Template for Developers of Molecular and Antigen Diagnostic COVID-19 Tests for Home Use [1]

This 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-Emergency Use Authorization (EUA) submission/EUA request for a SARS-CoV-2 molecular or antigen diagnostic test for home use. Home use tests may also be used in additional non-laboratory settings, such as offices, sporting events, airports, schools, etc., where an individual performs the test themselves, including reading and receiving the results themselves.[2] This template does not apply to home collection kits.[3] FDA generally recommends that the following validation studies be conducted for a SARS-CoV-2 molecular or antigen diagnostic assay: limit of detection (LOD), clinical evaluation, inclusivity, cross-reactivity, usability, and flex.

As described in the FDA guidance document *Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)*, [4] FDA is providing recommendations in this and other EUA templates regarding testing that should be performed to ensure appropriate analytical and clinical validity, including descriptions of appropriate comparators, for different types of tests.

The EUA templates[5] are intended to help test developers provide appropriate validation data and other information to FDA, but alternative approaches can be used. This template 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*.[6]

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[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] Operators of non-traditional testing sites should consult with the Centers for Medicare and Medicaid Services (CMS) to determine whether testing at their site would be considered "home use" or would be considered a laboratory under the Clinical Laboratory Improvement Amendments (CLIA). Please see https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA *(last accessed on July 6, 2021). Note this website is not controlled by FDA.*

[3] Please refer to the Home Specimen Collection Molecular Diagnostic Template available at https://www.fda.gov/media/138412/download.

[4] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised.

[5] All EUA templates can be found at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#covid19ivdTemplates.

[6] Available at https://www.fda.gov/media/97321/download.

Test developers interested in pursuing an EUA may submit a pre-EUA to begin discussions with the FDA or may submit an EUA request to covid19dx@fda.hhs.gov.

FDA recommends that all developers of molecular SARS-CoV-2 tests include the Molecular Diagnostic EUA Templates Cover Sheet[7] when submitting their EUA request to CDRH-EUA-Templates@fda.hhs.gov to help streamline the routing, triage, and review of EUA requests.

GENERAL INFORMATION ABOUT THIS TEMPLATE

- Text highlighted in yellow ***[Text]*** should be completed by test developers as applicable to their specific test. Text in **bold** outlines the FDA's additional recommendations for the developers' consideration when completing the suggested information in each section.
- Not all portions of this template may be relevant for all developers/tests. FDA recommends developers complete all portions that are relevant to facilitate a streamlined review.
- This template addresses tests intended for use with respiratory samples or saliva; if you are considering non-respiratory samples (e.g., blood, stool, etc.), please contact FDA at CDRH-EUA-Templates (covid19dx@fda.hhs.gov) to discuss your validation strategy.
- This template is for developers of molecular or antigen diagnostic tests for home use, including non-laboratory settings outside of the home (such as offices, sporting events, airports, schools etc.), that are intended to detect SARS-CoV-2 from individuals.
- A test authorized under an EUA is only authorized for emergency use while the EUA is in effect.
- We may update the template as appropriate as we learn more about COVID-19 and gain experience with the EUA process for these tests.
- A developer that has provided data to the FDA may grant a right of reference to other developers, either broadly or to individual developers, to leverage that data. A right of reference provides a developer the ability to rely upon, and otherwise use, existing information in one regulatory submission for the purpose of supporting a different regulatory submission. In these cases, if the data is applicable to the new developer's test, the new developer may not have to repeat that validation for its submission to the FDA or FDA may recommend a bridging study. Any developer seeking to leverage data regarding another developer's EUA-authorized assay must obtain a right of reference from that developer.

[7] Available at https://www.fda.gov/media/152768/download.

EXAMPLE TEMPLATE:

A. PURPOSE FOR SUBMISSION

Emergency Use Authorization (EUA) request for distribution and/or use of the ***[test name]*** for the *in vitro* qualitative detection of ***[ribonucleic acid (RNA) or antigen]*** from SARS-CoV-2 in ***[add all sample types, e.g., nasal swab or saliva]***. This test is for ***[prescription and/or over-the-counter (OTC) use]*** at home and other non-laboratory sites.

B. MEASURAND

Specific nucleic acid sequences from the genome of SARS-CoV-2 **[*please specify the targeted gene(s) of the pathogen*]**.
OR
Specific antigen(s) from SARS-CoV-2 **[*please specify the targeted antigen(s)*]**.

C. APPLICANT

[Official name, address, and contact information (including phone number and email address) of applicant and primary correspondent.]

