Contains Nonbinding Recommendations

Draft – Not for Implementation

Consideration of Enforcement Policies for Tests During a Section 564 Declared Emergency

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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For questions about this document, contact the CDRH Guidance Program in the Office of Policy at CDRH-Guidance@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

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Consideration of Enforcement Policies for Tests During a Section 564 Declared Emergency

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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[1]

FDA plays a critical role in protecting the United States (U.S.) from emergencies and public health threats such as emerging infectious diseases and chemical agents. In certain circumstances, emergencies and threats could lead to an HHS Secretary declaration under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) enabling FDA to issue emergency use authorizations (EUAs). After such a declaration, FDA also may decide to issue an enforcement policy to help expand availability of certain devices. FDA is issuing this draft guidance that, when finalized, will describe the factors FDA plans to assess in deciding whether to issue an enforcement policy regarding test manufacturers'[2] offering of certain devices,[3]

[1] This draft guidance has been prepared by the Center for Devices and Radiological Health (CDRH) in consultation with the Center for Biologics Evaluation and Research (CBER).

[2] For purposes of this document, we use "manufacturers" for those entities conducting any activity that constitutes manufacturing as described in FDA regulations (e.g., design, preparation, propagation, assembly, and processing). See 21 CFR 807.3(d) and 820.3(o).

[3] Under section 201(h)(1) of the FD&C Act, the term "device" is defined as follows:

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is--

(A) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(B) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(C) intended to affect the structure or any function of the body of man or other animals, and

specifically unapproved tests[4] and unapproved uses of approved tests,[5] for the diagnosis of disease or other conditions during a declared emergency.[6]

In general, FDA's guidance documents 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 guidances means that something is suggested or recommended, but not required.

II. Background

Appropriately safe and effective diagnostic tests are critical to the diagnosis, treatment, tracking, and interruption of transmission of infectious diseases during outbreaks, as well as for diagnosing and treating diseases or conditions caused by chemical, biological, radiological, and nuclear (CBRN) threat agents. Tests are also critical for evaluating the impact or effectiveness of certain public health interventions. In the event of these types of emergencies and threats, often there is no available FDA-approved test to diagnose the disease or condition.

Under section 564 of the FD&C Act, FDA may authorize emergency use of unapproved medical products, or unapproved uses of approved medical products, when certain criteria are met, after the HHS Secretary has made a declaration of emergency or threat justifying authorization of emergency use, to diagnose, treat, or prevent diseases or conditions caused by CBRN threat agents, as well as other agents that may present a heightened risk to the U.S. military forces. For information on FDA's implementation of this and other emergency use authorities, see FDA's guidance "Emergency Use Authorization of Medical Products and Related Authorities."[7] FDA has issued EUAs for tests for H1N1 (2009), H7N9 (2013), MERS-CoV (2013), Ebola (2014),

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term 'device' does not include software functions excluded pursuant to section 520(o)" of the FD&C Act.

[4] Consistent with section 564 of the FD&C Act and other FDA authorities, "unapproved tests" refers to a test that is not approved, licensed, granted or cleared under section 510(k), 513(f)(2) or 515 of the FD&C Act or section 351 of the Public Health Service Act (PHS Act), as applicable. The terms "approved test" and "FDA-approved test" refer to a test that is approved, licensed, granted or cleared under section 510(k), 513(f)(2) or 515 of the FD&C Act or section 351 of the PHS Act, as applicable. See "unapproved product" in section 564(a)(2)(A) of the FD&C Act.

[5] Consistent with section 564 of the FD&C Act and other FDA authorities, "unapproved use of an approved test" refers to a test that is approved, licensed, granted or cleared under section 510(k), 513(f)(2) or 515 of the FD&C Act or section 351 of the PHS Act, but for which the specific use is not an approved, licensed, granted or cleared use of the product. See "unapproved use of an approved product" in section 564(a)(2)(B) of the FD&C Act. Examples of unapproved uses of approved tests would be the over-the-counter use of a test approved for prescription use only or the use of nasal swab samples with a test approved for use with nasopharyngeal swab samples.

[6] For purposes of this guidance, "unapproved tests" refers to unapproved tests and unapproved uses of approved tests.

