Enforcement Policy for Modifications to FDA-Cleared Molecular Influenza and RSV Tests During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

---

Guidance for Industry and Food and Drug Administration Staff

October 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number FDA-2020-D-1138 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, and the FDA webpage titled "Search for FDA Guidance Documents," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive an additional copy of the guidance. Please include the document number 20046 and complete title of the guidance in the request.

Questions

For questions about this document, contact CDRH-EUA-Templates@fda.hhs.gov or call 1-888-INFO-FDA.

Table of Contents

Enforcement Policy for Modifications to FDA-Cleared Molecular Influenza and RSV Tests During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

---

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

FDA plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to provide a policy to help expand access to certain FDA-cleared molecular assays intended for detection and identification of influenza (flu) viruses, including those molecular influenza assays that also detect and identify respiratory syncytial viruses (RSV), during the influenza season and for the duration of the COVID-19 public health emergency.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Secretary of Health and Human Services (HHS) on January 31, 2020, effective January 27, 2020, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act) (42 U.S.C. 247d(a)(2)).

Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled "Process for Making Available Guidance Documents Related to Coronavirus Disease 2019," *available at* https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the

Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 371(h)(1)(C)) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

In general, FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

There is currently a pandemic of respiratory disease caused by a novel coronavirus. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.[1] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[2]

There is significant overlap in warning signs and symptoms between SARS-CoV-2 and other respiratory viral infections, including influenza and RSV and the diagnostic tests for these infections generally use many of the same components. For example, many FDA-cleared molecular influenza tests require specific specimen collection devices to obtain a sample from the patient and specific transport media to transport the clinical specimens to a laboratory for testing. These specimen collection devices and transport media that are required to perform molecular influenza tests are also critical components required to perform most molecular diagnostic SARS-CoV-2 assays that have been issued an Emergency Use Authorization (EUA). FDA believes this enforcement policy regarding the use of certain alternative specimen collection devices and transport media with cleared molecular influenza tests may help address availability concerns regarding these tests and critical components during the COVID-19 pandemic.

Increased availability of molecular influenza tests during the COVID-19 pandemic is important due to the similarity in symptoms between COVID-19 and the seasonal influenza. In addition, due to the similarity of the symptoms, and for convenience of patients, molecular influenza tests are often offered as part of a panel of tests including RSV, which generally shares an increased rate of onset during the influenza season. The importance of an accurate diagnosis of influenza can provide timely information for those patients during the COVID-19 pandemic suspected of respiratory viral infection(s). FDA believes the policy set forth in this guidance may help address public health concerns regarding the availability of molecular influenza tests during the COVID-19 pandemic and in particular during the influenza season.

[1] Secretary of Health and Human Services Alex M. Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020, renewed April 21, 2020, July 23, 2020, and October 2, 2020, effective October 23, 2020), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.

[2] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/.

III. Scope

The enforcement policy described in this guidance applies to FDA-cleared qualitative molecular assays that are intended to detect and identify influenza viruses (including Influenza A and Influenza B) from individuals exhibiting warning signs and symptoms of respiratory infection, including those assays that also detect and identify RSV (including RSV subtype A and RSV subtype B) (hereafter referred to as "molecular influenza and RSV tests").

These molecular influenza and RSV tests are class II devices regulated under 21 CFR 866.3980 (Respiratory viral panel multiplex nucleic acid assay) and may be assigned product codes OCC, OZE, or OEP. This policy only applies to those devices intended for use as described above.

This policy does not apply to the following devices:

- Devices classified under 21 CFR 866.3980 that are intended to detect and identify other viruses (i.e., viruses that are not influenza or RSV) such as human metapneumovirus, rhinovirus, or adenovirus, or bacteria, as FDA has concerns that the modifications described below may negatively impact the device's ability to detect and identify those microorganisms. These devices for which this policy does not apply are assigned product codes OEM, OOU, OQW, OTG, OZX, OZY, OMG, and OZZ;
- Antigen-based influenza tests classified under 21 CFR 866.3328 (assigned product code PSZ);
- Multiplex respiratory panels for detecting and identifying emerging respiratory pathogens and common respiratory pathogens, classified under 21 CFR 866.4001 (assigned product codes PZF and QDS); and
- Molecular diagnostic multiplex tests that have been issued an EUA under section 564 of the FD&C Act and are intended to diagnose and differentiate SARS-CoV-2 infection from other viruses, including influenza viruses and RSV.

IV. Policy

A. Overview

FDA recognizes that during the COVID-19 pandemic, there may be issues regarding the availability of molecular influenza tests due to increased pressures on the supply chain for the critical components necessary to perform these tests and the likelihood for increased demand of molecular influenza and RSV tests to differentiate these respiratory viruses from COVID-19. The guidance entitled "Enforcement Policy for Viral Transport Media During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency"[3] describes FDA's enforcement policy for transport media during the COVID-19 public health emergency and applies to the transport media necessary to perform molecular influenza and RSV tests. As such, developers of transport media should refer to that guidance.

