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

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Guidance for Industry and Food and Drug Administration Staff

Document issued on September 23, 2025.

The draft of this document was issued on May 6, 2024.

For questions about this document, contact CDRH at CDRH-OIR-Policy@fda.hhs.gov.



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

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Preface

Public Comment

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

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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[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 for certain devices (or other medical products) 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 guidance that describes the factors FDA plans to assess in deciding when to issue an enforcement policy regarding in vitro diagnostic test manufacturers'[2]

[1] This 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).

offering of certain devices,[3] specifically unapproved in vitro diagnostic tests[4] and unapproved uses of approved in vitro diagnostic tests,[5] for the diagnosis of disease or other conditions during a declared emergency (collectively referred to hereafter as "unapproved in vitro diagnostic tests") and when to end such an enforcement policy.

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 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. In vitro diagnostic 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 in vitro diagnostic 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 relevant declaration of emergency or threat justifying authorization of emergency use, to diagnose, treat, or prevent diseases or conditions caused by

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[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
>
> 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 in vitro diagnostic test" 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. See "unapproved product" in section 564(a)(2)(A) of the FD&C Act. 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.

[5] Consistent with section 564 of the FD&C Act and other FDA authorities, "unapproved use of an approved in vitro diagnostic 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.

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."

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 in vitro diagnostic tests, FDA may find it appropriate to also issue an enforcement policy regarding the distribution and use of certain unapproved in vitro diagnostic tests for which EUAs have not been issued to help further expand access to such in vitro diagnostic tests as quickly as possible. During the COVID-19[6] and mpox[7] responses, FDA issued guidance with enforcement policies for certain in vitro diagnostic tests to help facilitate availability and quickly increase national testing capacity. Those enforcement policies helped to supplement the availability of in vitro diagnostic tests when, even with access to EUA-authorized or FDA-approved in vitro diagnostic tests, there were still insufficient tests to meet demand during the emergencies. These guidance documents also discussed the FDA's intended review priorities for EUA requests to address public health needs.

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."[8] 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."[9] In determining when to begin and end any enforcement discretion policy, FDA will consider the public health needs and the benefits and risks of such a policy to address those needs. As part of this consideration, and as discussed further in the next section of this guidance, FDA believes the factors in this guidance will help to ensure that appropriate tests are included in such a policy and that a timeframe is determined that is appropriate for the circumstances of the particular public health emergency. This will allow FDA to end any such policy at a time when the benefits no longer outweigh the risks, such as when emergency use authorized tests are sufficiently available.

This guidance describes the factors FDA intends to consider in determining when to begin and end an enforcement policy regarding unapproved in vitro diagnostic tests for which EUAs have not been issued during a declared emergency.[10]

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[6] See "Policy for Coronavirus Disease-2019 Tests (Revised)."
[7] See "Policy for Monkeypox Tests to Address the Public Health Emergency."
[8] Available at https://www.gao.gov/products/gao-22-104266
[9] See footnote 8.
[10] We note that this guidance relates to the time period after the exposure or outbreak results in an applicable section 564 declaration.

III. Factors to Consider in Deciding When to Begin and End an Enforcement Policy for Unapproved In Vitro Diagnostic Tests

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 and unauthorized in vitro diagnostic 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 in vitro diagnostic 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 when to begin and end an enforcement policy for certain unapproved in vitro diagnostic tests for which EUAs have not been issued, FDA intends to assess, among other things: (1) the need for accelerated availability of such in vitro diagnostic tests, (2) the known or potential benefits and risks when such in vitro diagnostic tests are used, (3) the availability of appropriate alternative in vitro diagnostic tests that are authorized or approved, and (4) the availability of sufficient mitigations to address risks of false results, as discussed more fully below:

- **Public Health Need**: FDA intends to look at the testing needs in the context of the emergency response. This may include consideration of the number of, and access to, FDA-approved/authorized in vitro diagnostic tests available and how time sensitive the need for a test is (i.e., if there is sufficient time to wait for an in vitro diagnostic test to be cleared, granted, 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 in vitro diagnostic tests needed to address the testing needs, considering the patient population(s) in need of in vitro diagnostic testing, including estimates based on appropriate modeling for transmission or exposure, and whether the ability to scale up production to account for the needed in vitro diagnostic test capacity should be accounted for in an enforcement policy. In determining need, FDA also intends to examine the type of in vitro diagnostic 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 in vitro diagnostic 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 in vitro diagnostic 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 approved or authorized in vitro diagnostic tests. For example, in the early stages of the COVID-19 pandemic, FDA issued an enforcement policy to help increase in vitro diagnostic 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 in vitro diagnostic tests for which increased access was still appropriate.