D. PROPRIETARY AND ESTABLISHED NAMES

Proprietary Name - ***[test name]***
Established Name - ***[test name]***

E. REGULATORY INFORMATION

Approval/Clearance Status:

The ***[test name]*** test is not cleared, CLIA waived, approved, or subject to an approved investigational device exemption.

[If the test has been previously reviewed in an EUA request or pre-EUA submission, please provide the submission number.]

Product Code:

QJR-molecular diagnostic for SARS-CoV-2

OR

QKP-coronavirus antigen detection test system

F. PROPOSED INTENDED USE

1) Intended Use (IU):

The proposed intended use will be finalized based on, among other things, the data provided and recommendations from public health authorities at the time of authorization. Example text is provided below for a home use qualitative molecular or antigen test that detects organism RNA or antigen in adults and children 2 years and older, but may be adapted according to the specific emergency situation addressed by the device.

The ***[test name]*** is a ***[specify test technology such as, real-time reverse-transcriptase-polymerase chain reaction (RT-PCR) test, lateral flow immunoassay, etc.]*** intended to detect ***[RNA, [protein name] antigen]*** from the SARS-CoV-2 virus that causes COVID-19 in ***[describe all the sample types, e.g., anterior nasal swab, saliva]*** from ***[individuals age 2 years and older; describe the testing population requested, such as symptomatic individuals who are suspected of COVID-19 by a healthcare provider, or individuals with or without symptoms or other epidemiological reasons to suspect COVID-19 infection]***.

Persons who test positive with the **[test name]** should seek follow up care with their physician or healthcare provider as additional testing and public health reporting may be necessary. Positive results do not rule out bacterial infection or co-infection with other viruses. Persons who test negative and continue to experience COVID-19 like symptoms of fever, cough and/or shortness of breath may still have SARS-CoV-2 infection and should seek follow up care with their physician or healthcare provider.

Laboratories within the United States and its territories are required to report all results to the appropriate public health authorities.

The ***[test name]*** is intended for home use ***[and/or, as applicable for a lay user testing another person],*** including self-testing in a non-laboratory setting ***[and, as applicable, for healthcare provider testing of another person in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, that meet the requirements to perform moderate complexity, high complexity, or waived tests and, as applicable, Point of***

Care (POC), i.e., in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance, or Certificate of Accreditation].

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

2) Special Conditions for Use Statements:

For prescription use only **(as applicable)**
For *in vitro* diagnostic use
For Emergency Use Authorization only

3) Special Instruments:

The ***[test name]*** test is to be used with the ***[list all instruments, software, cameras, smart phones, operating systems, other applicable instrumentation, etc.]***.

If your test system includes an instrument, the instrumentation manual should be submitted as part of the EUA request. If your test system includes an instrument that was not previously cleared, approved, or authorized by FDA, please see additional discussion in the Product Manufacturing section and note that additional labeling information may be discussed during the EUA review.

G. DEVICE DESCRIPTION AND TEST PRINCIPLE

[Provide a Device Description and Test Principle consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.] **For new technologies, FDA may request additional information so we can adequately assess the known and potential risks and benefits associated with the device.**

Because of the greater potential for error in testing of samples collected at home, FDA recommends that the test include an internal control to indicate that adequate human sample was collected and placed into the test for analysis. If your assay does not have such a control, you should address this risk using another mitigation, such as video observation of user by a trained healthcare professional or a design feature of the collection device.

FDA recommends that your test use either anterior nares (nasal) swabs, mid-turbinate swabs (collected using the appropriate swab type), or saliva as sample types. Generally, FDA does not consider self-collection of nasopharyngeal (NP) and oropharyngeal swabs by lay persons to be safe because such collection requires training to accurately collect

the sample from the proper anatomical location. Moreover, incorrect technique can result in patient harm such as nose bleeds or esophageal spasms and choking.

1) Product Overview/Test Principle:

[Describe the technology of the test and how this technology works to identify the measurand (i.e., the test principle), the instruments/reader employed/required to perform the test from sample collection to result (include all instruments, software, mobile applications, etc.), and the sample types for which you claim to have specific performance characteristics, as described below. If applicable, list all primer and probe sets and briefly describe what they detect. Please include the nucleic acid sequences for all primers and probes used in the test. Please indicate if the test uses biotin-Streptavidin/avidin chemistry in any of the steps for coupling reagents.]

2) Description of Test Steps:

[List and describe in detail all the steps of the test sequentially from sample collection to assay report.]

