U.S. FOOD & DRUG ADMINISTRATION

November 1, 2022

To: Developers of Antigen In Vitro Diagnostics (IVDs) Authorized for Emergency Use for Coronavirus Disease 2019 (COVID-19) as of Today's Date

Re: Revisions Related to Serial (Repeat) Testing for the EUAs of Antigen IVDs

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.[1] FDA subsequently authorized the emergency use of numerous in vitro diagnostics (IVDs) for detection and/or diagnosis of SARS-CoV-2, the virus that causes COVID-19.[2]

Pursuant to Section 564 of the Act, and in response to new data regarding performance of antigen tests from a study assessing at-home COVID-19 antigen test performance ("the antigen

[1] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. 85 FR 7316 (February 7, 2020)

[2] In Vitro Diagnostics EUAs: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas, includes links to tables of currently authorized IVD EUAs for SARS-CoV-2.

study"),[3] FDA is revising the authorized uses[4] and requiring updates to product labeling of all tests that are within the scope of this letter. This revision also establishes one additional Condition of Authorization, and eliminates one Condition of Authorization, on EUAs that are within the scope of this revision (Section I).

The additional condition of authorization established by this revision concerns updates to the authorized labeling[5] to reflect the revised authorized use for tests that are within the scope of this revision. FDA's determination that the Condition of Authorization established by this revision is necessary or appropriate to protect the public health is based on the available scientific evidence and FDA's continuing efforts to evaluate the performance of authorized antigen IVDs with respect to the use of serial testing. The eliminated condition of authorization concerns the collection of additional data to evaluate the performance of authorized antigen IVDs with respect to the use of serial testing. FDA's determination that the Condition of Authorization eliminated by this revision is no longer necessary or appropriate to protect the public health in light of the antigen study.

Having concluded that the revisions to the EUAs of tests that are within the scope of this letter (section I) are appropriate to protect the public health or safety, I am hereby revising all such EUAs pursuant to Section 564(g)(2)(C), including to revise the authorized use and to establish the additional condition set forth in this letter as permitted by Section 564(e) of the Act. This

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[3] COVID-19 antigen tests are less likely to detect the SARS-CoV-2 virus than molecular tests, such as polymerase chain reaction (PCR) tests. However, repeat, or serial, antigen testing has been shown to improve the ability of an antigen test to detect the virus in time for an individual to take actions to contain the spread of disease. To investigate the performance of SARS-CoV-2 antigen serial testing and generate data to support regulatory decisions, FDA collaborated with the National Institutes for Health (NIH) and the University of Massachusetts Chan Medical School to design and implement a study (*Finding a Needle in the Haystack: Design and Implementation of a Digital Site-less Clinical Study of Serial Rapid Antigen Testing to Identify Asymptomatic SARS-CoV-2 Infection* - https://www.medrxiv.org/content/10.1101/2022.08.04.22278274v1, referred to as "the antigen study" in this letter) to assess at-home COVID-19 antigen test performance. Results from the antigen study (*Performance of Screening for SARS-CoV-2 using Rapid Antigen Tests to Detect Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infection: findings from the Test Us at Home prospective cohort study* - https://www.medrxiv.org/content/10.1101/2022.08.05.22278466v1) show that repeat testing over multiple days improves test performance and increases the likelihood that an at-home COVID-19 antigen test will accurately detect an infection. These results have informed the FDA's general understanding that repeat testing after a negative result with an at-home COVID-19 antigen test reduces the risk of a false negative result. On August 11, 2022, based on the results of the antigen study, FDA advised individuals to perform repeat, or serial, testing following a negative result on any at-home COVID-19 antigen test, to reduce the risk an infection may be missed (false negative result) and to help prevent individuals from unknowingly spreading the SARS-CoV-2 virus to others. The FDA recommended repeat testing following a negative result whether or not an individual has COVID-19 symptoms. (https://www.fda.gov/medical-devices/safety-communications/home-covid-19-antigen-tests-take-steps-reduce-your-risk-false-negative-fda-safety-communication).

[4] Generally, the authorized uses of antigen tests are described in, among other locations, the "indication" discussion and "authorized product detail" section in the letters of authorization, and in an "intended use" section in the authorized labeling.

