Template for Manufacturers of Molecular and Antigen Diagnostic COVID-19 Tests for Non-Laboratory Use [1]

This template (the "template") provides FDA's current recommendations concerning what data and information should be submitted to FDA in support of a pre-EUA/EUA submission for a molecular or antigen diagnostic test for SARS-CoV-2 for use in a non-laboratory setting. Such settings are likely to include a person's home or certain non-traditional sites such as offices, sporting events, airports, schools etc. This template does not apply to home collection kits.

As outlined in Section V.A. and V.B. of the FDA guidance document *Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)*, [2] FDA recommends that the following validation studies be conducted for a SARS-CoV-2 molecular or antigen diagnostic assay: Limit of Detection, Clinical Evaluation, Inclusivity, Cross-reactivity, Usability and Flex Studies. This template is intended to help manufacturers provide these 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*.[3]

GENERAL INFORMATION ABOUT THIS TEMPLATE

- Text highlighted in yellow ***[Text]*** should be completed by the test manufacturer (sponsor) as applicable to their specific test. Text in **bold** outlines the Food and Drug Administration's (FDA) additional recommendations for the sponsors' consideration when completing the suggested information in each section.
- This template is intended for testing with respiratory specimens or saliva; if you are considering non-respiratory specimens (e.g., blood, stool, etc.), please contact FDA at CDRH-EUA-Templates (CDRH-EUA-Templates@fda.hhs.gov) to discuss your validation strategy.
- This template applies to developers of molecular or antigen diagnostic tests, for use in non-laboratory settings (such as person's home or certain non-traditional sites such as offices, sporting events, airports, schools etc.), intended to detect SARS-CoV-2 from individuals.

[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/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised

[3] https://www.fda.gov/media/97321/download

- A test 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 these kinds of tests.

EXAMPLE TEMPLATE:

A. PURPOSE FOR SUBMISSION

Emergency Use Authorization (EUA) request for distribution and/or use of the ***[test name]*** to ***[indicate non-laboratory testing sites]*** for the *in vitro* qualitative detection of ***[RNA or antigen]*** from the SARS-CoV-2 in ***[add all claimed specimen types, e.g., nasal swab or saliva]***. This test is for ***[prescription use at home and other non-laboratory sites and/or OTC use at home and other non-laboratory sites]***. All test results will 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 provided by CDC.

B. MEASURAND

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

C. APPLICANT

[Official name, address and contact information of applicant]

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.

Product Code:

QJR-molecular diagnostic for SARS-CoV-2

OR

QKP-antigen diagnostic for SARS-CoV-2

F. PROPOSED INTENDED USE

1) Intended Use for Molecular Assays:

The proposed Intended Use will be finalized based on the available information including data and recommendations from public health authorities at the time of authorization – example text is provided below for a home use qualitative molecular test that detects organism RNA in adults and children 2 years and older, but may be adapted according to the specific emergency situation addressed by the device.

[***Test name***] is a [***specify test technology such as, real-time RT-PCR test, lateral flow immunoassay***] intended to detect [***RNA, [protein name] antigen***] from the SARS-CoV-2 virus that causes COVID-19 in [***describe all the specimen types, e.g.,* nasal swab, saliva**] from ***[individuals age 2 years and older]*** or ***[for prescription use only tests, describe the patient 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.

All test results will 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 provided by CDC.

The ***[test name]*** is intended for self-use ***[and/or, as applicable for a lay user testing another person]*** 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 to perform moderate or high complexity tests and as applicable, Point of Care (POC) testing at 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 Emergency Use Authorization (EUA) only
[For prescription use only or For prescription use and over-the-counter use.]
For in vitro diagnostic use only

3) Special Instrument Requirements:

The ***[test name]*** test is to be used with the [***list all instruments, smart phones, operating systems, camera and software requirements***].