1. ***[Step one]***
2. ***[Step two]***
3. ***[Etc.…]***

3) Control Material(s):

[For any controls that you intend to be used with your test, please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

4) Quick Reference Instructions:

You should develop a test procedure that will be easy to follow in the format of a Quick Reference Instructions (QRI). User instructions should be oriented to users at no higher than a 7th grade level. It is highly recommended that developers consider adding pictures and diagrams to facilitate performance of the test by a lay user and that the instructions be limited to 1-2 pages. Web or mobile application-based material such as videos may be particularly helpful. We recommend you perform Human Usability Studies on your device using the QRI before conducting your final clinical study as the final QRI should be evaluated in the clinical study.

The QRI may eliminate the need for a separate Patient Fact Sheet if the QRI contains all necessary elements of a Patient Fact Sheet.

5) Test Result Reporting:

All test results are to be reported to healthcare providers and relevant public health authorities in accordance with local, state, and federal requirements, using appropriate LOINC and SNOMED codes, as defined by the *Laboratory In Vitro Diagnostics (LIVD) Test Code Mapping for SARS-CoV-2 Tests*[8] provided by CDC. Core diagnostic data elements[9] are to be collected for all tests, which have been defined by the Department of Health and Human Services (HHS), along with technical specifications for implementation for lab-based [10] and non-lab-based[11] tests.

[You should describe how you will ensure all users of the test can report all test results to public health and/or other authorities to whom reporting is required, in accordance with local, state, and federal requirements. Please note whether identified information will be sent to local public health authorities and/or if de-identified information will be sent to CDC. If the test produces results that will be used as part of a CDC recommended testing algorithm, please indicate what follow-up testing/process should be conducted, if applicable. Please also describe how test reporting will capture the appropriate LOINC and SNOMED codes, in addition to location data, and other patient information that may be relevant or required.] **The approach adopted should facilitate reporting by all users and be easy to use and understand. There are several options to allow for reporting of test results, including automatic reporting through a mobile application, instructions directing users to a website where reporting is easily facilitated, etc. FDA is open to alternative approaches that ensure appropriate reporting.**

Note that in some cases, developers may add a reporting mechanism post-authorization to ensure that all test results are reported in accordance with local, state, and federal requirements.

6) Mobile Applications and Software

Any smartphone application should be simple. Error messages should be readily understandable, and troubleshooting should be included in the device instruction. The display should promote understanding of results and what individuals should do next, including how to care for themselves and when to seek follow up care. The application should automatically report all test results when appropriate in accordance with local,

[8] Available at https://www.cdc.gov/csels/dls/sars-cov-2-livd-codes.html *(last accessed on July 7, 2021). Note this website is not controlled by FDA.*
[9] Available at https://www.hhs.gov/coronavirus/testing/covid-19-diagnostic-data-reporting/index.html *(last accessed on July 24, 2021). Note this website is not controlled by FDA.*
[10] Available at https://www.hhs.gov/sites/default/files/hhs-guidance-implementation.pdf *(last accessed on July 24, 2021). Note this website is not controlled by FDA.*
[11] Available at https://www.hhs.gov/sites/default/files/non-lab-based-covid19-test-reporting.pdf *(last accessed on July 24, 2021). Note this website is not controlled by FDA.*

state, and federal requirements. If your application is intended to interpret test results or otherwise function as part of the test system, it should be included in your analytical and clinical validation studies.

[Please list and describe any mobile applications, software, or web applications used with the test and provide the following information:

- ***A summary of the verification and validation performed on your software/application. To validate use of your application with a smartphone, you should develop a set of minimum smartphone specifications (e.g., memory, processor capability, minimum operating system (OS) requirements, etc.). You should validate the software on smartphones with each OS that meets those minimum hardware specifications. Full functionality for the application should be demonstrated for the full range of platforms intended for use (e.g., if a web application, then demonstrating on popular modern browsers such as Chrome, Firefox, Microsoft Edge; if a mobile application, then demonstrating on popular modern smartphones and other mobile devices such as Android, and iOS-based devices, etc.).***
- ***Address the cybersecurity of your device, including information that may be contained on your device or in a mobile application or web application. For communications between components (e.g., application to reader, application to cloud service provider), the security of the communications protocol should be described (including version number, configuration, cipher suite), tested, and assessed for risks, especially when the communication security could impact the integrity of the results. For cloud-based functionality, the security of the application programming interface (API), communications, and updates should also be described, tested, and assessed for risks.***
- ***A software update plan that covers mobile application updates, algorithm updates, and web application updates that may impact the performance or safe reporting of the device.]***

H. INTERPRETATION OF RESULTS

Results that are displayed to the user should be simple and easy to interpret (e.g., positive, negative, and invalid). Additional information about test results should also be provided that instructs the users to seek follow up care from a healthcare physician if their symptoms persist or if they are concerned about their health.