[5] Authorized labeling impacted by the additional condition of authorization established by this letter includes some combination of the following documents: Instructions for Use (IFU), Quick Reference Instructions (QRI), laboratory Standard Operating Procedures (SOPs), electronic labeling and applications, and Fact Sheets. Note that the Fact Sheets are generated by FDA who will update the documents after it receives the supplement request to update the test's other labeling consistent with this revision.

action is based on the available scientific evidence[6] on the impact of serial testing on the performance of SARS-CoV-2 antigen tests.

## I. Scope of this Revision

This letter revises all current EUAs for antigen SARS-CoV-2 IVD devices[7] as of today's date by:

(1) revising the authorized use to be for serial testing at least twice over three days for individuals with symptoms of COVID-19 and, for tests previously authorized for testing individuals without symptoms, revising the authorized use to be for serial testing at least three times over five days for individuals without symptoms of COVID-19, as set forth in Appendix A of this letter,
(2) establishing a new condition of authorization, as set forth in Section III of this letter, on such authorizations, and
(3) eliminating a condition of authorization, as set forth in Section III of this letter, on such authorizations.

This revision does not apply to EUAs for non-antigen based authorized assays (e.g., molecular, serology), EUAs for authorized IL-6 assays, EUAs for standalone specimen collection devices, or EUAs for standalone home collection kits.

All updated labeling will be added to FDA's webpage and posted with the EUA after it is submitted to FDA as required by Condition of Authorization (1) of this letter.

## II. Waiver of Certain Requirements

This revision does not change the waiver of any requirements included in the EUAs being revised.

## III. Revisions to Conditions of Authorization

A. Pursuant to Section 564(e) of the Act, I am establishing the additional condition below with respect to repeat testing on all authorized tests within this letter's scope.

**Developer (You)**

(1) You must update your authorized labeling to reflect the revised authorized use in Appendix A and as set forth in Appendix B of this letter by submitting your proposed updated labeling to FDA as a supplement to your EUA within 10 business days of today's date, unless otherwise agreed to by the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics

[6] *Performance of Screening for SARS-CoV-2 using Rapid Antigen Tests to Detect Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infection: findings from the Test Us at Home prospective cohort study* - https://www.medrxiv.org/content/10.1101/2022.08.05.22278466v1

[7] Please see the following link for currently authorized Antigen IVD devices for SARS-CoV-2: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2.

/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH). Following FDA's concurrence with the supplement, you must update your electronic labeling and electronic/mobile applications (apps) within 20 business days. You must update your paper labeling within 30 business days of FDA's concurrence and all tests distributed subsequently must be accompanied by the updated paper labeling.

B. Pursuant to section 564(g)(2)(C) of the Act, and in consideration of the establishment of Condition of Authorization (1) above, I am eliminating the following condition (or similar condition) from EUAs within the scope (section I above):

**Developer (You)**

You must evaluate the clinical performance of your product to support the serial screening claim in an FDA agreed upon post authorization clinical evaluation study within 4 months of the date of this letter (unless otherwise agreed to with DMD/OHT7/OPEQ/CDRH). After submission to and concurrence with the data by FDA, you must update the authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH.

Sincerely,

_____
Namandjé N. Bumpus, Ph.D.
Chief Scientist
Food and Drug Administration

Enclosure

## Appendix A
## Revised Authorized Uses

The authorized uses for tests that are within the scope (Section I) of this letter are revised as follows:

1) Where a test was previously authorized for testing of symptomatic individuals (e.g., within the first [*number specific to each test*] days of symptom onset), the test is now authorized for use at least twice over three days with at least 48 hours between tests.
2) Where a test was previously authorized for testing of asymptomatic individuals (e.g., individuals without symptoms or other epidemiological reasons to suspect COVID-19), the test is now authorized for use at least three times over five days with at least 48 hours between tests.

## Appendix B
## Required Changes to Authorized Labeling

As required by Condition of Authorization (1), you must update your authorized labeling to include the labeling elements, sections, and statements below:

1. **Intended Use:**[8]

   In addition to name, technology, analyte specific information and other validated claims, the Intended Use must include the updated frequency of testing for symptomatic and asymptomatic individuals (as applicable).

   - For tests referenced in Appendix A, #1, this means including language that the test is for serial testing for use at least twice over three days with at least 48 hours between tests;
   - For tests referenced in Appendix A, #2, this means including language that the test is for serial testing for use at least three times over five days with at least 48 hours between tests and removing language regarding testing at least twice over two or three days with at least 24 and no more than 36 hours between tests.