[7] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

Enterovirus D68 (2015), Zika (2016), Coronavirus Disease 2019 (COVID-19) (2020), and mpox (formerly monkeypox) (2022).[8]

In certain situations, even when there is a relevant declaration under section 564 of the FD&C Act and FDA has issued EUAs for certain tests, FDA may find it appropriate to also issue an enforcement policy regarding the distribution and use of certain unapproved tests for which EUAs have not been issued to help further expand access to such tests as quickly as possible. During the recent COVID-19[9] and mpox[10] responses, FDA issued guidance with enforcement policies for certain tests to help facilitate availability and quickly increase national testing capacity. Those enforcement policies helped to supplement the availability of tests when, even with access to EUA-authorized or FDA-cleared tests, there were still insufficient tests to meet demand during the emergencies.

In May 2022, following a request by Congress to review FDA's oversight of tests for COVID-19, the U.S. Government Accountability Office (GAO) published a report to Congress titled "FDA Took Steps to Help Make Tests Available; Policy for Future Public Health Emergencies Needed."[11] In this report, GAO recommended "that FDA develop a policy for the use of enforcement discretion regarding unauthorized tests in future public health emergencies. This policy should include the conditions under which FDA would begin and end the use of such discretion."[12]

This draft guidance describes the factors FDA intends to consider in determining whether to issue an enforcement policy regarding use of unapproved tests during a declared emergency.[13]

III. Factors to Consider in Deciding Whether to Issue an Enforcement Policy for Unapproved Tests

[8] The year in each parentheses represents when the first emergency declaration under section 564 of the FD&C Act was issued for each outbreak justifying the emergency use authorization of unapproved tests. For some of the declared emergencies there have been subsequent declarations issued under section 564 of the FD&C Act for emergency use authorization of unapproved tests as the emergency evolved.

[9] See "Policy for Coronavirus Disease-2019 Tests (Revised)," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised

[10] See "Policy for Monkeypox Tests to Address the Public Health Emergency," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-monkeypox-tests-address-public-health-emergency

[11] Available at https://www.gao.gov/products/gao-22-104266

[12] See footnote 11.

[13] We note that this draft guidance relates to the time period after the exposure or outbreak results in an applicable section 564 declaration. FDA has issued another draft guidance that describes an enforcement policy for certain laboratory manufacturers offering certain unauthorized in vitro diagnostic devices (IVDs) for immediate response to CBRN agents in the absence of a declaration applicable to IVDs under section 564 of the FD&C Act. See FDA draft guidance document "Enforcement Policy for Certain In Vitro Diagnostic Devices for Immediate Public Health Response in the Absence of a Declaration under Section 564" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-certain-in-vitro-diagnostic-devices-immediate-public-health-response-absence

FDA may decide it is appropriate to issue an enforcement policy (or policies) indicating its intent not to object to the limited offering of certain unapproved tests for the diagnosis of a specific disease or other condition under certain circumstances, such as to help quickly increase test availability, during a declared emergency under section 564 of the FD&C Act. FDA intends to outline any such policy in guidance that identifies, among other things, the intended scope of the enforcement policy regarding certain legal requirements (e.g., premarket review, quality system), the rationale for the policy, FDA's general performance expectations for tests offered as described in the policy, and the intended duration of the policy. FDA may also identify any applicable legal requirements that are outside the scope of the enforcement policy (e.g., complying with applicable medical device reporting (MDR) requirements under 21 CFR Part 803) and clarify that the enforcement policies would not apply to tests falling outside the scope of the guidance.

In determining whether to issue an enforcement policy for certain unapproved tests, FDA intends to assess, among other things: (1) the need for accelerated availability of such tests, (2) the known or potential risks of such tests, (3) the availability of appropriate alternative tests that are authorized or approved, and (4) the availability of sufficient mitigations to address risks of false results, as discussed more fully below:

- **Need:** FDA intends to look at the testing needs of the emergency response. This may include consideration of the number of, and access to, FDA-approved/authorized tests available and how time sensitive the need for a test is (i.e., if there is sufficient time to wait for a test to be cleared, approved, or authorized for emergency use). In considering the time sensitivity of the need, factors such as the transmission levels, potential for asymptomatic infections, the size of the population potentially exposed, and morbidity and mortality rates may be considered. FDA also may consider the volume of tests needed to address the testing needs, considering the patient population(s) in need of testing, including estimates based on appropriate modeling for transmission or exposure, and whether the ability to scale up production to account for the needed test capacity should be accounted for in an enforcement policy. In determining need, FDA also intends to examine the type of test best suited to assist in the response. This may include highly accurate or high-throughput molecular diagnostic tests that can rule out infection, antigen diagnostic tests that may be less accurate but more accessible and less costly, or in rare cases, serology tests that can detect recent infection. Different types of tests may be helpful to the response depending on the type of emergency. For example, while molecular diagnostic tests may be appropriate for detection of a virus, different types of specialized tests may be needed for a radiological exposure. Further, while serological tests may not always be useful during an initial outbreak, during the Zika outbreak, serology tests were important for understanding whether a pregnant person had a recent infection. Evaluation of need may also include consideration of the turnaround time for results with authorized tests. For example, in the early stages of the COVID-19 pandemic, FDA issued an enforcement policy to help increase testing options when FDA became aware that a backlog of specimens was contributing to test results taking many days to be processed. Later in the COVID-19 pandemic, FDA narrowed the enforcement policy to focus only on specific types of tests for which increased access was still needed.