[Please describe the testing algorithm/calculation that is used by the device to return the simple qualitative result, for example a ratio value, fluorescence reading, cycle threshold and cut-off, etc. Please also provide any text for users that will accompany test results. Please clearly indicate how invalid results will be displayed to the user and how the user will resolve invalid results, e.g., if repeat testing may be required, call hotline for replacement, etc.]

I. PRODUCT MANUFACTURING

The ***[test name]*** has been validated using only the components referenced in this request and will not be changed after authorization without prior concurrence from the FDA.

1) Overview of Manufacturing and Distribution:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

2) Components and Other Materials/Information Included with the Test:

Components manufactured by ***[test developer's name and FDA registration number (if applicable)]*** and supplied with the test include:

[List all components and other materials/information included with your test, including a description of the primers and probes, volumes, concentrations, quantities, buffer components, etc.]

[Present a detailed assessment of the toxicology profile of the components of your assay, and propose assay labeling that informs users of the risks associated with use of your device, as well as any recommendations for personal protective equipment. Please specify the volumes and concentrations of each reagent included in your test kit.] **FDA will conduct an independent risk assessment to determine if the proposed mitigations are appropriate.**

[If you plan to use non-traditional sources of swabs or media, please describe your qualification testing and validation procedures.]

Example: Kit components

Name	Description	Quantity	Material Supplier	Catalog Number

3) Software Validation:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

4) Basic Safety and Essential Performance:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

5) Electromagnetic Compatibility (EMC) Testing

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

6) Manufacturing and Testing Capabilities:

[Please provide the number of kits you can manufacture per day/week for distribution in the United States.]

7) Distribution Plan:

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

8) Reagent Stability

[Briefly describe the stability test plan for reagents and include any accelerated stability information, if available.] **Reagent stability studies generally 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. You should consider the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate, when designing your stability study.**

J. PERFORMANCE EVALUATION

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate, with additional considerations and recommendations specific to Home Use Tests provided here.]

The following validation studies should be performed to support your EUA request. Please note that, particularly for new technologies, FDA may request additional studies so we can adequately assess the risks and benefits associated with the candidate test. ***[For each validation study, you should provide a study protocol that includes a detailed, step-by-step description of how samples were prepared and how testing was conducted. You should also include the study data from each validation study in an Excel-compatible format.]***

1) Limit of Detection (LoD) - Analytical Sensitivity:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

2) Inclusivity (Analytical Sensitivity):

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.]

3) Cross-reactivity (Analytical Specificity):

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers or Molecular Diagnostic Template for Test Developers, as appropriate.] **Additionally, for home use tests, FDA recommends wet testing of Cross-reactivity and Microbial Interference in addition to in silico analysis.**

a) Cross-reactivity (organisms tested in the absence of SARS-CoV-2)
b) Microbial Interference Studies (organisms tested in the presence of SARS-CoV-2)
c) Endogenous Interference Substances Studies (including common household items such as cleaners, lotions, soap etc.)

4) Biotin interference for antigen tests:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers.]

5) High-dose Hook Effect Study for antigen tests:

[Please provide information consistent with the recommendations in the Antigen Template for Test Developers.]

6) Flex Studies:

Flex studies assess the robustness of an assay performed with the device in its final design/format and should be performed in-house by staff who have been trained in the use of the test. The flex studies should evaluate the most common or likely sources of error based on the use locations and test procedure. Flex studies should be conducted by testing a negative sample and a low positive sample (at 1.5 - 2 times LoD) for each condition being evaluated. In general, the flex studies should be conducted to the point of failure to determine the maximum deviation that will still generate accurate results. We recommend testing 3 replicates per condition per sample concentration. ***[You provide the line data from each flex study in an Excel-compatible format.]*** **If erroneous**

results are observed during studies evaluating the robustness of the device, adequate mitigation(s) should be provided.