   In addition, the Intended Use must include the following statements:

   - "negative results are presumptive"
   - "The [*Test Name*] is only for in vitro diagnostic use under the Food and Drug Administration's Emergency Use Authorization. This product has not been FDA cleared or approved."

2. **Outer Box and Subassembly Labeling (as applicable):**

   - Expiration date (sticker): Based on component of kit with the earliest expiration date
   - Summary of box contents
   - Items necessary to use the test but not provided in the test kit: *[e.g., access to computer/smartphone, internet, email account]*
   - Storage temperature
   - Summary of how the kit works

   Statements that must be present on the outer box:

   - For Emergency Use Authorization (EUA) only
   - For in vitro diagnostic use
   - In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an EUA.

[8] As discussed in footnote 4, generally the authorized uses of antigen tests are described in, among other locations, an "intended use" section in the authorized labeling. If such uses are discussed elsewhere in the authorized labeling, you must also make appropriate updates to that labeling to reflect the revised authorized uses.

- This product has been authorized only for the detection of proteins from SARS-CoV-2 [*for multi-analyte tests please insert the additional on-panel analytes, e.g., influenza A/B]*, not for any other viruses or pathogens.
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- Determining a negative result requires multiple tests. 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.

**3. Instructions for Use**

**a. <u>Lay User Labeling (applicable only to tests authorized for home use)</u>**

**i. Test Interpretation**

Repeat testing is needed to improve test accuracy. Please follow the table below when interpreting test results for COVID-19.

| Status on First Day of Testing | First Result Day 1 | Second Result Day 3 | Third Result Day 5 | Interpretation |
|---|---|---|---|---|
| With Symptoms | Positive | N/A | N/A | Positive for COVID-19 |
| | Negative | Positive | N/A | Positive for COVID-19 |
| | Negative | Negative | N/A | Negative for COVID-19 |
| Without Symptoms | Positive | N/A | N/A | Positive for COVID-19 |
| | Negative | Positive | N/A | Positive for COVID-19 |
| | Negative | Negative | Positive | Positive for COVID-19 |
| | Negative | Negative | Negative | Negative for COVID-19 |

Results should be considered in the context of an individual's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.

***<u>COVID-19 Positive (+)</u>***

If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible [*color*] test (T) line with the control line (C) should be read as positive.

**You do not need to perform repeat testing if you have a positive result at any time.**

A positive test result means that the virus that causes COVID-19 was detected in your sample and it is very likely you have COVID-19 and are contagious. Please contact your doctor/primary care physician or your local health authority immediately and adhere to the local guidelines regarding self-isolation. There is a very small chance that this test can give a positive result that is incorrect (a false positive).

***COVID-19 Negative (-)***

If the Control (C) line is visible, but the Test (T) line is not visible, the test is negative.

**To increase the chance that the negative result for COVID-19 is accurate, you should:**

- **Test again in 48 hours if you have symptoms on the first day of testing.**
- **Test 2 more times at least 48 hours apart if you do not have symptoms on the first day of testing.**

A negative test result indicates that the virus that causes COVID-19 was not detected in your sample. A negative result is presumptive, meaning it is not certain that you do not have COVID-19. You may still have COVID-19 and you may still be contagious. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR. If you test negative and continue to experience COVID-19-like symptoms, (e.g., fever, cough, and/or shortness of breath) you should seek follow up care with your health care provider.

***Invalid***

If the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test device.

### ii. How to Use This Test

The Lay User labeling must include a specific section "How to Use this Test" with the following information:

- Serial testing should be performed in all individuals with negative results; individuals with symptoms of COVID-19 and initial negative results should be tested again after 48 hours. Individuals without symptoms of COVID-19, and with initial negative results, should be tested again after 48 hours and, if the 2nd test is also negative, a 3rd time after an additional 48 hours. You may need to purchase additional tests to perform this serial (repeat) testing.
- If you test negative but continue to have symptoms of COVID-19, and both your first and second tests are negative, you may not have COVID-19, however you should follow-up with your healthcare provider.
- If your test is positive, then proteins from the virus that causes COVID-19 have been found in your sample and you likely have COVID-19.