G. DEVICE DESCRIPTION AND TEST PRINCIPLE

We recommend providing a Device Description and Test Principle consistent with the recommendations in the Antigen Template for Manufacturers or Molecular Diagnostic Template for Manufacturers, as applicable. Please note that for new technologies, FDA is more likely to request additional detailed information so we can adequately assess the risks and benefits associated with the device.

Because of the greater potential for error in specimen collection at home, FDA recommends that the assay, which per the intended use allows specimens to be collected outside of a healthcare facility, have 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 professional or a design feature of the collection device.

1) Product Overview/Test Principle:

Describe the technology of the test and how this technology works to identify the measurand, the instruments employed/required to perform the test from sample collection to result (include all instruments, software, mobile app, etc.), and the specimen 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 specimen collection to detection. Please note that FDA generally does not consider self-collection of nasopharyngeal, 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. As such, we recommend that your test use either anterior nares (nasal) swabs, mid-turbinate swabs or saliva as sample types.

3) Control Material(s) to be Used: This section only applies to devices intended for high-volume use in non-laboratory settings. FDA believes that having control materials available for quality control and training is important in these non-laboratory settings and does not believe such materials will be necessary when these tests are intended only for use in an individual's home or other non-laboratory low-volume settings.

List all control materials (provided with the test kit and/or required but not provided with the test kit) and describe what they are, how they are expected to work, where in the testing process they are used, and the frequency of use. If a control is commercially available, provide supplier's name and catalog number or other identifier.

Please note that any control recommended to be used with your device (provided with the kit or not) should be validated in the context of your analytical and clinical study (i.e., you should run these controls as part of your studies). In instances where control material is not readily available through 3rd party vendors (which is often the case at the beginning of an outbreak), FDA may request that you include suitable control material with your device. Please note that external control materials are considered particularly important when GMP requirements are waived and reagent stability studies are limited.

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). Because these tests are intended for use in non-laboratory settings and may be intended for parents to test children, we recommend you develop and test for usability and develop at least two sets of instructions: one for self-testing and one for a lay user testing another person (child and/or adult as appropriate per your IFU). User instructions should be oriented to users at no higher than a 7th grade level. It is highly recommended that sponsors 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 should be provided in both English and Spanish at a minimum.

5) **Test Result Reporting*:***

All test results will 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 provided by CDC.

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. 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, but not limited to: *automatic reporting through mobile app, instructions directing users to a website where reporting is easily facilitated, etc.* FDA is open to alternative approaches to reporting that ensure appropriate reporting.

You should 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.

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 patients should do next, including how to care for themselves and when to seek follow up care.

Please list and describe any mobile applications, software or web applications used with the test. You should include the following information:

Verification & Validation:

- **To validate use of your App 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 models of Smartphones for each OS that meet those minimum hardware specifications.**
- **You should summarize the verification and validation performed on your software/app.**
- **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.).**

- **You should address the cybersecurity of your device and any private health information that may be contained on your device or in a mobile app or web application.**
- **You should have a software update plan that covers mobile app updates, algorithm updates and web application updates that may impact the performance of the device**
- **The application should automatically report all test results when appropriate in accordance with local, state, and federal requirements.**

H. INTERPRETATION OF RESULTS

Results that are displayed to the user should be simple and easy to interpret (e.g., positive, negative, and invalid).

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.

You should also describe how results will be reported 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.

Additional information about negative results should also be provided that instruct the user to seek follow up care from a healthcare physician if their symptoms persist or if they are concerned about their health.

I. PRODUCT MANUFACTURING

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*]**.

***Under the Emergency Use Authorization (EUA) any of the 21 CFR Part 820 Quality System Regulation (QSR) requirements can be waived for the duration of the EUA but FDA recommends that developers follow comparable practices as much as possible if such requirements are waived. Among other things, FDA may consider previous compliance history when determining whether or not to waive certain QSR requirements for a specific product. Please note adverse events, as per 21 CFR Part 803, have to be reported for authorized devices (see Section P).**

2) Components Included with the Test

Components manufactured by [***manufacturer's name and FDA registration number (if applicable)***] and supplied with the test include:
List all components and reagents for your test, including a description of the primers and probes, 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 and other test components that contains hazardous or irritating materials (such as guanidinium salts) should not be used for home (or other non-laboratory) testing unless the collection device has specific safety features to reduce the risk of patient exposure. FDA will conduct a safety review of all test components.

