Guides for the U.S. FDA's Emergency Use Authority for Speedy Approval of Covid-19 Diagnostics and Treatments

Heemin (Herman) Rhee, Ph.D.

President, Health Research International
Senior Advisor, Korean-American Professional Association in Life Sciences

11320 Coral Gables Drive
North Potomac, Maryland 20878 U.S.A.
Tel: 1-301-762-7211
Email: rheehm41@gmail.com

News on Seegene's Activities around the World

- Seegene has received emergency use approval from the Korea Ministry of Food and Drug Safety for an assay to detect the Covid-19 on 2/18/2020(US FDA 4/21).
- Seegene's automated system and analysis software, providing test results in four hours. The system also runs the firm's high multiplex respiratory assay portfolio that screens and identifies 19 respiratory viruses and seven pneumonia bacteria with similar symptoms to COVID-19.
- Seegene has the capability to manufacture 100,000 COVID-19 tests per day.
- The agreement with Mexico's agriculture department covers studies to evaluate molecular detection assays for bovine TB, as well as studies on zoonotic TB diagnosis.
- Seegene announced that it has formed a cancer diagnostics research and development alliance with Spain's Institut Català d'Oncologia (ICO).

Coronavirus Tests From Seegene, DiaSorin, Others Get Health Canada Approval: 4/13/2020

- Health Canada recently approved tests for SARS-CoV-2, the virus that causes COVID-19, permitting their marketing and use in that country. Recent approvals include the Seegene Allplex 2019-nCoV and DiaSorin Molecular Simplexa COVID-19 Direct, both of which are real-time RT-PCR assays.
- Seegene: the Health Canada approval will enable Canadian hospitals and licensed labs to run the assay immediately for high-volume testing. Seegene's SARS-CoV-2 assay is already being used in more than 40 countries, and that it is manufacturing and delivering more than 3 million of the tests per week globally.
- Osang Healthcare and SeeSun BioMaterials were obtained the U.S. FDA EUA for Covid-19 on April 18 and April 28, respectively.

Maryland purchased 500,000 Covid-19 tests from Korea

- On 4/20/2020, Maryland Gov. Larry Hogan announced that Maryland has purchased 500,000 Coronavirus tests from South Korean LabGenomics.
- Maryland's deal with South Korea began nearly a month ago. Governor Hogan and his wife, Yumi Hogan were actively participated for the deal.
- The couple had visited Lee Soo Hyuck, the Republic of Korea's ambassador to the United States with other governors a few weeks earlier when Korean President Moon Jae In also called.
- That call set in motion 22 straight days of vetting, testing, negotiations, and protocols between our scientists and doctors, eight Maryland state government agencies and Korean counterparts.
- He said negotiations took place almost nightly, and "sometimes, it seemed like all night." The state was busy securing last-minute approvals from federal agencies, including the FDA/EUA.

FDA Emergency Use Authorization (EUA) Guidances

- FDA's EUA authority allows FDA to help strengthen the nation's public health protections against chemical, biological, radiological, or nuclear (CBRN) threats by facilitating the availability and use of medical countermeasures (MCMs) needed during public health emergencies.
- EUA and Pre-EUA Guidances
- COVID-19 EUA Guidances
  - In Vitro Diagnostic Products
  - High Complexity Molecular-Based Laboratory Developed Tests
  - Personal Protective Equipment
  - Ventilators and Other Medical Devices
  - Therapeutic Medicines and Vaccines for Covid-19
- Other Current Pre-IND EUAs

A simpler FDA template for Emergency Use Authorization

- FDA relaxed EUA requirements to enable highly-complex labs in the US to develop tests. It has also made the CDC's EUA almost like an umbrella authorization to cover certain kit lots from a reagent supplier, Integrated DNA Technologies, as long as the lots have been validated at CDC.
- The submission for EUA is different now because it is a rolling process involving an electronic template. The FDA has engaged with more than 70 diagnostics developers, and the initial conversation is the first step in the application for negotiation with FDA.
- After the negotiation with the FDA until finally everything is agreed upon, and the data are entered into the form sheet, and it is usually a week until the EUA is granted. By the end of the process, FDA knows what is coming in the final document because the FDA has been reviewing it all along.
- The FDA template with yellow highlighted areas where they want YOU to fill in the blanks and they have done all the work, and they even give YOU the cover letter that the FDA wants.
- Rheonix applied for funding through the Office of Biomedical Advanced Research and Development Authority (BARDA), and the EZ-Broad Agency Announcement template that is used in that case is also incredibly simplified, and only 20 pages.