### iii. Warnings, Precautions, and Safety Information

The Lay User labeling must include the following warnings, precautions and/or safety information:

- Read all instructions carefully before performing the test. Failure to follow the instructions may result in inaccurate test results.
- In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization. This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- **Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals. You may need to purchase additional tests to perform this serial (repeat) testing.**
- An anterior nasal swab sample can be self-collected by an individual age [*X*] years and older. Children age 2 to [*X*] years should be tested by an adult.
- Do not use on anyone under 2 years of age.
- Wear a safety mask or other face-covering when collecting a specimen from a child or another individual.
- Do not use if any of the test kit contents or packaging is damaged.
- Test components are single-use. Do not re-use.
- Do not use kit past its expiration date.
- Do not touch the swab tip.
- Once opened, the test card should be used within [*X*] minutes.
- Do not read test results before [*X*] minutes or after [*Y*] minutes. Results read before [*X*] minutes or after [*Y*] minutes may lead to a false positive, false negative, or invalid result.
- If applicable: Keep testing kit and kit components away from children and pets before and after use. Avoid contact with your [e.g., *skin, eyes, nose, or mouth*]. Do not ingest any kit components. The reagent solution contains harmful chemicals (see table below). If the solution contacts your [e.g., *e.g., skin, eyes, nose, or mouth]*, flush with large amounts of water.

  **If irritation persists, seek medical advice: https://www.poisonhelp.org or 1-800-222-1222**. *[Note: Please do not use the following website in your labeling: https://www.poison.org/contact-us. Also, please populate the following table as appropriate for your device and per FDA toxicological assessment of your device:*]

| **Chemical Name** | **GHS Code for each Ingredient** | **Concentrations** |
|---|---|---|
| e.g., Microcide III | H315, skin irritation | 0.2% |
| | | |

- For more information on EUAs please visit: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- For the most up to date information on COVID-19, please visit: www.cdc.gov/COVID19

### iv. Limitations

- There is a higher chance of false negative results with antigen tests than with laboratory-based molecular tests due to the sensitivity of the test technology. This means that there is a higher chance this test will give a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between [*month, year and month, year*]. The clinical performance has not been established for all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- All COVID-19 antigen test negative results are presumptive and confirmation with a molecular assay may be necessary. If you continue to have symptoms of COVID-19, and both your first and second tests are negative, you may not have COVID-19, however you should follow-up with a healthcare provider.
- If the test is positive, then proteins from the virus that causes COVID-19 have been found in the sample and you likely have COVID-19.
- This test is read visually and has not been validated for use by those with impaired vision or color-impaired vision.
- Incorrect test results may occur if a specimen is incorrectly collected or handled.

### v. Frequently Asked Questions (FAQ):

The following FAQ section should be added to the Lay User IFU (and, if applicable, the QRI) for those Lay User IFUs that also contain the information typically found in a Patient Fact Sheet for OTC tests:

**WHAT ARE THE KNOWN AND POTENTIAL RISKS AND BENEFITS OF THE TEST?**

Potential risks include:

- Possible discomfort during sample collection.
- Possible incorrect test result (see Warnings and Result Interpretation sections for more information).

Potential benefits include:

- The results, along with other information, can help you and your healthcare provider make informed recommendations about your care.
- The results of this test may help limit the potential spread of COVID-19 to your family and others in your community.

For more information on EUAs go here: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

**WHAT IS THE DIFFERENCE BETWEEN AN ANTIGEN AND MOLECULAR TEST?**

There are different kinds of tests for the SARS-CoV-2 virus that causes COVID-19. Molecular tests detect genetic material from the virus. Antigen tests, such as the [*Test Name*], detect proteins from the virus. Due to the lower sensitivity of antigen tests, there is a higher chance this test will give you a false negative result when you have COVID-19 than a molecular test would.

**HOW ACCURATE IS THIS TEST?**

Clinical studies have shown that antigen tests more accurately determine whether you are infected with the virus that causes COVID-19 when taken multiple times across several days. Repeat testing improves test accuracy. This serial testing approach is recommended to minimize the risk of incorrect results. For more information on the performance of the test and how the performance may apply to you, please refer to the performance data in the Healthcare Provider Instructions for Use (IFU), available at [***insert developer's website's address***].

**WHAT IF I HAVE A POSITIVE TEST RESULT?**

A positive result means that it is very likely you have COVID-19 because proteins from the virus that causes COVID-19 were found in your sample. You should self-isolate from others and contact a healthcare provider for medical advice about your positive result.