3) Testing Capabilities

Briefly describe current sample throughput capacity, total time required to perform the test (from clinical specimen collection, to result), and, if applicable, number of tests that can be performed per instrument run and per day.

4) EMC (electrical and mechanical safety) Testing:

We recommend that EMC testing be conducted on any device that uses a battery or power source. Please provide FDA with any standards that were followed for EMC testing.

5) **Reagent Stability:**

Briefly describe stability test plan for reagents and include accelerated stability information, if available. Based on FDA's experience thus far, FDA believes that reagent stability studies generally would not need to be completed at the time of EUA issuance, however, the study design generally will be agreed upon during interactive review and the stability studies started immediately following authorization, if not before. You should consider the following recommendations when designing your stability study:

- **You could 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 premarket submission.**
- **We recommend testing a known positive diluted patient sample at 3-5x LoD rather than positive control material to establish reagent stability. Use of DNA material is unlikely to be appropriate.**
- **If you are claiming multiple clinical specimen types in which similar LoDs are determined, you should use the most challenging clinical matrix for this study.**
- **We typically recommend your stability study design includes the evaluation of at least 5 replicates. You should also evaluate, if available, 3 different lots of reagents.**
- **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 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 is acceptable for EUA submissions while the real-time studies are on-going. However, please note real-time stability data is generally needed to support regular pre-market submissions.**
- **Shipping Stability - Unopened kit: You should evaluate the anticipated handling and shipping times and temperatures expected for unopened kits.**

- **In-use/Opened Kit Stability: Depending on your device, your stability study design should also support in-use stability of the kit reagents once the kit has been opened, e.g., storage at 2-8 ºC for 7 days.**
- **Inverted stability (if applicable): Study should support stability for kits if stored inverted or in the wrong orientation.**
- **FDA recommendations for analysis of 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 intended use population and the risk of false results to public health.**

J. PERFORMANCE EVALUATION

We recommend including the studies listed below (as applicable) in 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 device:

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

   Please provide information consistent with the recommendations in the Antigen Template for Manufacturers or Molecular Diagnostic Template for Manufacturers.

2) **Inclusivity (analytical sensitivity)**

   Please provide information consistent with the recommendations in the Antigen Template for Manufacturers or Molecular Diagnostic Template for Manufacturers.

3) **Cross-reactivity (Analytical Specificity)**

   Please provide information consistent with the recommendations in the Antigen Template for Manufacturers or Molecular Diagnostic Template for Manufacturers. For all tests intended for use in a non-laboratory setting (e.g., a complete home test), 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) **High-dose Hook Effect Study for antigen tests**

   Please provide information consistent with the recommendations in the Antigen Template for Manufacturers.

5) **Biotin interference, if applicable**

   Please provide information consistent with the recommendations in the Antigen Template for Manufacturers.

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 1.5x - 2x 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 allow for generating accurate results. We recommend 3 replicates per condition per sample concentration. Data for each condition evaluated (i.e., line data) should be provided. 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**

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

iv. **40°C and 95% RH (mimicking hot and humid climates)**
v. **Delay in sample testing**
vi. **Delay in operational steps**
vii. **Delay in reading results**
viii. **Sample volume variability (if applicable)**
ix. **Buffer volume variability (if applicable)**
x. **Mixing/swab expression variability (if applicable)**
xi. **Disturbance during analysis**
xii. **Placement on non-level surface**
xiii. **Impact of different light sources (if applicable)**
xiv. **If hand-held, positioning at 90° angle (simulating placing device in pocket or lifting to see result display screen)**

Please see Appendix A for more in depth study designs for Flex Studies. Alternative sources of information that may be applicable to your device can be found on the FDA CDRH website containing CLIA Waiver by Application Decision Summaries (https://www.fda.gov/about-fda/cdrh-transparency/clia-waiver-application-decision-summaries).