Each study should be performed using a pre-defined study protocol that includes the following:

i. **The objective of the study**
ii. **Detailed test procedure**
iii. **Materials used**

Examples of some conditions that may be evaluated as potential user errors and anticipated environmental stresses (temperature and humidity extremes) are shown below:

- **40°C and 95% relative humidity (RH) (mimicking hot and humid climates)**
- **Delay in sample testing**
- **Delay in operational steps**
- **Delay in reading results**
- **Sample volume variability (if applicable)**
- **Buffer volume variability (if applicable)**
- **Environmental stability of electronics (temperature and humidity, in combination)**
- **Vibrations**
- **Mixing/swab expression variability (if applicable)**
- **Disturbance during analysis**
- **Placement on non-level surface**
- **Impact of different light sources (if applicable)**
- **Sensitivity to power failures (e.g., surge protection, battery power failure)**
- **Error reporting and device failure handling instructions**
- **Electrical interference testing (e.g., validation of system functions in the presence of potential EM interference sources including cell phones, Bluetooth, Wi-Fi radios, medical equipment expected in the intended environment, etc.)**

Please see Appendix A for detailed Flex Study designs. CLIA Waiver by Application Decision Summaries[12] available on the FDA website may include additional alternative flex study designs potentially applicable to your test.

Please contact FDA to discuss the design of a flex study for a multiplexed test.

7) Usability Study:

FDA recommends a usability study be performed to evaluate the ability of users to perform the test when the test design or instructions for use are not similar to

[12] Available at https://www.fda.gov/about-fda/cdrh-transparency/clia-waiver-application-decision-summaries.

previously authorized home use COVID-19 tests. If you believe that your test design and instructions for use are similar to previously authorized home use COVID-19 tests, such that a usability study may not be needed, FDA recommends that you provide information to help FDA understand how the proposed test design and instructions for use are similar to currently authorized tests and why any differences do not reduce the usability of the test. FDA recommends that you include a comprehensive description of the similarities and differences between the new test and previously authorized tests.

FDA encourages developers to submit their usability study protocols, including questions for study participants, to FDA for feedback prior to conducting the study. This is especially important for multiplexed tests.

It may be possible to combine the usability study with the clinical evaluation study; however, this presents risk of a failed clinical study if there are problems with the instructions for use. FDA strongly recommends you discuss this option with FDA before design and execution.

FDA recommends evaluating the ability of users to perform the entire workflow in an actual use environment or simulated environment as follows:

- **The study should have pre-defined acceptance criteria and a defined strategy to mitigate risk of errors identified in the study (e.g., modifying the instructions).**
- **For home use tests, we recommend evaluating a minimum of 30 participants split evenly into two sections: 15 participants testing themselves and 15 participants testing another person (child or adult, depending on your intended use population). FDA generally expects demonstrated usability for nasal swab samples for children ≥ 2 years of age when collected by an adult and for saliva samples for school aged children.**
- **Participants with prior medical or laboratory training or prior experience with self-collection or self-testing (including infectious disease home tests) should be excluded.**
- **The entire workflow should be performed by each individual participant using the kit, including kit registration, sample collection, testing, and results interpretation.**
- **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.**
- **Enrollment population should represent different socioeconomic and educational backgrounds. You should collect data on any controls that are run during the test to assess sample adequacy. These data should support that individuals can effectively collect an adequate sample and run the test without introducing contaminants or inhibitors.**
- **After the entire process is completed, participants should be given a questionnaire to assess the ease of use of sample collection, test procedure, and results interpretation**

as well as the user's ability to understand the consequences if steps are not performed correctly. The participants should be able to provide comments.

[Please provide FDA with the version of the instructions that was used in the usability study and resulting summary and line data from your usability study]

8) User Comprehension of Test Results/Procedure:

FDA recommends performing a study to evaluate user comprehension of test results (i.e., interpreting positive, negative, and invalid results) and instructions for use when the test design or instructions for use are not similar to previously authorized home use COVID-19 tests. This is particularly important for tests intended to be run by lay users without involvement of a physician, as there are significant risks associated with misinterpretation and misuse of test results.

If you believe that your test design and instructions for use are similar to previously authorized tests home use COVID-19 tests, such that a user comprehension study may not be needed, FDA recommends that you provide information to help FDA understand how the proposed test design and instructions for use, including reading and interpreting results, are similar to currently authorized tests and why any differences do not reduce the user comprehension for the test. FDA recommends that you include a comprehensive description of the similarities and differences between the new test and previously authorized tests.

[Please provide FDA with user comprehension study data to verify that users can accurately interpret the test results and carry out any follow up actions.]