General Information about EUA TEMPLATE of Covid-19

- EUA template is only for use by CLIA certified high-complexity laboratories with experience developing and validating molecular diagnostics for viral pathogens. Use of the template is applicable only for testing of respiratory specimens.
- Text highlighted in yellow with brackets ***[Text]*** should be completed by the laboratory/sponsor. The remaining text should be unchanged. Text in ***italic bold*** outlines FDA suggestions and clarifications.
- If authorized, the EUA means that this SARS-CoV-2 IVD is temporarily authorized for use until further notice, the public health emergency is terminated or the EUA is revoked by the FDA.
- This template must be completed and submitted within 15 business days following completion of assay validation and FDA notification in accordance with the Interim FDA Guidance available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-diagnostics-testing-laboratories-certified-perform-high-complexity-testing-under-clia-prior.
- If you need additional information completing this EUA template, would like to know how to submit your Pre-EUA/EUA submission to FDA or wish to consider use an alternative specimen type, please contact the Division of Microbiology devices at (301) 348-1778 or email CDRH-EUA-Templates@fda.hhs.gov

General Information about EUA TEMPLATE of Covid-19

- **A. PURPOSE FOR SUBMISSION:** EUA request for use of a SARS-CoV-2 molecular diagnostic test …
- **B. MEASURAND:** Specific nucleic acid sequences from the genome of the SARS-CoV-2 ***[please specify the targeted gene(s) of the pathogen; assays with more than one target are recommended]***.
- **C. LABORATORY/SPONSOR:** ***[Official name, address and contact information of applicant and all locations where specimen testing will be performed]***
- **D. REGULATORY INFORMATION:** ***Approval/Clearance Status:*** The SARS-CoV-2 assay test is not cleared, CLIA waived, approved, or subject to an approved investigational device exemption.
- **E. PROPOSED INTENDED USE:**
- ***1. Intended Use:*** The SARS-CoV-2 assay is a [***specify test technology such as, real-time RT-PCR test***]
- ***2. Instruments Used with Test:*** The ***[test name]*** test is to be used with the [***list all RT-PCR Instruments, software, automated extraction instruments***].

General Information about EUA TEMPLATE of Covid-19

- **F. DEVICE DESCRIPTION AND TEST PRINCIPLE: N*ote the accelerated template is intended for use only with existing, well-established technologies.***
- ***1. Product Overview/Test Principle:*** The assay is a real-time (rRT -PCR) test. The SARS-CoV-2 primer and probe set(s) is designed to detect RNA from the SARS-CoV-2 in respiratory specimens from patients as recommended …
- ***2. Description of Test Steps: [Please describe in abbreviated form the steps for performing your assay in sequential order as a numbered list, including extraction methods.***
- ***3. Control Material(s) to be Used: [Please describe the assay controls to be performed in the laboratory, including the following: The positive and negative control; ideally the positive control will be used to confirm performance near the test limit of detection (LoD). If a template control is used, please describe in general terms the sequence used, the extraction control, the internal control, if present.***
- ***4. Assay results and interpretation: [Please describe the results of your assay procedure, e.g., reactive (positive/detected), non-reactive (negative/non-detected), or Invalid (no result reported)]***

General Information about EUA TEMPLATE of Covid-19

- **G. PRODUCT MANUFACTURING:** Under the EUA 21 CFR 820 Quality System Regulation (QSR) requirements can be waived for the duration of the EUA.
- **H. PERFORMANCE EVALUATION**
- ***1. Limit of Detection (LoD)-Analytical Sensitivity: Lab. should document the LoD of their SARS-CoV-2 assay. It is acceptable to spike RNA or inactivated virus into artificial or real clinical matrix (e.g., Bronchoalveolar lavage fluid, sputum, etc.) for LoD determination.***
- ***2. Inclusivity (analytical sensitivity): Lab. should document the results of an inclusivity study that demonstrates the strains of SARS-CoV-2 that can be detected by the proposed molecular assay.***
- ***3. Cross-reactivity (Analytical Specificity): FDA defines in silico cross-reactivity as greater than 80% homology between one of the primers/probes and any sequence present in the targeted microorganism.***
- ***4. Clinical Evaluation: In the absence of known positive samples available for testing, lab. should confirm the performance of their assay with a series of contrived clinical specimens by testing a minimum of 30 contrived reactive and 30 non-reactive specimens in a RCT. FDA defines the acceptance criteria for the performance as 95% agreement at 1x-2x LoD, and 100% agreement at all other concentrations and for negative specimens.***