7) **Human Usability Study**

- **Testing should include a minimum of 100 participants for non-prescription (OTC) tests and 30 participants for prescription only tests, and take place in an actual use environment or simulated environment. For OTC tests for use at non-laboratory sites, we recommend you split the usability study into two sections: 50 participants testing themselves and 50 participants testing another person (child or adult, depending on your intended use population). For prescription only tests for use on children, you should have 15 of the 30 usability participants be parents or legal guardians performing the test on their children.**
- **The entire workflow should be performed by each individual participant using the kit, including kit registration, sample collection, testing, and results interpretation (if possible: we recommend users see a mock result to interpret).**
- **You should collect data for your assay on any controls that are run during the test to assess sample adequacy. The data from this Usability Study should support that patients can effectively collect an adequate sample and run the assay without introducing contaminants or inhibitors.**
- **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 sample collection, test procedure and results interpretation as well as understanding the consequences if steps are not performed correctly. The participant should be able to provide comments if needed.**
- **Participants should represent varying education levels and ages. A portion of your users should be Spanish speaking, and should be provided with instructions written in Spanish. A portion of your users should collect samples from themselves, while a subset should collect samples from others, including children. Participants with prior medical or laboratory training should be excluded. Participants who have prior experience with self-collection or self-testing (including glucose testing) should also 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. It may be possible to combine the Human Usability with the Clinical Evaluation; however, this study design does involve more risk as problems with the instructions for use could lead to a failed clinical study. FDA strongly recommends you discuss this option with FDA before design and execution.

8) Clinical Evaluation:

FDA recommends using natural clinical specimens for the clinical evaluation. You should conduct a clinical study to evaluate your device's performance in symptomatic and asymptomatic individuals. This study design evaluates performance in asymptomatic individuals as well as symptomatic individuals. Since there is no mechanism to limit OTC testing to symptomatic individuals, FDA recommends this study design for all developers requesting an OTC claim. This study design is also recommended for developers requesting prescription use, unless the test is intended to be limited to symptomatic individuals.

1. **Testing Sites**

    - **The sponsor should attempt to set up a minimum of 2 testing sites to encourage diverse enrollment or recruit for an at home clinical study through the internet. Conducting the study at home will generally be acceptable, but the following issues may arise and should be considered:**
        - **Comparator samples should be collected at home using an FDA authorized home collection kit and SARS-COV-2 molecular assay.**
        - **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.**
        - **Possible injury during sample collection (applies to mid-turbinate swabs).**

  - **Observed usability study recommended prior to at home clinical study to evaluate clarity and demonstrate robustness in using the instructions for use, etc.**
- **Testing sites should be set up such that when a user is performing the test, they are unable to see/hear other patients performing the test (can be in separate rooms or areas partitioned with curtains)**
- **The following testing situations are possible, all of which should have an observer present:**
  - **Parent or legal guardian collects a sample from their child (e.g., age 3-13) and parent performs the test. The age of children that are tested by their parent or legal guardian should be consistent with the device's intended use.**
  - **Older child (e.g., age 14-17) self-collects sample and child performs the test (parent or legal guardian should not be present to intervene). The age range of children that self-collect should be consistent with the device's intended use.**
  - **Adults (age 18 and older) self-collect the sample and perform the test themselves.**
  - **Adult (adult 1) collects a sample from another adult (adult 2) and adult 1 performs the test.**

2. Patient Enrollment

- **Study population should include individuals across all ages 2y-65+y**
  - **<14 years of age (target ~20%)**
  - **14-24 years of age (target ~10-15%)**
  - **24-64 years of age (24-64y target ~30-35%)**
  - **≥65 years of age (target ~35%)**
- **Parents or legal guardians must consent for children as required by law**
- **Enrollment population should represent different socioeconomic and educational backgrounds**
- **Study should include symptomatic and asymptomatic individuals**
- **High risk individuals should not be excluded from the study**
- **You should exclude participants who regularly use home use diagnostic tests, such as glucose meters.**