9) Clinical Evaluation:

FDA recommends conducting a prospective, randomized clinical evaluation in the intended use population in which fresh samples are collected, tested, and interpreted by lay-users and results are compared to paired samples evaluated with an authorized high sensitivity molecular test. Please contact FDA regarding recommendations for clinical evaluation designs of multiplexed tests.

a) Testing Sites

- **The clinical evaluation should generally include a minimum of 2 testing sites in the United States to encourage diverse enrollment. This may include an at home clinical study or a study at a testing site with a simulated home environment.**
- **Prior to conducting the at home clinical study, you should first complete an observed usability study to evaluate clarity and demonstrate robustness in using the instructions for use, unless you have provided information to FDA as to why a usability study may not be needed, as described in Section J(7) above.**

- **Recruitment by internet, especially if using monetary incentives, can drastically bias the population who enrolls in the study. We recommend that you consult FDA before starting a recruitment involving a monetary incentive.**
- **Sample types should be non-invasive and safe to prevent possible injury during sample collection. Mid-turbinate swabs may need additional safety features to be appropriate, specifically for pediatric populations.**
- **If collected at home, comparator samples should be collected using an FDA authorized home collection kit, which in combination with a SARS-COV-2 molecular assay comprise the comparator test for the study.**
- **Testing sites should be set up in a way that precludes a user from seeing or hearing other users performing the test (e.g., in separate rooms or areas partitioned with curtains).**
- **The entire workflow should be performed by each individual participant using the kit, including kit registration, sample collection, testing, and results interpretation.**

b) Patient Enrollment

- **Parents or legal guardians must consent for children as required by law.**
- **Enrollment population should represent different socioeconomic and educational backgrounds.**
- **High risk individuals should not be excluded from the study.**
- **If you are seeking an OTC or prescription authorization for a home test for use in all patient populations, including individuals with or without symptoms or other epidemiological reasons to suspect COVID-19, you should evaluate both symptomatic and asymptomatic individuals and include an adequate number of pediatric subjects from ages 2-13 years of age. We recommend testing at least 30 children between the ages of 2-13 years of age between your usability and clinical evaluations, to ensure that your proposed sample collection techniques can be conducted by parents or guardians in a home use setting. Study population should include individuals across all ages 2 years - 65+ years**
  - **<14 years of age, where the Parent or legal guardian collects a sample from their child (e.g., age 2-13) and performs the test**
  - **14-24 years of age**
  - **24-64 years of age**
  - **≥65 years of age**
- **If you believe that your test design and instructions for use are similar to previously authorized home use COVID-19 tests, such that inclusion of pediatric subjects may not be needed to confirm performance across different age ranges, FDA recommends that you provide information to help FDA understand how the proposed test design and instructions for use are similar to currently authorized tests and why any differences do not impact the performance of the test across different age ranges. FDA recommends that you include a comprehensive description of the similarities and differences between the new test and previously authorized tests.**

- **If you are not able to enroll sufficient asymptomatic individuals in your clinical validation study, you may consider seeking an OTC or prescription home use authorization for use only in individuals with symptoms of COVID-19. For antigen tests, all recommended elements of the clinical study data should be provided, including the days since symptom onset for each symptomatic individual included in your clinical validation study. If your clinical validation study includes symptomatic individuals only (or insufficient numbers of asymptomatic individuals) and you are interested in seeking authorization for serial testing of asymptomatic individuals based on this data, please consult the "Supplemental Template for Molecular and Antigen Diagnostic COVID-19 Tests for Screening with Serial Testing".** [13]

c) Reference Sample/Comparator method

- **FDA recommends the comparator sample type be either a health care provider-collected NP or mid-turbinate swab sample (collected from each patient in the study within a reasonable time frame from when the test sample was obtained/tested, preferably during the same visit) or a home-collected nasal swab. If you conduct the study remotely without in-person visits with health care professionals, the comparator sample should be collected with an FDA authorized home collected nasal swab.**
- **You should describe your randomization approach for swab collection, as applicable. If study participants are collecting the reference sample for comparator testing and the study sample, you should clearly describe the order in which swabs will be collected and describe how swab order was randomized to ensure that bias is not introduced due to an unequal distribution of viral materials. If healthcare providers are collecting the reference sample for comparator testing, you should ensure that study participants are not provided additional training by observing how healthcare providers collected a sample, particularly if collected from the same anatomical area as the study sample.**
- **All comparator samples should be tested with a comparator test. The comparator test selected should be an authorized highly-sensitive RT-PCR test that uses both a chemical lysis step and solid phase extraction of nucleic acids (e.g., silica bead extraction). The comparator test should be one of the more sensitive RT-PCR assays authorized by FDA. We encourage you to review the results from the FDA SARS-CoV-2 Reference Panel[14] and contact us to discuss your choice of comparator test. The same comparator test should be used for all samples, if possible. Evaluations with the comparator test should be conducted per the authorized instructions for use. If any modifications are made to the**

[13] Available at https://www.fda.gov/media/146695/download.