General Information about EUA TEMPLATE of Covid-19

- **I. UNMET NEED ADDRESSED BY THE PRODUCT: *This section will be completed by FDA***
- **J. APPROVED/CLEARED ALTERNATIVE PRODUCTS:**
- **K. BENEFITS AND RISKS: *This section will be completed by FDA.***
- **L. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS: Include proposed Fact Sheets for Patients and Healthcare Providers - *see examples for authorized EUA tests on our website and templates will be made available.***
- **M. INSTRUCTIONS FOR USE/PROPOSED LABELING/PACKAGE INSERT: In lieu of a package insert or labeling please include your Laboratory SOP/protocol.**
- **N. RECORD KEEPING AND REPORTING INFORMATION TO FDA:** The lab. will track adverse events and a website is available to report on adverse events.
- **O. FDA ADMINISTRATIVE INFORMATION: This section will be finalized by the FDA Reviewer upon completion of the review process. This will document any interactions of communications with the lab., the interactive review of this submission and any conclusions resulting from the interactive review.**

FDA Releases New EUA Guidance for Covid-19 Test

- FDA released new guidance for EUA for molecular-based lab. developed tests (LDTs) detecting SARS-CoV-2 for qualitative detection of nucleic acid from SARS-CoV-2 in respiratory specimens that are authorized for use by the developing lab. can be performed, but only in the CLIA-certified lab. in which the test was developed.
- Tests are eligible for authorization under the EUA if the lab. has submitted an EUA request for the LDT with required data, and if they are either new and not covered at the time of the EUA request or significantly different from an existing EUA-authorized test. The test must also be a reverse transcription PCR test using authorized material components and control materials.
- The new guidance follows the FDA's pathway "Policy A," which allows labs to use validated SARS-CoV-2 LDTs on patient samples as soon as they are validated internally if they have notified the FDA and file an EUA application within 15 days.
- Yale New Haven Hospital's Clinical Virology Laboratory was granted an EUA for its SARS-CoV-2 RT-PCR test under the new guidance on March 31, 2020.

FDA updates its guidance for COVID-19 diagnostic tests

- 3/16 Policy B: State authorization within their jurisdictions that will be run in high-complexity CLIA labs. The tests covered by Policy B can be used on patients as soon as they are validated and the FDA is notified, and a subsequent EUA is not required. Washington, Nevada, New York, and Maryland have notified FDA of their intent to pursue this pathway.
- Policy C applies to molecular, antigen, and antibody tests that can be used in clinical labs and at the point-of-care, and the policy does not apply for tests intended to be used at home. 4 manufacturers have notified FDA that they are distributing kits under the Policy C path since the March 16 guidance. The agency's website lists those developers as Becton Dickinson, Qiagen, BGI and Co-Diagnostics.
- For commercial manufacturers of COVID-19 tests, a pathway called "Policy C" will apply. In this pathway, a manufacturer can launch its test and platform as soon as it is validated, provided it has notified the FDA and will submit an EUA application within 15 business days.
- Policy D applies only to antibody-based serology tests. These tests, whether they come from a commercial manufacturer or are developed by a high-complexity lab, do not need to submit an EUA application at all, and makers can begin selling them and using them on patients as soon as they are validated.