3. Reference Sample/Comparator method

- **FDA recommends the comparator be either a health care provider-collected NP swab sample (collected from each patient in the study within a reasonable time frame from when the test sample was obtained/tested same visit preferred) or a home-collected nasal or mid-turbinate swab. If you will conduct the study remotely, in a way where patients do not have in person visits with health care professionals, the comparator should be an FDA authorized home collected nasal or mid-turbinate swab. If you have difficulty in sourcing NP swabs, finding patients who consent to the NP swab procedure or finding clinical sites willing to collect NP swabs, please**

contact FDA about potential alternative swab types, such as mid-turbinate, oropharyngeal and nasal and the additional considerations for these comparator samples.

- **All comparator samples should be tested with a comparator method. The comparator method selected should be one of the more sensitive EUAs on the FDA website (supported by peer reviewed literature, comparative studies in lab, etc.) that uses both a chemical lysis step and solid phase extraction method. Ideally the same comparator would be used for all samples.**

4. Discrepant analysis

- **A plan for discrepant testing should be developed and should be implemented if a large number of discordant results are obtained in the clinical study.**
- **Like with the original comparator method, discordant samples should be tested with a second EUA from FDA's website that has also demonstrated high sensitivity, and which uses both a chemical lysis step and solid phase extraction method.**
- **Discrepant analysis should not be used to alter the performance data but may be added to the performance table as a footnote.**
- **If necessary, to help with discrepant resolution, positive samples can also be serially diluted and tested in parallel with the test device and a comparator method to demonstrate reduced or improved analytical sensitivity.**

5. Study Size

All Comers Testing

- **Patients should be enrolled in an "all comers" style, including both symptomatic and asymptomatic patients. Study testing should be continued until 30 positives are obtained. The overall study size should not be less than 150 individuals.**
- **You should aim to have at least 10 positives from asymptomatic individuals.**
- **If you would like to enrich your study to obtain positives more rapidly, you can enrich your population by including patients who have already tested positive by another assay. Please contact FDA for feedback on potential alternatives for enriching prospective positive patients in a clinical study.**

6. Performance

- For non-prescription (OTC) tests intended for use in non-laboratory settings, FDA recommends that tests have a PPA and NPA as follows: **Positive Percent Agreement (PPA) ≥90% for asymptomatic and symptomatic**
- **Negative Percent Agreement (NPA) ≥99% (LB >95%)**

9. Additional Studies

FDA Reference Material Testing

- **All assays for use in non-laboratory settings should demonstrate high analytical sensitivity as determined by testing with the FDA SARS-CoV-2 Reference Panel or a recognized International Standard. If you do not have access to either the FDA SARS-CoV-2 Reference Panel or a recognized international standard then please contact CDRH-EUA-templates@fda.hhs.gov to discuss options.**

10. Alternative Clinical Study Approaches:

A) Adding Asymptomatic Testing Post-Authorization

If your assay is already authorized for non-laboratory use without an asymptomatic claim, you may request the addition of asymptomatic testing through a post-authorization study. For a post-authorization study we generally recommend testing a minimum of 20 consecutively collected asymptomatic positive specimens and at least 100 consecutively collected negative specimens based on the results of the candidate test. All specimens should then be tested with another EUA authorized molecular assay. Using estimates of the predictive values and the percentage of positive results, this study can be used to establish the sensitivity (PPA) and specificity (NPA) of your test in an asymptomatic population, as this is an important performance metric for tests intended for asymptomatic screening of large populations. The FDA generally expects that PPA should be ≥95% and NPA should be ≥98% (with a lower bound of the two-sided 95% confidence interval >95%).

B) Symptomatic Patient Testing (prescription use only)

If you wish to limit your assay to symptomatic individuals you may do this by offering your test by prescription only. Since there is no mechanism to limit OTC testing to symptomatic individuals, FDA recommends developers requesting an OTC claim consider the clinical study and performance recommendations for asymptomatic testing, as described above.

