is in effect.
- This is an EUA interactive review template for Pre-EUA/EUA submissions. We plan to update the template as appropriate as we learn more about the COVID-19 disease and gain experience with the EUA process for this home collection kit.
- FDA recommends distributors of home collection specimen kits contact the Pipeline and Hazardous Materials Safety Administration (PHMSA) within the Department of Transportation (DOT) to confirm their packaging and shipping instructions will ensure users are in compliance with the hazardous materials regulations for shipping medical material. PHMSA can be contacted at HMInfo@dot.gov.

EXAMPLE TEMPLATE:

A. PURPOSE FOR SUBMISSION

Emergency Use Authorization (EUA) request for distribution and/or use of the ***[name of collection device]*** for the [***collection or collection and stabilization***] of ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]*** in ***[add transport media or dry tube]*** to transport viral SARS-CoV-2 RNA, from patients suspected of COVID-19 by a healthcare provider. The specimen collection device is for use in conjunction with molecular diagnostic testing performed at a clinical laboratory using an *in vitro* diagnostic (IVD) test for the detection of SARS-CoV-2 that is authorized for use with the home collected kit.

B. APPLICANT

[Official name, address and contact information of applicant]

D. PROPRIETARY AND ESTABLISHED NAMES

Proprietary Name - ***[device name (home collection kit name)]***
Established Name - ***[device name (home collection kit name)]***

C. REGULATORY INFORMATION

Approval/Clearance Status:
The ***[device name]*** device is not cleared, approved, or subject to an approved investigational device exemption.

Product Code:

QJR

D. PROPOSED INTENDED USE

1) Intended Use:
The proposed IU will be finalized based on, among other things, the data and recommendations from Public Health authorities at the time of authorization – example text is provided below.

Example text for a home collection kit where the manufacturer does not hold the COVID-19 NAAT test EUA:
The ***[name of collection device]***is intended for use by individuals to self-collect ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]***at home, when determined by a healthcare provider to be appropriate based on [***include mechanism via which the individual is determined to be appropriate for COVID-19 testing by a healthcare provider – to facilitate prescription use. For example (1) the results of an online***

COVID-19 questionnaire, or (2) telephone or online video appointment, etc. with a healthcare provider]. Specimens collected using the ***[name of collection device]*** are transported at ambient temperature for testing at a laboratory. SARS-CoV-2 RNA from the ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]*** is maintained in the specimen packaging and is suitable for use in molecular diagnostic testing performed using an in vitro diagnostic (IVD) test for the detection of SARS-CoV-2 that has been issued an EUA for use with Home Collection Kits, that includes the ***[name of collection device]***.

Testing is limited to laboratories designated by ***[name of manufacturer]*** and certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests. Testing is also limited to molecular diagnostic tests that are authorized for use with Home Collection Kits for collection of nasal swab specimens, including the ***[name of collection device]***.

The ***[name of collection device]***is only for use under the Food and Drug Administration's Emergency Use Authorization.

Example text for a home collection kit where the manufacturer also holds the COVID-19 NAAT test EUA (e.g., an already issued EUA is being revised to authorize home specimen collection as an option):

The [***name of the EUA test***] is a real-time reverse transcription polymerase chain reaction (rRT-PCR) test for the qualitative detection of nucleic acid from SARS-CoV-2 in [***name typical respiratory specimens collected, e.g., upper and lower respiratory specimens such as nasal, nasopharyngeal or oropharyngeal swabs, sputum, lower respiratory tract aspirates, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal aspirate***] collected from individuals suspected of COVID-19 by their healthcare provider.

This test is also for use with the [***name of home collection device***] to self-collect [***name specimens, nasal swab or saliva***] specimens at home by individuals when determined by a healthcare provider to be appropriate based on [***include mechanism via which the individual is determined to be appropriate for COVID-19 testing by a healthcare provider – to facilitate prescription use. For example (1) the results of an online COVID-19 questionnaire, or (2) telephone or online video appointment, etc. with a healthcare provider***].

Testing is limited to [***specify laboratory/laboratories***] certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests.

Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in **[*name specimen type*, *e.g.*** upper respiratory**]** 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 positive results to the appropriate public health authorities.

Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiological information.

The ***[test name]*** is intended for use by **[*include intended user, e.g., qualified and trained clinical laboratory personnel specifically instructed and trained in the techniques of real-time PCR and in vitro diagnostic procedures*]**. The ***[test name]*** is only for use under the Food and Drug Administration's Emergency Use Authorization.

2) Special Conditions for Use Statements:

For Emergency Use Authorization (EUA) only.
For prescription use only.
For in vitro diagnostic use only.
For professional use only.
For use by people 18 years of age or older.
The ***[name of collection device]*** collection device is only authorized for use in conjunction with an in vitro diagnostic (IVD) test for the detection of SARS-CoV-2 that has been issued an EUA and is authorized for use with this collection device.

E. DEVICE DESCRIPTION

Example text has been added below, please modify for your specific collection device. Please note that for new technologies FDA may request additional detailed information so we can adequately assess the risks and benefits associated with the device.

1) Device Description:

Describe the basic design of the collection device and the components included in the kit.

The ***[name of collection device]*** collection device consists of a ***[e.g., swabs, collection tube containing stabilizing liquid, gel pack, return shipping box/envelope, insulated pack, instructions]***.

2) Home Collection Kit Ordering and Processing:

Describe how individuals are selected as acceptable for receiving the home collection kit and who writes the prescription for the test. For example, do individuals fill out an online questionnaire that is reviewed by a physician before the home collection kit is shipped to the requesting individual? You should note if the screening follows CDC recommendations for testing prioritization. As a prescription use device, the home collection kit is not to be dispensed to the patient before the prescription for the test is written. Describe how the specimen is collected and then transferred into the collection device. Include details of all reagents/materials included in the kit and their function. Include how the components of the collection device stabilize the specimen and protect

the virus/viral RNA for shipment. Describe the shipping conditions during transit [for example; use of a drop box, sample waiting for pick up outside, etc.]and how the transit/shipping time will be tracked. How does the home user know where to send their specimens? Are there specific shipping instructions? Please identify the company(ies) shipping specimens and if specimens will be placed in drop boxes or mail boxes for pickup. You should have an accessioning SOP for all laboratories to use when accepting [name of collection device] samples for testing, before entering them into the work flow.

Individuals may request the [***name of collection device***] collection device [***describe the mechanism via which individuals request the home collection kit and how they are determined appropriate for COVID-19 testing by a prescribing healthcare provider***].

The ***[name of collection device]*** collects and stabilizes [***virus/viral RNA]*** from ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]*** specimen***(s)***; it can also be used for the transportation and [***short/long-term room temperature storage***] of a sample. The ***[name of collection device]*** is a non-invasive alternative for collecting high quality and quantity [***virus/viral RNA]*** by/from individuals who are suspected of COVID-19 by their healthcare provider for use in molecular COVID-19 diagnostic assays that are authorized for use with the ***[name of collection device]***.

The ***[name of collection device]*** consists of [***e.g., a swab, a collection tube, stabilizing liquid optional sponges for assisted collection***]. The individual using the ***[name of collection device]*** to collect ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]*** specimen***(s)*** performs the following steps to collect the initial specimen.

After ***[add all claimed specimen types, i.e., nasal swabs and/or saliva]*** specimen***(s)*** is collected, the [***swab is inserted, stabilizing liquid is mixed with the sample***].

Upon contacting [***e.g. clinical specimen, saliva cells, the stabilizing liquid lyses cellular and nuclear membranes to release and stabilize nucleic acids***]. For device shipping, the individual must [***describe steps and expected timeframe***].

Specimens received at the clinical laboratory for testing with the [***name of EUA test***] undergo the following accessioning prior to acceptance for testing [***describe the specimen log in, acceptance and rejection criteria, mechanism for handling rejected specimens, etc.***]

Test results are communicated back to individuals that used the ***[name of collection device***] via ***[describe the mechanism via which results are returned to patients that use the home collection device].***

3) ***Specimen Collection Control:***
The accessioning process should include some type of control for adequate human specimen. This could include using an EUA authorized assay that includes some form of human sample control (e.g. RNaseP) to determine if sufficient sample was collected by the user. Alternatively, the laboratory could run a separate RT PCR in parallel for

each sample type that targets a human housekeeping gene. A design feature of the collection device, such as changing color in the presence of human material, may also be an appropriate control. Sample collection visually observed by a healthcare provider through a telemedicine visit, and a method/procedure for the laboratory to confirm this, could also serve as this control.