Coronavirus Emergency Use Authorizations Progressing

- The COVID-19 was uncovered Dec. 31, and the virus sequenced and viral genome publicly available on Jan. 5.
- When the US emergency was declared on Jan. 31, and US Centers for Disease Control and Prevention submitted its SARS-CoV-2 real-time RT PCR test to FDA on Feb. 3 and was granted EUA on Feb. 4.
- The CDC and/or the DoD were always the first to get EUA from FDA, usually within a few days of the emergency being declared for H7N9 influenza, Middle East Respiratory Syndrome, Ebola (Ebola virus disease), EV-D68(echovirus and coxsachievirus), and Zika(mosquitos) virus.
- Ebola emergency declaration on 8/5/2014: DoD got EUA on 10/10/2014 (BioFire Diagnostics was granted EUA 81 days after the emergency was declared, on10/25/2014 and Altona Diagnostics was granted EUA on Nov. 26).
- Zika emergency issued 2/26/2016: CDC received EUA that same day (Quest Diagnostics on April 28, while Altona got EUA 77 days after 5/13/2016, and Hologic got EUA for a test on June 17).
- MERS emergency on 5/29/2013: CDC was granted EUA 6/5/2013, and commercial MERS test to get EUA was from Altona Diagnostics, granted on 7/17/2015.
- SARS-CoV-2 in December, 2019, is a newly emerged pathogen that bloomed from local to global spread very quickly.

FDA Issues New Policy to Help Expedite Availability of Diagnostics for Coronavirus (COVID-19)

- The new policy is for certain labs that develop and begin to use validated COVID-19 diagnostics before the FDA has completed review of their EUA requests.
- The FDA can issue an EUA to permit the use, based on scientific data, of certain medical products that may be effective in diagnosing, treating or preventing a disease or condition when there is a determination, by the Secretary of Health and Human Services (HHS), that there is a public health emergency or a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens, and a declaration that circumstances exist justifying the medical products' emergency use.
- Rapid detection of COVID-19 cases in the U.S. requires wide availability of diagnostic testing to control the emergence of a rapidly spreading, severe illness. The FDA has authorized one EUA for COVID-19 that is in use by the U.S. CDC and some public health labs across the country.

NIOSH-Approved Disposable Filtering Facepiece Respirators for Use in Health Care Settings for the COVID-19 Public Health Emergency

- On March 2, 2020, the FDA issued an EUA for emergency use of,
- (1) all disposable filtering facepiece respirators (FFRs) approved by the National Institute for Occupational Safety and Health (NIOSH), in accordance with 42 CFR Part 84, as non-powered air-purifying particulate FFRs, and
- (2) FFRs that were NIOSH-approved but have since passed the manufacturers' recommended shelf-life, for use in healthcare settings by healthcare personnel (HCP) to prevent wearer exposure to pathogenic biological airborne particulates during FFR shortages resulting from the COVID-19 outbreak.
- Letter of Authorization
- Appendix A: NIOSH-approved FFRs
- Appendix B: Authorized Respirators (as of March 6, 2020)
- 인공호흡기 전문기업 멕아이씨에스(대표이사 김종철) had a sale contract of respirators with Future Medical on April 28, 2020.

II. Scope of Authorization: Authorized Respirators

- FDA will add a respirator from Appendix A to the list of authorized respirators in Appendix B upon submission of request from CDC, the manufacturer, or strategic stockpiler to FDA, as described in the Scope of Authorization Section of this letter (Section II) and pursuant to the Conditions of Authorization in this EUA.
- Current CDC recommendations on optimizing respirator use, please visit CDC's webpage: Strategies for Optimizing the Supply of N95 Respirators.
- CDC or the Office of AS for Preparedness and Response (ASPR)/HHS may request the authorization of additional respirators that were NIOSH-approved that have been held beyond their manufacturer-intended shelf life or expiration date (e.g., N95s in federal Strategic National Stockpile), which may be authorized by FDA in consultation with, and with concurrence of, the Office of Strategic Partnerships and Technology Innovation (OST)/CDRH, Division of Infection Control and Plastic and Reconstructive Surgery/CDRH, and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC).
- Manufacturers may request the authorization of additional respirators, upon submission of an attestation from the manufacturer to FDA with a copy to CDC (CVSDBadmin@cdc.gov) specifying the NIOSH-approval number, model number, and place of manufacture.