- **Risk:** FDA intends to consider the risks to public health when unauthorized, and potentially inaccurate, tests are used. This includes consideration of the seriousness of the life-threatening disease or condition, the complexity of the technology of the test, and the experience of test manufacturers, among other things. For example, certain tests for radiological exposure are very complex and require a high level of training. FDA considered these factors for COVID-19 and mpox, and the different public health risks led to different enforcement policies. FDA also intends to consider other risks as appropriate, such as risks associated with sample collection or certain test components.

- **Alternatives**: FDA intends to look at whether there are appropriate alternatives to diagnose the disease or condition. In considering the adequacy of alternatives, FDA intends to look at the manufacturing capacity of any alternatives and ability for the alternative(s) to meet the testing need. For example, when considering whether to issue an enforcement policy for COVID-19 tests at the beginning of the emergency, FDA considered that there was only one test authorized for emergency use, and supply was limited. When considering whether to issue an enforcement policy for mpox tests, FDA considered that there was an FDA-cleared diagnostic test for the detection of non-variola Orthopoxvirus DNA that was able to detect mpox,[14] but the cleared test was limited to use by certain laboratories and the turnaround times for results were up to a few days.

- **Mitigations:** FDA intends to consider the availability of other factors that may mitigate the risk of false results from unapproved tests. False results not only negatively impact the individual patient relying on a test but can also have an impact on broad public health decisions during an emergency. FDA intends to consider such factors as manufacturer experience (e.g., manufacturers who have successfully been issued an EUA for a test during a public health emergency, received approval or clearance for a diagnostic test, or have similar experience and are manufacturers for whom FDA does not have current compliance concerns), participation in a government evaluation program such as the National Institutes of Health (NIH) Rapid Acceleration of Diagnostics (RADx) Tech program's Independent Test Assessment Program (ITAP),[15] certain validation recommendations, certain labeling statements, availability of confirmatory testing, public disclosure by manufacturers that the tests have not been reviewed by FDA, and submission of an EUA request within a reasonable period of time, among others. FDA intends to provide any relevant recommendations for test validation specific to a particular emergency or potential emergency in the guidance document for a specific enforcement policy, as appropriate.

When issuing an enforcement policy, FDA generally intends to describe the circumstances in which the agency intends to exercise enforcement discretion, including, for example, when the

[14] The CDC non-variola Orthopoxvirus test was first cleared in 2018. In 2022, the FDA cleared additional 510(k)s from CDC, which expanded testing capacity through use of additional components and in additional laboratories. At the time of issuance of the enforcement policy for mpox, the latest cleared 510(k) was K222558, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K222558

[15] For more information on ITAP, see https://www.nibib.nih.gov/covid-19/radx-tech-program/ITAP

test has been validated. Any such policy may include recommendations for validation procedures and labeling, among other considerations. FDA's COVID-19 and mpox test guidances both described validation procedures and labeling for tests offered as described in those guidances.

In any such enforcement policy, FDA may identify an initial period in which the enforcement policy is intended to be in effect. FDA may adjust, including shortening or lengthening this period, as appropriate.

Consistent with 21 CFR 10.115(k), FDA will periodically review any issued enforcement policy guidance to determine whether it needs to be changed or withdrawn. For example, during the COVID-19 declared emergency, FDA issued six updates to the "Policy for Coronavirus Disease-2019 Tests (Revised)" guidance to reflect the changes in the country's needs and test landscape.

Regardless of an enforcement policy, FDA retains discretion to pursue enforcement action against the offering of unapproved tests with respect to violations of the FD&C Act, Public Health Service (PHS Act), or FDA regulations, and FDA intends to pursue such actions in individual cases when appropriate for public health.