4) ***Partnering Laboratories:***
Fill out the table below to identify all laboratories that samples will be sent to and all tests that will be run with the samples at each laboratory.

Laboratory	**EUA Assay**	**Lab Testing Capacity (per day or week)**
Lab Name Address Phone: CLIA #:	Assay Name **Identify if Commercial Assay or LDT**	

We recommend requesting a letter from the developer of each test permitting FDA to discuss their submission with you.

Additionally, each test developer should submit an EUA or EUA amendment for authorization with [collection device name]. Please provide a right of reference to each test developer to allow the data validating your home collection device to be incorporated by reference in the test developer's EUA request.

F. PRODUCT MANUFACTURING

The ***[name of collection device]*** has been validated using only the components referenced in this submission.

1) Overview of Manufacturing and Distribution:

The product will be manufactured at [***manufacturer's name and FDA registration number (if applicable)]*** by [***manufacturer name***] personnel consistent with practices for the production of **[*types of devices*]** based on [***type of quality system****]**.** Material manufactured by [***manufacturer's name***] may be bottled and kitted by [***packager name***] manufacturing facility.

The current manufacturing capabilities include the ability to manufacture approximately **[*please insert the approximate number of units/products that can currently be manufactured per week at the manufacturing facility*]** products per week; however, in the event of a surge in demand, this could be increased to **[*please insert the approximate maximum number of units/products that could potentially be manufactured per week at the manufacturing facility if there was a surge in demand*]** product per week within a **[*please specify in weeks/months the expected timeframe required to increase product production if required*]** timeframe.

The product will be distributed by **[*please describe the distribution plan for the product and list all current distributors*]**.

2) Components Included with the Home Collection Kit

Components manufactured by [***manufacturer's name and FDA registration number (if applicable)***] and supplied with the home collection kit include:

List all components and reagents provided for your home collection kit, including a description, volumes, concentrations, quantities, buffer components, etc. If you plan to use non-traditional sources of swabs or media, please describe your qualification testing and validation procedures. Collection media that contains hazardous or irritating materials (such as guanidinium salts) should not be used for home collection unless the collection device has specific safety features to reduce the risk of patient exposure (such as releasing preservative only when the container lid is closed). FDA will conduct a safety review of all collection media and containers.

Kit components

Name	Description	Quantity	Material Supplier

3) Collection Device Stability:

Briefly describe stability test plan for [name of collection device] reagents and include any accelerated stability information if available. Please note that reagent stability studies do not need to be completed at the time of EUA issuance, however the study design should be agreed upon during interactive review and the stability studies started immediately following authorization, if not before. When designing your stability study, general recommendations are outlined below, for your consideration.

- For EUAs, you may follow the current FDA recognized CLSI Standard EP25 – Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline when evaluating the suitability of stability study designs. If you are planning to pursue a De Novo/510(k) for your device, we recommend discussing in more detail your stability design to facilitate potential use of the EUA data in your regular premarket submission.
- We recommend testing a known positive diluted patient sample at 3-5x LoD rather than positive control material to establish reagent stability.
- You should design your study to provide data for a timeframe that is about 10% longer than the one to be claimed – for example; a claim of 18 months should be supported by stability data out to 20 months and a claim of 7 days should include stability data out to 8 days.

- FDA considers 15-30°C to represent room temperature conditions. Ideally you should evaluate stability at both 15°C and 30°C, however, for the purposes of the EUA evaluation at 30°C is acceptable as the worse-case scenario.
- Shelf-Life Stability- Unopened kit:
    - You should evaluate real-time kit stability studies with unopened kits stored at the claimed storage temperature for your test.
    - Accelerated stability evaluations for unopened kits may be included in EUA submissions while the real-time studies are on-going. However, please note real-time stability data may be needed to meet the required statutory standard for pre-market approval/clearance and for EUA issuance.
- Shipping Stability - Unopened kit: Study should evaluate the anticipated handling and shipping times and temperatures expected for unopened kits.