IV. Conditions of Emergency Use Authorization

- CDC will inform relevant stakeholders, such as manufacturers and HCPs, of this EUA, including the terms and conditions herein and any updates.
- CDC will post on its website the following statement: "For information about the FDA-authorized EU of NIOSH-approved FFRs, please see: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use- authorizations."
- CDC will provide FDA any updates to their complete listing of all NIOSH-approved FFR manufacturers, contact information for each manufacturer, and model numbers.
- CDC or ASPR/HHS may request the authorization of respirators that were NIOSH-approved that have been held beyond their manufacturer-intended shelf life or expiration date (e.g., N95s in federal Strategic National Stockpile) for authorized use under this EUA without manufacturer's attestation. Such requests will be made by CDC or ASPR/HHS in consultation with, and require concurrence of, OST/CDRH, Division of Infection Control and Plastic and Reconstructive Surgery/CDRH, and OCET/OCS/OC.
- CDC is authorized to issue additional recommendations and instructions related to the emergency use of the authorized respirators in this letter of authorization, to the extent that additional recommendations and instructions.

FDA updates its guidance for COVID-19 diagnostic tests

- 3/25, FDA held a webinar to flesh out its evolving policies, providing key insights on regulatory paths for molecular and serological diagnostic testing in commercial and state labs, and for commercial test products and devices.
- The FDA had previously issued EUA guidance for COVID-19 on Feb. 28. It then expanded the guidance on March 16. CDRH: organized four pathways for COVID-19 tests, and offered some information on the numbers of tests.
- Policy A has been set out for high-complexity CLIA labs that wish to launch validated COVID-19 laboratory-developed tests, including molecular tests, or antigen or antibody tests. Labs are permitted to begin using tests on patient samples as soon as they are validated internally, provided they have notified FDA and subsequently file an EUA application within 15 days.
- FDA received 98 notifications from laboratories running LDTs to date.

FDA updates its guidance for COVID-19 diagnostic tests

- 12 developers have notified FDA they are pursuing the Policy D path. A list on the FDA's website now includes 19 developers of antibody tests. The FDA has not reviewed the validation of tests offered by these developers, who will not be pursuing EUAs, and is including this list … to provide transparency regarding the notifications submitted to FDA.
- The FDA granted 16 EUA to date, including for commercial tests and labs, and state labs, the agency offered insights on test validation, and the role it intends to play in regulating tests that involve slight modifications of existing tests or protocols, including modified commercial tests. It also provided information on non-CLIA labs doing testing, and the types of samples and sample collection locations that can be used.
- The validation requirements in the guidance pertain to determining clinical agreement and cross reactivity for all tests: Molecular tests require an inclusivity study and limit of detection determination. The latter applies to antigen tests as well, which must also be validated with a microbial interference study.

FDA updates its guidance for COVID-19 diagnostic tests

- Molecular tests run in highly complex CLIA labs are supposed to have an additional validation, comparing the first 5 positive and 5 negative patient samples to a previously validated test.
- Labs that wish to modify an EUA test or protocol to suit their equipment availability need to run a bridging study. Since you are validating something new, just confirm the first 5 positives and negatives with someone else who is already set up and using an EUA authorized assay, as a check, which may not be required, unless the lab was developing its own lab developed test from scratch.
- FDA does not intend to object to the use of a test without a new or amended EUA where the test is validated using a bridging study to an EUA-authorized test. A lab can take an authorized test, whether it is CDC's or somebody else's, make some changes to it —whether it is a new platform, a new component—and if they do the appropriate bridging study, or rely on somebody else who has done a bridging study for that change, then they don't need to come in with an EUA or a notification.

FDA updates its guidance for COVID-19 diagnostic tests

- FDA would review the bridging study data. If the data supports the modification, and, if the lab or other entity who own that data agrees to FDA sharing that information on our website, FDA would intend to update [FAQ's] so other labs can refer to that validation for their testing without having to conduct their own bridging study for the same modification.
- If a manufacturer wishes to modify its own EUA products, it can send the FDA an amendment for the change and implement the change immediately, while the FDA reviews it.
- For Policy C—the commercial tests seeking EUA that can now launch a test as soon as it is validated and you have 15 business days to submit your EUA package, all the while you can stay on the market, provided the developers post the package insert and performance data on their websites.