[14] Available at https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data.

authorized comparator test, additional bridging studies may be necessary. Please contact FDA if you are considering using a modified configuration of an authorized RT-PCR assay. *[Please submit the instrumentation and detailed laboratory protocols, including the platform and extraction kit, for each RT-PCR assay used in your validation studies.]*

d) Discrepant analysis

- **You can establish a discordant analysis plan prior to your clinical study, if preferred. Discordant samples should be tested with a second authorized RT-PCR test that has also demonstrated high sensitivity, and which uses both a chemical lysis step and solid phase extraction of nucleic acids (e.g., silica bead extraction). Results from a Discrepant analysis should not be included in the calculation of negative percent agreement (NPA) and positive percent agreement (PPA) but may be added to the performance table as a footnote.**

e) Study Size

- **Individuals should be consecutively enrolled (i.e., in an "all comers" style) until 30 positives and 30 negatives are obtained.**
- **If your test is intended for use in asymptomatic individuals not suspected of COVID-19, you should enroll at least 10 positive individuals without symptoms or other epidemiological reasons to suspect COVID-19 infection. Additional post-authorization studies in individuals with or without symptoms or other epidemiological reasons to suspect COVID-19 infection may be recommended. If you do not enroll at least 10 positive individuals without symptoms, you may consider the approach in the "Supplemental Template for Molecular and Antigen Diagnostic COVID-19 Tests for Screening with Serial Testing".[15]**
- **If using an enrichment strategy to speed enrollment, you should carefully consider how you will randomize and blind study participants to their infection status or the infection status of the individual they are testing and describe how you will minimize potential bias when conducting self-testing. Blinding study participants to their infection status, particularly if positive, raises potential ethical issues and should be discussed with FDA and the study IRB. Data from an enriched study design should represent the full range of viral loads, with both low and high positives samples. Therefore, it is not appropriate to use a rapid antigen test to enrich for participants, as it will select for strong positive samples. We strongly recommend discussing your proposed enrichment strategy with FDA prior to conducting your clinical validation study.**

f) Performance

FDA believes that data should generally demonstrate the following:

- **NPA ≥98%**

[15] Available at https://www.fda.gov/media/146695/download.

- **PPA**
  - **For OTC single-use testing in all patient populations, including individuals with or without symptoms or other epidemiological reasons to suspect COVID-19: ≥ 80% PPA demonstrated in a clinical evaluation including both symptomatic and asymptomatic individuals;**
  - **For OTC testing in all patient populations, including individuals with or without symptoms or other epidemiological reasons to suspect COVID-19, with additional mitigations such as serial screening, as discussed in the "Supplemental Template for Developers of Molecular and Antigen Diagnostic COVID-19 Tests for Screening with Serial Testing"[16]: ≥ 80% PPA with a lower bound (LB) of the two sided 95% confidence interval (CI) ≥70%, demonstrated in a clinical evaluation including symptomatic individuals only or both symptomatic and asymptomatic individuals;**
  - **For prescription home use single-use testing in individuals suspected of COVID-19 by their healthcare provider: ≥ 80% PPA demonstrated in a clinical evaluation including symptomatic individuals only (note that, for antigen tests, the indication may be limited to symptomatic individuals within a certain number of days of symptom onset, depending on the data); or**
  - **For OTC single-use testing in symptomatic individuals: ≥80% PPA demonstrated in a clinical evaluation including symptomatic individuals only (note that, for antigen tests, the indication may be limited to symptomatic individuals within a certain number of days of symptom onset, depending on the data).**

The indications for use for tests with PPA <95% should be limited to providing presumptive negative results.

10) Standard Material Testing

All molecular tests for home use should demonstrate high analytical sensitivity as determined by testing with a recognized international standard. If you do not have access to a recognized international standard, then please contact CDRH-EUA-templates@fda.hhs.gov to discuss options. If this is not completed prior to submission of an EUA request, it may be required as a Condition of Authorization.

K. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

[16] Available at https://www.fda.gov/media/146695/download.

L. APPROVED/CLEARED ALTERNATIVE PRODUCTS

There is no adequate, approved, and available alternative to the emergency use of the product.

M. BENEFITS AND RISKS:

This section will be completed by FDA.

N. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

During review, FDA will make available Fact Sheet templates. See examples for authorized tests on our website. [17]

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

[*You should include Instructions for Use, Box Labels, Vial Labels and any other proposed 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.