- FDA analysis recommendations for real time stability studies are as follows:
    - Baseline of the study (t=0 of stability study) should not exceed a month from bottling
    - Clear baselines should be described (e.g., a month from bottling) for each stability claim under each study
    - Claims should be determined based on regression analysis. Any %change (%shift) from time zero (baseline) should 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. When formulating your acceptance criteria for evaluating the shift from baseline you should consider the reproducibility of your device. However, generally, the shift at the target claim due to storage should not exceed 10-15%. The target stability is the next to last tested point that was within +/- 10% of time zero.
    - Acceptance criterion may be different, depending on the test samples analyte concentration distribution in the intended use population and the risk, in other words, the impact of false results to public health.

G. PERFORMANCE EVALUATION

The following recommended validation studies should be performed during your device development:

Home Collection Sample Stability Study Design

If your kit will use foam or wrapped polyester nasal swabs transported in 0.9% saline, PBS or dry tubes you may reference stability studies conducted by Quantigen Biosciences, with support from The Gates Foundation and UnitedHealth Group and do not have to perform your own separate stability study for sample transport. 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.

If you are shipping a dry swab you should also provide a rehydration SOP for laboratories to use and provide validation data for the rehydration protocol.

The proposed study design is for validation of home sample collection for nasal swab samples in media (you should test all media you intend to use for shipping), or saliva. Testing should include 20 spiked samples at 2xLoD (low positives) and 10 spiked samples at 5-10x LoD (high positives). We also recommend testing 10 negative samples to monitor for false positives. Spiked samples for swab samples should be generated by spiking virus onto swabs and placing the swab in media, if appropriate. **Diluted clinical samples** can be used for spiking. Ideally, spiking material should be prepared with clinical matrix to most closely replicate a clinical specimen.

Table1: Sample Panel

Sample	Replicates	Titer
Low Positive	20	2xLoD
High Positive	10	5-10x LoD
Negatives	10	N/A
Total	**40**	

The shipping study is designed to simulate the following situations in one study during home sample collection and shipping:

- Storage of samples before the customer ships the sample
- Sample sitting in mailbox or drop box waiting for pick-up
- Shipping conditions after pick up, when the sample is shipped to testing lab

Total # of samples: 40

General Acceptance Criteria:
Low Positive Samples: ≥95% agreement with expected results. High Positive Samples: 100% agreement with expected results. Negative Samples: 100% agreement with expected results.

The table below describe each temperature profile to replicate worst case scenario shipping conditions (for spring/summer) for an 8 hour wait at the customer's house before shipping and then a subsequent 48-hour shipping cycle. We also included a Winter Profile for testing if you plan to continue shipping your product past August 2020. If you plan to allow testing of samples that have been shipped by 3-5-day mail, please expand the shipping study times below. The sample panel in Table 1 should be cycled through the temperatures & times below and then tested with an assay that your lab will use that produces a Ct value. FDA expects that the samples not only remain positive but that the Ct value does not appreciably increase (more than 3 Ct).

Table 2: Summer Profile *

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

Winter Profile*

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

*Shipping conditions for cycle periods 2 through 5 are modeled after ISTA 7D 2007 shipping standard (48-hour domestic freight transport) where for cycle period 3 and 5 the temperature has been increased from 35°C to 40°C. The cycle period 1 (8 hours) has been included for the time delay between collection of the sample and shipment of the sample. The remaining time (48 hours) covers the domestic shipment within the continental U.S. Cycle periods are sequential with the "cycle period hours" required per cycle listed in the table. After each cycle period, the "total time hours" increments by the number of hours in the cycle period.