[3] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-viral-transport-media-during-coronavirus-disease-2019-covid-19-public-health

Manufacturers of molecular influenza and RSV tests are required to submit a premarket notification under section 510(k) of the FD&C Act and receive FDA clearance prior to marketing these devices, as well as comply with certain post-marketing requirements. Many FDA-cleared molecular influenza and RSV tests are indicated specifically for use with specific specimen collection devices (e.g., nasopharyngeal swabs) and/or indicated specifically for use with specific transport media (e.g., viral transport media (VTM)). These FDA-cleared molecular influenza and RSV tests may not be marketed for use beyond their clearance, meaning use with new specimen types, new collection specimen devices, or new transport media generally require a new premarket notification (i.e., a new 510(k) clearance) and changes to the device's labeling prior to marketing the modified test. In light of the importance of having increased availability of molecular influenza tests during the COVID-19 pandemic and in particular during the influenza season, FDA does not intend to object to the types of modifications to FDA-cleared molecular influenza and RSV tests described in section III for the duration of the public health emergency where such modification does not create an undue risk, as described in more detail below, without prior submission of a premarket notification as required by section 510(k) of the FD&C Act and 21 CFR 807.81.[4]

Because FDA does not intend to enforce compliance with the requirement to submit a 510(k) for certain modifications, FDA also does not intend to enforce the special controls identified in 21 CFR 866.3980(b)[5] pertaining to the information that should be included in a 510(k) submission, for manufacturers who do not to submit a 510(k) for these limited modifications as described in this guidance. However, when a manufacturer does submit a 510(k) for a device modification, FDA would expect the manufacturer to follow the special controls regarding the information that should be included. Moreover, this policy does not apply to compliance with other applicable requirements identified in the special controls under 21 CFR 866.3980(b), including any applicable labeling requirements.[6, 7]

[4] For further guidance on modifications that trigger the requirement that a manufacturer submit a new premarket notification (510(k)) to FDA, refer to "Deciding When to Submit a 510(k) for a Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff," https://www.fda.gov/regulatory-information/search-fda-guidancedocuments/deciding-when-submit-510k-change-existing-device.

[5] The special controls applicable to molecular influenza and RSV tests are the "Respiratory Viral Panel Multiplex Nucleic Acid Assay - Class II Special Controls Guidance for Industry and FDA Staff," available at https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/respiratory-viral-panel-multiplex-nucleic-acid-assay-class-ii-special-controls-guidance-industry-and, and the "Testing for Detection and Differentiation of Influenza A Virus Subtypes Using Multiplex Assays - Class II Special Controls Guidance for Industry and FDA Staff," available at https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/testing-detection-and-differentiation-influenza-virus-subtypes-using-multiplex-assays-class-ii.

[6] See section 7 of the special controls document "Respiratory Viral Panel Multiplex Nucleic Acid Assay - Class II Special Controls Guidance for Industry and FDA Staff."

[7] For molecular influenza and RSV tests that detect and differentiate influenza A virus subtype H1 and subtype H3, see section 7 of the special controls document "Testing for Detection and Differentiation of Influenza A Virus Subtypes Using Multiplex Assays - Class II Special Controls Guidance for Industry and FDA Staff."

B. Modifications

For the duration of the public health emergency, FDA does not intend to object to the following modifications to certain FDA-cleared molecular influenza and RSV tests without prior submission of a 510(k) premarket notification that do not create an undue risk in light of the public health emergency:

1) Modifications are made to the FDA-cleared indications, labeling, or materials of an FDA-cleared molecular influenza and RSV test in order to add sterile phosphate buffered saline (PBS) (including molecular grade PBS and other similar formulations such as Dulbecco's PBS), and sterile normal saline as additional transport media types when the device was previously indicated for VTM; or

2) Modifications are made to the FDA-cleared indications, labeling, or materials, of an FDA-cleared molecular influenza and RSV test cleared for use with nasopharyngeal swabs only to add use with healthcare provider collected anterior nares specimens and/or mid-turbinate specimens.

Based on current information and experience, FDA believes the modifications in the examples below would create an undue risk:

1) Adding a sample type not identified above to an FDA-cleared molecular influenza and RSV test;

2) Adding an indication for use with self-collected specimens to an FDA-cleared molecular influenza and RSV test;

3) Adding a transport media not identified above to an FDA-cleared molecular influenza and RSV test; or

4) Adding an over-the-counter (OTC) use or new patient population (e.g., pediatrics) to the indication for an FDA-cleared molecular influenza and RSV test.

C. Labeling and Validation

Molecular influenza and RSV tests are devices subject to the labeling requirements in 21 CFR Parts 801 and 809 and the labeling requirements in the special controls for these devices identified in 21 CFR 866.3980. Manufacturers should refer to those regulations for the complete list of labeling requirements for *in vitro* diagnostic devices. The additional labeling and performance recommendations described in this section are intended to help ensure that molecular influenza and RSV tests under this policy do not create an undue risk in light of the public health emergency and to help users understand the device modification(s) under this policy.

FDA believes that molecular influenza and RSV tests should use labeling that helps users better understand the device modifications, such as:

- Instructions for specimen collection using the alternative collection devices as a result of this policy (e.g., instructions for collecting anterior nares specimen type) and instructions for handling of collected specimens, including storage instructions, and transport conditions instructions in accordance with 21 CFR 809.10(b)(7);
- Results and specific performance criteria using any alternative collection devices and/or transport media as a result of this policy in accordance with 21 CFR 809.10(b)(9) and 21 CFR 809.10(b)(12);
- Indications of compatibility including indications for use with alternative specimen type(s), collection devices and transport media; and
- A clear distinction delineating FDA-cleared indications and technical specifications from those that are not FDA-cleared. In addition, FDA recommends the labeling include a clear statement that the test has not been reviewed by FDA for use with [insert new specimen collection device] or using [insert transport media].

Additionally, we believe it is important for modifications to FDA-cleared molecular influenza and RSV tests to be appropriately validated prior to distribution to reduce the risks of inaccurate test results. Under design controls, manufacturers are required to conduct verification and validation (21 CFR 820.30(f) and (g)) and must verify and/or validate the performance of their modified molecular influenza and RSV test. Manufacturers must document changes to their device in their device master record and change control records and make this information available to FDA, if requested, in accordance with 21 CFR 820.30 and 21 CFR 820.180.