The following limitations should be included in the Instructions for Use of a home use test, as applicable:

- **Testing for asymptomatic individuals should be performed at least twice over three days, with at least twenty-four hours and no more than 48 hours between tests. You may need to purchase additional tests to perform this serial (repeat) testing.**
- **There is a higher chance of false negative results with home use tests than with laboratory-based molecular tests. This means that there is a higher chance this test will give you a negative result when you have COVID-19.**
- **Serial testing (i.e., testing every day or every other day) is more likely to detect COVID-19, especially when you do not have any symptoms.**

The following should be included on the outer box of a home use test, as applicable:

- **Expiration date (sticker): Based on component of kit with the earliest expiration date**
- **For Emergency Use Authorization (EUA) only**

[17] A list of EUA-authorized tests and their accompanying fact sheets are available at https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas.

- **For in vitro diagnostic use**
- **Must be 18+ to use this kit**
- **If you have symptoms of COVID-19, you can use a single test**
- **If you do not have symptoms of COVID-19, you will need at least two tests per person**
- **You may need to purchase additional tests to perform serial (repeat) testing**
- **This test is more likely to give you a false negative result when you have COVID-19 than a lab-based molecular test**
- **Storage temperature**
- **Summary of box contents**
- **Items necessary to use the kit: e.g., access to computer/smartphone, internet, email account**
- **Summary of how the kit works**
- **Warnings and related information from EUA letter of authorization**

P. RECORD KEEPING AND REPORTING INFORMATION TO FDA:

As allowed by Section 564(e) of the FD&C Act, FDA may require certain conditions as part of an EUA. FDA generally includes the following record keeping and reporting information requirements in the EUA.

[***Test Developer name***] will track adverse events and report to FDA under 21 CFR Part 803. A website is available to report on adverse events, and this website is referenced in the Fact Sheet for Health Care providers as well as through the [***Test Developer name***] Product Support website: [***Include link to Test developer's Website***]. Each report of an adverse event will be processed according to [***Test Developer name]***'s Non-Conformance Reporting Requirements, and Medical Device Reports will be filed with the FDA as required. Through a process of inventory control, [***Test Developer name]*** will also maintain records of device usage/purchase. [***Test Developer 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 [***Test Developer name]*** becomes aware. [***Test Developer 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.

Appendix A: Recommended Flex Study Design Details, as appropriate for the device:

If incorrect results are observed under the test conditions, the test developer should implement adequate mitigations to prevent reporting of erroneous results.

1) **Reading Time:**
   You should evaluate test results at multiple reading times four-fold below and three-fold above the recommended reading time for the candidate test. For example, where the recommended read time is 20 minutes, you should evaluate read times of 5, 10, 15, 20, 30, and 60 minutes, at a minimum. If incorrect results are observed, the developer should propose adequate mitigations.

2) **Sample Volume:**
   You should evaluate candidate test results at sample volumes two times below and two times above the recommended sample volume, and the maximum possible added. For example, where the recommended sample volume is 10 µL, you should evaluate sample volumes of 5, 10, and 20 µL, as well as at the maximum sample volume. If incorrect results are observed at either 5 or 20 uL, additional testing at 7.5 and/or 15 uL may be needed. The amount of diluent/buffer added should be that specified in the instructions for use.

3) **Sample Diluent/Buffer Volume:**
   You should evaluate candidate test results at diluent/buffer volumes at two times below and two times above the recommended diluent/buffer volume specified in the instructions for use and the maximum volume. For example, where the recommended buffer/diluent volume is 2 drops, you should evaluate sample diluent volumes of 1, 2, 3, 4 drops and the whole bottle.

4) **Sample Elution:**
   You should evaluate how mixing the swab in elution buffer (or other reagent) affects candidate test results. You should evaluate all extremes from not-mixing to vigorous shaking, including generating bubbles and intermediate mixing (i.e. swirling 1 or 2 times).

5) **Temperature and Humidity:**
   You should evaluate candidate test results at temperature and humidity extremes that are likely to occur in the United States (i.e., 40°C and 95% RH to mimic a hot and humid climate and 5°C and 5% RH to mimic a cold and dry climate.)

6) **Light:**
   You should evaluate candidate test results in different lighting conditions that would be expected during use (i.e., fluorescent, incandescent, and natural lighting mimicking the outside environment.)

7) **Disturbance during analysis:**
   You should evaluate the effect on expected candidate results of moving the candidate test while the candidate test is running. This could include dropping the candidate test while it is being run, moving the candidate test to another surface, unplugging the candidate test, receiving a phone call while the mobile app is running, etc.

8) **Device Orientation:**
   You should evaluate unique device characteristics, as determined by a robust risk analysis. For example, if the candidate test is intended to be run upright, you should evaluate candidate test results if the candidate test is run horizontally, or vice versa.