**WHAT IF I HAVE A NEGATIVE TEST RESULT?**

A negative test result indicates that antigens from the virus that causes COVID-19 were not detected in your sample. However, if you have symptoms of COVID-19, and your first test is negative, you should test again in 48 hours since antigen tests are not as sensitive as molecular tests. If you do not have symptoms and received a negative result, you should test at least two more times with 48 hours in between tests for a total of three tests. If you have a negative result, it does not rule out SARS-CoV-2 infection; you may still be infected and you may still infect others. It is important that you work with your healthcare provider to help you understand the next steps you should take.

**WHAT DOES AN INVALID TEST RESULT MEAN?**

An invalid result means the test was not able to tell if you have COVID-19 or not. If the test is invalid, a new swab should be used to collect a new nasal specimen and you should test again with a new test.

**IMPORTANT**

Do not use this test as the only guide to manage your illness. Consult your healthcare provider if your symptoms persist or become more severe.

Individuals should provide all results obtained with this product to their healthcare provider.

**b. HCP Labeling**

**i. Test Interpretation**

Repeat testing is needed to improve test accuracy. Please follow the table below when interpreting test results.

| Status on first day of Testing | First Result Day 1 | Second Result Day 3 | Third Result Day 5 | Interpretation |
|---|---|---|---|---|
| With Symptoms | Positive | N/A | N/A | Positive for COVID-19 |
| | Negative | Positive | N/A | Positive for COVID-19 |
| | Negative | Negative | N/A | Negative for COVID-19 |
| Without Symptoms | Positive | N/A | N/A | Positive for COVID-19 |
| | Negative | Positive | N/A | Positive for COVID-19 |
| | Negative | Negative | Positive | Positive for COVID-19 |
| | Negative | Negative | Negative | Negative for COVID-19 |

Results should be considered in the context of an individual's recent exposures, history, and the presence of clinical signs and symptoms consistent with COVID-19.

***COVID-19 Positive (+)***

If the Control (C) line and the Test (T) line are visible, the test is positive. Any faint visible [*color*] test (T) line with the control line (C) should be read as positive.

**Repeat testing does not need to be performed if patients have a positive result at any time.**

A positive test result means that the virus that causes COVID-19 was detected in the sample, and it is very likely the individual has COVID-19 and is contagious. Please contact the patient's doctor/primary care physician (if applicable) and the local health authority immediately and instruct your patient to adhere to the local guidelines regarding self-

isolation. There is a very small chance that this test can give a positive result that is incorrect (a false positive).

Positive results do not rule out bacterial infection or co-infection with other viruses. The agent detected may not be the definite cause of disease. Individuals who test positive with the [*Test Name*] should self-isolate and seek follow up care with their physician or healthcare provider as additional confirmatory testing with a molecular test for positive results may also be necessary, if there is a low likelihood of COVID-19, such as in individuals without known exposures to COVID-19 or residing in communities with low prevalence of infection.

***COVID-19 Negative (-)***

If the Control (C) line is visible, but the Test (T) line is not visible, the test is negative.

**To increase the chance that the negative result for COVID-19 is accurate, you should:**

- **Test again in 48 hours if the individual has symptoms on the first day of testing.**
- **Test 2 more times at least 48 hours apart if the individual does not have symptoms on the first day of testing.**

A negative test result indicates that the virus that causes COVID-19 was not detected in the sample. A negative result does not rule out COVID-19. There is a higher chance of false negative results with antigen tests compared to laboratory-based tests such as PCR tests. If the test is negative but COVID-19-like symptoms, e.g., fever, cough, and/or shortness of breath continue, follow up testing for SARS-CoV-2 with a molecular test or testing for other respiratory disease should be considered. If applicable, seek follow up care with the primary health care provider.

All negative results should be treated as presumptive and confirmation with a molecular assay may be necessary if there is a high likelihood of SARS-CoV-2 infection, such as in an individual with a close contact with COVID-19 or with suspected exposure to COVID-19 or in communities with high prevalence of infection. Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions.

***Invalid***

If the control (C) line is not visible, the test is invalid. Re-test with a new swab and new test device.

### ii. Warnings, Precautions, and Safety Information

The following Warnings, Precautions, and Safety Information should be included in the full HCP IFU; in addition, the warning statements of the first three bullet points below should also be included in the Quick Reference Guide (QRI) of all tests authorized for point-of-care (PoC) use.