FDA updates its guidance for COVID-19 diagnostic tests

- For serology products being imported under Policy D, once the importer, distributor, or the foreign test manufacturer notifies the FDA of the intent to market the test in the U.S., the test is permitted to be distributed in the U.S.
- CLIA-waivable serology tests can be distributed to CLIA-waived labs, even though the guidance specifies that manufacturers are not allowed to make claims about CLIA waived status.
- For additional sample types, the FDA is trying to be very precise, and where there is insufficient data to recommend something, they make that clear. FDA updated its guidance on the FAQ page to say that while nasopharyngeal swabs are still the preferred sample type, mid-turbinate and lower nasal samples from symptomatic patients are now acceptable. Looking at study data which is not public yet, but which the UnitedHealth Group will hopefully publish very soon.
- Regarding the FAQ page, the FDA would encourage you to check that out because the FDA are updating it almost daily with new information.

FDA Allows Covid-19 Test for Patient At-Home Sample Collection

- FDA re-issued the EUA for the Laboratory Corporation of America (LabCorp) COVID-19 RT-PCR Test to permit testing of samples self-collected by patients at home using LabCorp's Pixel by LabCorp COVID-19 Test home collection kit.
- FDA authorization of more than 50 diagnostic tests and engagement with over 350 test developers: for tests that include home sample collection.
- This reissued EUA for LabCorp's molecular test permits testing of a sample collected from the patient's nose using a designated self-collection kit that contains nasal swabs and saline. Once patients self-swab to collect their nasal sample, they mail their sample, in an insulated package, to a LabCorp lab for testing. LabCorp intends to make the Pixel by LabCorp COVID-19 Test home collection kits available to consumers in most states, with a doctor's order, in the coming weeks.
- The LabCorp home self-collection kit includes a specific Q-tip-style cotton swab for patients to use to collect their sample. Due to concerns with sterility and cross-reactivity due to inherent genetic material in cotton swabs, other cotton swabs should not be used with this test at the present time. This authorization only applies to the LabCorp COVID-19 RT-PCR Test for at-home collection of nasal swab specimens using the Pixel by LabCorp COVID-19 home collection kit

How to Submit a Pre-EUA Package for In vitro Diagnostics

- A Pre-EUA package contains data and information about the safety, quality, and efficacy of the product, its intended use under a future or current EUA, and information about the emergency or potential emergency situation.
- The pre-EUA process allows FDA scientific and technical subject matter experts to begin a review of information and assist in the development of conditions of authorization, fact sheets, and other documentation that would be needed for an EUA in advance of an emergency and facilitate EUA requests during a current emergency declaration.
- Request the most recent EUA review template: Please include a brief description of your IVD (target pathogen, device technology – assay based on molecular, antigen or antibody detection, etc.) at Email CDRH-EUA-Templates@fda.hhs.gov
- After you receive the EUA review template, populate the draft template with the information and data that you currently have for your IVD test.
- Send the draft template back to FDA for review as a Pre-EUA submission using the instructions that are provided along with the EUA review template (which includes sending 1 hard copy and 1 electronic copy to the Document Control Center).
    - The Pre-EUA review is a very interactive process. The draft review template is a shared "work-in-progress" document which you will populate with information and data about your test. FDA will review and provide feedback to you.

How to Submit a Pre-EUA Package for In vitro Diagnostics

- Are you interested in submitting a Pre-EUA for an IVD test for a pathogen that does not have a current EUA declaration?
- If so, FDA is interested in learning about your IVD test from a biopreparedness perspective and recommends the following steps:
- Email Device@fda.hhs.gov to express your interest.
- Please include in the email the following information about your device:
  - A detailed description of your IVD (target pathogen, device technology - assay based on molecular, antigen or antibody detection, etc.)
  - The proposed Intended Use
  - Summary of any analytical (LoD, inclusivity, exclusivity, Interfering substances, Hook effect, etc.) and clinical data collected for this device to date
  - Summary of any analytical or clinical studies planned but not yet started
- On receipt of this request FDA will contact you and outline the specific steps for submitting a Pre-EUA for your IVD test.