For a Prescription Non-Laboratory Test for symptomatic patients, you should follow the study design above with the recommended changes to Study Size and Performance below.

Study Size For Prescription Non-Laboratory Use Only

- Testing in symptomatic individuals should be continued until 30 positives and 30 negatives are obtained. (a population size of 150, in a prospective study, would be expected to yield 30 positive results if prevalence is 20%).

Lower PPA and NPA may be acceptable for prescription non-laboratory use assays for symptomatic patients because the inclusion of symptoms as a requirement for testing increases the pre-test probability of a positive result (higher prevalence) and therefore increases the Positive Predictive Value of the test. FDA believes that a Positive Predictive Value of a test with below 90% PPA would be insufficient without this mitigation (confirming symptoms).

Performance For Symptomatic Use Only

For symptomatic use only tests, FDA recommends that the test have a PPA and NPA as follows:

- Positive Percent Agreement (PPA) ≥80% for symptomatic
- Negative Percent Agreement (NPA) ≥99% (LB >95%)

K. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

L. APPROVED/CLEARED ALTERNATIVE PRODUCTS

Currently no methods for the detection of the SARS-CoV-2 have been approved/cleared by FDA.

M. BENEFITS AND RISKS:

This section will be completed by FDA.

N. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

Include proposed Fact Sheets for Patients and Healthcare Providers ***- see examples from authorized EUA tests on our website. Templates will be made available at sponsor's request.***

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

Include Instructions for Use, Box Labels, Vial Labels and any other proposed labeling.

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 emergency use authorization. FDA will generally include the following record keeping and reporting information requirements in the EUA which FDA believes are necessary to protect the public health.

[***Manufacturer 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 [***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.

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

1) **Reading Time:**
   You should evaluate test results at reading times four times below and three times above the recommended reading time. For example, for a test where the recommended read time is 20 minutes, reading time times would be performed to evaluate at least read times of 5, 10, 15, 20, 30, and 60 minutes. If incorrect results are observed, the sponsor should propose adequate mitigations for how the incorrect timing can be addressed.

2) **Specimen Volume:**
   You should evaluate test results at specimen volumes two times below and two times above the recommended specimen volume, and the maximum possible added. For example, for a test where the recommended specimen volume is 10 µL, specimen volume testing would be performed to evaluate at least specimen volumes of 5, 10, 20 µL and 100uL (whole 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 diluent/buffer amount added should be that specified in the instructions for use

3) **Sample Diluent Volume:**
   You should evaluate test results at diluent/buffer volumes at two times below and two times above the recommended diluent/buffer volume and the maximum volume. For example, for a test where the recommended buffer/diluent volume is 2 drops, sample diluent volume testing would be performed to evaluate at least sample diluent volumes of 1, 2, 3, 4 drops and whole bottle. The sample volume added should be that specified in the instructions for use.

4) **Sample Elution:**

You should evaluate how mixing the swab in elution buffer (or other reagent) affects results. You should evaluate all extremes from not-mixing to vigorous shaking, generating bubbles as well as intermediate mixing, i.e. Swirling 1 or 2 times, instead of the prescribed number from the instructions.

5) **Temperature and Humidity:**
You should evaluate test results at temperature and humidity extremes that are likely to occur in the United States. For example, 40°C and 95% RH, mimicking hot and humid climate, and 5°C and 5% RH mimicking cold and dry climates.

6) **Light:**
You should evaluate test results in different lighting conditions that would be expected during use of the device, for visually read devices. For example, fluorescent, Incandescent, and natural lighting mimicking the outside environment.

7) **Disturbance during analysis:**
You should evaluate the effect of moving the device while the test is running on expected test results. This could include; dropping the test while it is run, moving the test to another surface, unplugging the 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 device is intended to be run upright, evaluating test results if the device is used horizontally, or vice versa.