- Read all instructions carefully before performing the test. Failure to follow the instructions may result in inaccurate test results.
- In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization. This product has been authorized only for the detection of proteins from SARS-CoV-2 [*for multi-analyte tests please insert the additional on-panel analytes, e.g., influenza A/B*], not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
- **Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals. You may need to purchase additional tests to perform this serial (repeat) testing**.
- An anterior nasal swab sample can be self-collected by an individual age [*X*] years and older. Children age 2 to [*X*] years should be tested by an adult.
- Do not use on anyone under 2 years of age.
- Wear a safety mask or other face-covering when collecting a specimen from a child or another individual.
- Do not use if any of the test kit contents or packaging is damaged.
- Test components are single-use. Do not re-use.
- Do not use kit past its expiration date.
- Do not touch the swab tip.
- Once opened, the test card should be used within [*X*] minutes.
- **Do not read test results before [*X*] minutes or after [*Y*] minutes. Results read before [*X*] minutes or after [*Y*] minutes may lead to a false positive, false negative, or invalid result.**
- **Keep testing kit and kit components away from children and pets before and after use. Avoid contact with your [*e.g., skin, eyes, nose, or mouth]*. Do not ingest any kit components. The reagent solution contains harmful chemicals (see table below). If the solution contacts your [e.g., *skin, eyes, nose, or mouth]*, flush with large amounts of water. If irritation persists, seek medical advice: https://www.poisonhelp.org or 1-800-222-1222**.

  *[Note: Please do not use the following website in your labeling: https://www.poison.org/contact-us. Also, please populate the following table as appropriate for your device and per FDA toxicological assessment of your device:*]

| Chemical Name | GHS Code for each Ingredient | Concentrations |
|---|---|---|
| e.g., Microcide III | H315, skin irritation | 0.2% |
| | | |

- For more information on EUAs please visit: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- For the most up to date information on COVID-19, please visit: www.cdc.gov/COVID19

### iii. Limitations

- The performance of this test was established based on the evaluation of a limited number of clinical specimens collected between [*month, year and month, year*]. The clinical performance has not been established for all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.
- There is a higher chance of false negative results with antigen tests than with laboratory-based molecular tests due to the sensitivity of the test technology. This means that there is a higher chance this test will give a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
- All COVID-19 antigen test negative results are presumptive and confirmation with a molecular assay may be necessary.
- If the patient continues to have symptoms of COVID-19, and both the patient's first and second tests are negative, the patient may not have COVID-19, however additional follow-up may be needed.
- If the test is positive, then proteins from the virus that causes COVID-19 have been found in the sample and the individual likely has COVID-19.
- This test is read visually and has not been validated for use by those with impaired vision or color-impaired vision.
- Incorrect test results may occur if a specimen is incorrectly collected or handled.
- This test detects both viable (live) and nonviable SARS-CoV-2. Test performance depends on the amount of virus (antigens) in the sample and may or may not correlate with viral culture results performed on the same sample.

### iv. Performance Section of HCP labeling

A prospective clinical study was conducted between January 2021 and May 2022 as a component of the Rapid Acceleration of Diagnostics (RADx) initiative from the National Institutes of Health (NIH). A total of 7,361 individuals were enrolled via a decentralized clinical study design, with a broad geographical representation of the United States. Per inclusion criteria, all individuals were asymptomatic upon enrollment in the study and at least 14 days prior to it and did not have a SARS-CoV-2 infection in the three months prior to enrollment. Participants were assigned to one of three EUA authorized SARS-CoV-2 OTC rapid antigen tests to conduct serial testing (every 48 hours) for 15 days. If an antigen test was positive, the serial-antigen testing result is considered positive.

At each rapid antigen testing time point, study subjects also collected a nasal swab for comparator testing using a home collection kit (using a 15-minute normalization window between swabs). SARS-CoV-2 infection status was determined by a composite comparator method on the day of the first antigen test, using at least two highly sensitive EUA RT-PCRs. If results of the first two molecular test were discordant a third highly sensitive EUA RT-PCR test was performed, and the final test result was based upon the majority rule.

Study participants reported symptom status throughout the study using the MyDataHelps app. Two-day serial antigen testing is defined as performing two antigen tests 36 - 48 hours apart. Three-day serial antigen testing is defined as performing three antigen tests over five days with at least 48 hours between each test.