How to Submit a Pre-EUA Package for In vitro Diagnostics

- **Contact FDA**
- If you are not sure which Pre-EUA process to follow, have a non-diagnostic device you would like considered for a Pre-EUA or have additional device-related questions with respect to EUA, contact Device@fda.hhs.gov. If you have general device-related questions that are not specific to EUA, we recommend you consult our Device Advice: Comprehensive Regulatory Assistance webpage that includes contact information for the Division of Industry and Consumer Education (DICE).
- If you are interested in Pre-EUA discussions for another product (such as a therapeutic or biological product), or have general questions about EUAs, contact EUA.OCET@fda.hhs.gov.
- **Related Links**
- Coronavirus Disease 2019 (COVID-19)
- FAQs on Diagnostic Testing for SARS-CoV-2
- Zika Virus Diagnostic Development – includes information on Zika reference materials available from FDA for NAT-based IVD devices and serological tests
- Guidance: Emergency Use Authorization of Medical Products and Related Authorities

Tests are eligible for authorization under this EUA if:

- 1. The test is the subject of an EUA request that includes submission of a completed "Accelerated" Template for Laboratories Certified to Perform High-Complexity Testing Under CLIA: EUA Template or equivalent data and the laboratory developed test procedure for performing the authorized test;
- 2. The test is a molecular-based test for the qualitative detection of nucleic acid from SARS-CoV-2 in respiratory specimens collected from individuals suspected of COVID-19 by their healthcare provider;
- 3. Testing is limited to the single laboratory that developed the test, and that is certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests;
- 4. The test is either new and not covered at the time of the EUA request by an existing commercially distributed EUA-authorized test, or the test represents a significant deviation from an existing commercially distributed EUA-authorized test and is not otherwise currently marketed in the U.S.

Tests are eligible for authorization under this EUA if:

- 5 The test is a typical real-time RT PCR test in which SARS- CoV-2 nucleic acid is first extracted, isolated and purified from human respiratory specimens, using authorized extraction methods. The purified nucleic acid is then RT into cDNA followed by nucleic acid amplification and detection using an authorized detection instrument;
- 6. The test uses test material components that are either designed and manufactured by the laboratory or represent commercially sourced materials, such as research use only (RUO) components from third party manufacturers in addition to other authorized materials and authorized ancillary reagents commonly used in clinical laboratories as described in the authorized test procedures submitted as part of the EUA request, and;
- 7. The test uses some combination of the following control materials, or other authorized control materials, that are to be run as outlined in the authorized procedures submitted as part of the EUA request. The controls when used in combination must evaluate all aspects of the authorized test procedure. All controls listed below must generate expected results in order for a test to be considered valid, as outlined in the authorized test procedures submitted as part of the EUA request:

All controls listed below must generate expected Results

- Internal Process Control (IPC) – included in each clinical sample and controls for specimen quality and demonstrates that nucleic acid was generated by the extraction process. Examples include endogeneous RNA control such as RNase P (RP) control and exogeneous RNA, such as MS2 bacteriophage.
- Extraction Control (EC) – serves both as a negative extraction control to monitor for any cross-contamination that occurs during the extraction process, and can validate extraction reagents and successful RNA extraction when used in combination with certain IPC. Example includes a previously characterized negative patient sample.
- External Positive Control or Positive Template Control (PTC) - contains SARS-CoV-2 genomic regions targeted by the test. The positive control is used to monitor for failures of rRT-PCR reagents and reaction conditions. Examples include in vitro transcript SARS-CoV-2 RNA, pseudo SARS-CoV-2 virus, previously characterized positive patient specimen.
- No Template (Negative) Control (NTC) - used to monitor non-specific amplification, cross-contamination during experimental setup, and nucleic acid contamination of reagents. Examples include nuclease-free, molecular- grade water or buffer.

EUA Format: Every EUA Included the followings:

- Fact Sheet for Healthcare Providers
- At this time, no FDA-approved/cleared tests that identify the existence of the novel influenza A(H7N9) virus in clinical specimens are available in the United States. Therefore, the CDC has developed this test to detect novel influenza A(H7N9) infections.
- Fact Sheet for Patients
- The CDC Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A(H7) [Eurasian Lineage] Assay is a laboratory test designed to detect the H7N9 virus. The FDA has not cleared or approved this test, and there are no FDA cleared or approved tests that can identify the H7N9 virus. However, based on data submitted by CDC, FDA has determined that this test can be used for emergency use under an EUA.
- Manufacturer Instructions/Package Insert
- WHO first reported 3 human infections with a new influenza A(H7N9) virus in China. Since then, additional cases have been reported. Most reported cases have severe respiratory illness and, in some cases, have died. This is a “novel” (non-human) virus and therefore has the potential to cause a pandemic if it were to change to become easily and sustainably spread from person-to-person.