Clinical Validation of Saliva as a sample type (if the COVID-19 NAAT test EUA does not have saliva as an acceptable validated sample type):

If you seek a claim for alternative respiratory specimens, such as saliva, oral fluid, buccal swabs, etc., you should test at least 30 paired, positive nasopharyngeal swabs and 30 of the same type of alternative respiratory specimen (e.g., all saliva). To minimize the occurrence of discordant results, the samples should be collected within short time of each other and both tested using your candidate EUA assay. FDA believes ≥95% positive agreement with similar Ct values for the paired specimen types is generally acceptable clinical performance. Please provide detailed information

regarding the type of collection device and transport medium you validated for use with your assay.
If you plan to conduct this study, we strongly suggest you submit a short study design to FDA for review before commencing.

Flex studies:
For oral saliva - Sample Volume Tolerance: You should conduct a study to evaluate the effect of over or under filling the collection device.

Human Usability Study: for home-collection and mailing the sample to a CLIA-certified lab for testing:

- Testing should include a minimum of 30 participants and takes place in an actual use environment or simulated environment.
- The entire workflow should be performed by each individual participant using the kit, including kit registration, sample collection, packaging of the sample, and mailing to the laboratory with pre-prepared label.
- The participants should be observed (either in person or by remote visual monitoring, such as a video conference) during sample collection and all difficulties should be noted.
- After the entire process is completed the user should be given the questionnaire to indicate the ease of use of the kit and sample collection as well as understanding the consequences if steps are not performed correctly. The participant should be able to provide comments if needed.
- The laboratory personnel should inspect the packaging and sample upon delivery and note all packaging errors and acceptability of the sample for testing.
- The samples collected during the study should be tested for specimen adequacy using a human sample control assay. This could include using an EUA authorized assay that includes a human sample control (e.g. RNaseP) to determine if sufficient sample was collected by the user. Alternatively, the laboratory could run a separate RT PCR for each sample that targets a human housekeeping gene. A design feature of the collection device, such as changing color in the presence of human material, may also be an appropriate control.
- Participants should include individuals representing varying education levels and ages. Participants with prior medical or laboratory training should be excluded. Participants who have prior experience with self-collection should be excluded.
- The study should have pre-defined acceptance criteria and defined strategy to mitigate risk of errors identified in the study (e.g., modifying the instructions).

We encourage sponsors to submit their usability study protocols and questions for participants for FDA review prior to conducting the study.

User Labeling:

You should submit for review your packaging and directions for your specimen collection kit. FDA will review these documents for their ease of use and clarity of instructions. We recommend all directions be written at a 7th grade reading level or below.

H. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

I. APPROVED/CLEARED ALTERNATIVE PRODUCTS

Currently no methods for specimen self-collection in conjunction with a laboratory-based molecular in vitro diagnostic EUA test for the detection of the SARS-CoV-2 have been approved/cleared by FDA.

J. BENEFITS AND RISKS:

This section will be completed by FDA.

K. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

As set forth in the EUAs, Fact Sheets for Patients and Healthcare Providers generally are to be provided with the assays that will be used with the home collection kit - ***see examples for authorized EUA tests on our website and templates will be made available.***

L. INSTRUCTIONS FOR USE/ PROPOSED LABELING/PACKAGE INSERT:

Include Instructions for Use, Box Labels, Vial Labels and any other proposed labeling for the test and/or home collection kit. You should also include copies of any questionnaires used to determine eligibility of the patient to receive the home collection kit.

M. RECORD KEEPING AND REPORTING INFORMATION TO FDA:

If authorized, conditions would likely be included in the EUA to require the following -

[***Manufacturer name***] will track adverse events and report to FDA under 21 CFR Part 803. A website is available to report adverse events, and this website is referenced through the [***Manufacturer name***] Product Support website: [***Include link to Website***].

Each report of an adverse event will be processed according to [***Manufacturer name]***'s Non-Conformance Reporting Requirements, and Medical Device Reports will be filed with the FDA as required. Through a process of inventory control, [***Manufacturer name]*** will also maintain records of device usage/purchase. [***Manufacturer name]*** will collect information on the performance of the test, and report to FDA any suspected occurrence of false positive or false negative results of which [***Manufacturer name]*** becomes aware. [***Manufacturer name]*** will maintain records associated with this EUA and ensure these records are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.