Out of the 7,361 participants enrolled in the study, 5,609 were eligible for analysis. Among eligible participants, 154 tested positive for SARS-CoV-2 infection based on RT-PCR, of which 97 (62%) were asymptomatic on the first day of their infection, whereas 57 (39%) reported symptoms on the first day of infection. Pre-symptomatic subjects were included in the positive percent agreement (PPA) of asymptomatic individuals, if they were asymptomatic on the first day of antigen testing, regardless of whether they developed symptoms at any time after the first day of testing.

Performance of the antigen test with serial testing in individuals is described in Table YYY.

**Table YYY**: Data establishing PPA of COVID-19 antigen serial testing compared to the molecular comparator single day testing throughout the course of infection with serial testing. Data is from all antigen tests in study combined.

| DAYS AFTER FIRST PCR POSITIVE TEST RESULT | ASYMPTOMATIC ON FIRST DAY OF TESTING | | | SYMPTOMATIC ON FIRST DAY OF TESTING | | |
|---|---|---|---|---|---|---|
| | Ag Positive / PCR Positive (Antigen Test Performance % PPA) | | | | | |
| | 1 Test | 2 Tests | 3 Tests | 1 Test | 2 Tests | 3 Tests |
| **0** | 9/97 (9.3%) | 35/89 (39.3%) | 44/78 (56.4%) | 34/57 (59.6%) | 47/51 (92.2%) | 44/47 (93.6%) |
| **2** | 17/34 (50.0%) | 23/34 (67.6%) | 25/32 (78.1%) | 58/62 (93.5%) | 59/60 (98.3%) | 43/43 (100%) |
| **4** | 16/21 (76.2%) | 15/20 (75.0%) | 13/15 (86.7%) | 55/58 (94.8%) | 53/54 (98.1%) | 39/40 (97.5%) |
| **6** | 20/28 (71.4%) | 21/27 (77.8%) | 16/18 (88.9%) | 27/34 (79.4%) | 26/33 (78.8%) | 22/27 (81.5%) |
| **8** | 13/23 (56.5%) | 13/22 (59.1%) | 4/11 (36.4%) | 12/17 (70.6%) | 12/17 (70.6%) | 7/11 (63.6%) |
| **10** | 5/9 (55.6%) | 5/8 (62.5%) | | 4/9 (44.4%) | 3/7 (42.9%) | |

1 Test = one (1) test performed on the noted days after first PCR positive test result. Day 0 is the first day of documented infection with SARS-CoV-2.

2 Tests = two (2) tests performed an average of 48 hours apart. The first test performed on the indicated day and the second test performed 48 hours later.
3 Tests = three (3) tests performance an average of 48 hours apart. The first test performed on the indicated day, the second test performed 48 hours later, and a final test performed 48 hours after the second test.

**4. Fact Sheets**

The Fact Sheet for Healthcare Providers (HCPs) and Fact Sheet for Patients and Fact Sheet for Individuals will be updated by FDA consistent with this revision, and FDA will provide them to you.

**5. Electronic Applications (e.g., Cell Phone Apps)**

Electronic applications (apps) should include a prominently placed warning for the requirement of repeat testing after a negative test result. App related software should be updated to accommodate the following minimal information:

- Test interpretation as outlined in section 3. a. i. above.
- How to Use This Test as outlined in section 3. a. ii. above
- Warning Statements:
  - In the USA, this product has not been FDA cleared or approved, but has been authorized by FDA under an Emergency Use Authorization. This product has been authorized only for the detection of proteins from SARS-CoV-2, not for any other viruses or pathogens. The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.
  - **Serial testing should be performed in individuals with negative results at least twice over three days (with 48 hours between tests) for symptomatic individuals and three times over five days (with at least 48 hours between tests) for asymptomatic individuals. You may need to purchase additional tests to perform this serial (repeat) testing.**
  - There is a higher chance of false negative results with antigen tests than with laboratory-based molecular tests due to the sensitivity of the test technology. This means that there is a higher chance this test will give a false negative result in an individual with COVID-19 as compared to a molecular test, especially in samples with low viral load.
  - All COVID-19 antigen test negative results are presumptive and confirmation with a molecular assay may be necessary. If you continue to have symptoms of

COVID-19, and both your first and second tests are negative, you may not have COVID-19, however you should follow-up with a healthcare provider.
  - This test is read visually and has not been validated for use by those with impaired vision or color-impaired vision.
- A link to an FAQ document as described in section 3. a. v. above.