- **Benefits and Risks**: FDA intends to consider the potential benefits and risks to public health when unapproved/unauthorized in vitro diagnostic tests are used. Consideration of potential benefits to public health include, among others, timely clinical management of patients and infection control. Consideration of potential risks to public health include the seriousness of the life-threatening disease or condition, the complexity of the technology of the in vitro diagnostic test, and the impact of a false result on patient care and spread of infection, among other things. FDA considered these factors for COVID-19 and mpox, and the different public health benefits and risks (along with different needs), among other things, led to different enforcement policies. FDA also intends to consider other benefits and risks as appropriate, such as benefits of rapid access, risks associated with sample collection, or risks presented by certain in vitro diagnostic test components. FDA may also consider the experience of in vitro diagnostic test manufacturers and users with the specific type of test needed.

  FDA intends to reconsider the potential benefits weighed against the potential risks of unapproved in vitro diagnostic tests at each stage of the declared emergency based on the available information.

In balancing the benefits and risks of the use of unapproved/unauthorized in vitro diagnostic tests in light of the particular public health needs, FDA also intends to consider the following factors:

- **Alternatives**: FDA intends to assess the extent to which appropriate alternative approved or authorized in vitro diagnostic tests to diagnose the disease or condition may be available. In considering the adequacy of such alternatives, FDA intends to look at the manufacturing capacity of any alternatives and ability for the alternative(s) to meet the in vitro diagnostic 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 in vitro diagnostic test authorized for emergency use, and supply was limited. When considering whether to issue an enforcement policy for mpox in vitro diagnostic tests, FDA considered that there was an FDA-cleared in vitro diagnostic test for the detection of non-variola Orthopoxvirus DNA that was able to

detect mpox,[11] but the cleared in vitro diagnostic 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 factors that may mitigate the risk of false results from unapproved/unauthorized in vitro diagnostic tests. False results not only negatively impact the individual patient relying on an in vitro diagnostic 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 an in vitro diagnostic test during a public health emergency, received approval, grant, or clearance for an in vitro diagnostic test, or have similar experience and are manufacturers for whom FDA does not have current compliance concerns), manufacturer 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),[12] 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 in vitro diagnostic test validation specific to a particular emergency or potential emergency in the guidance document for a specific enforcement policy, as appropriate.[13]

To summarize, while each public health emergency has unique factors that influence FDA's policy decisions, the general concepts discussed in this section describe how FDA considers the various factors in evaluating the benefits and risks relevant to initiating and ending an enforcement policy. FDA intends to begin any enforcement policy regarding the use of unapproved/unauthorized tests when it believes the potential benefits of such policy outweigh the potential risks, taking into consideration, for example, the critical and urgent need to test large portions of the population, available authorized tests, and likelihood of correct results based on the technology and experience of manufacturers. FDA will reconsider the public health needs and benefits/risks balance periodically during the declared emergency and adjust its enforcement policy as appropriate. FDA further intends to end any such enforcement policy when, for example, testing needs have declined and/or additional tests have been approved/authorized, such that testing needs can be met by available approved/authorized tests.

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 in vitro diagnostic test has been validated. Any such policy may include recommendations for

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[11] 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 testing 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

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

[13] In January 2025, FDA issued a draft guidance entitled "Validation of Certain In Vitro Diagnostic Devices for Emerging Pathogens During a Section 564 Declared Emergency." (When final, the guidance will represent FDA's current thinking on this topic.) Some of the concepts and information regarding diagnostic test validation described in the guidance, once finalized, may be applicable to in vitro diagnostic tests described in an enforcement policy during a relevant section 564 declaration.

validation procedures and labeling, among other considerations. FDA's COVID-19 and mpox test guidances both described recommended validation procedures and labeling for in vitro diagnostic 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. In accordance with FDA's Good Guidance Practices, FDA may adjust, including shortening or lengthening this period, as appropriate.

Additionally, as discussed in FDA's guidance "Emergency Use Authorization of Medical Products and Related Authorities," FDA intends to establish priorities for its review of requests to issue an EUA based on a variety of factors. FDA also described certain prioritization policies in COVID-19 and mpox guidances, as noted above. Similarly here, FDA has assessed the need for prioritization policies and intends to include such policies, as appropriate, when issuing a future enforcement policy to help expand availability of certain in vitro diagnostic tests during a declared emergency.

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 in vitro diagnostic test landscape.

Regardless of an enforcement policy, FDA retains discretion to pursue enforcement action against the offering of unapproved in vitro diagnostic 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.