# Frequently Asked Questions About Monkeypox Virus Test Regulations

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## 1. The current non-variola orthopoxvirus test for detecting the presence of monkeypox virus has FDA 510K clearance. What does this mean?

The 510(k) clearance process allows a medical device manufacturer—in this case, the US Centers for Disease Control and Prevention (CDC)—to obtain approval from the US Food and Drug Administration (FDA) to use a test. It should be noted that, legally, a 510(k) device clearance is not a true "approval," it simply gives the manufacturer permission to use its test based on comparison to a "predicate" test—a previously approved test designed, validated and manufactured under very similar conditions. The applicant for 510K clearance must demonstrate that the new device (or test) is "substantially equivalent" to one that has already been granted FDA approval and has been on the market or used in the field. The 510K clearance process does not require companies to provide safety or effectiveness data from clinical trials, though the FDA still evaluates the device's safety and effectiveness by comparing it to other devices.[1,2] The 510K process is substantially faster and less expensive than the alternate, pre-market approval (PMA) or de novo classification processes that are available to manufacturers.

## 2. Some manufacturers have developed monkeypox tests labelled as "RUO." Is it appropriate to use these tests for diagnosis of monkeypox virus infection and for the laboratory to report these results to the patient?

RUO means research use only. Similarly, some tests are called IUO, meaning investigational use only. To clarify these terms and how to use RUO or IUO labeled devices, the FDA issued guidance in 2013[3] that stated:

- The term RUO refers to devices (in this case, tests) that are in the laboratory phase of development by the manufacturer.
- The term IUO refers to devices (tests) that are in the product testing phase of development by the manufacturer.
- The RUO and IUO labeling is meant to serve as a warning to users, to prevent such products from being used in clinical diagnosis or patient management. These tests should therefore not be used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. In the case of monkeypox virus, the result of a RUO or IUO test would have to be confirmed with the FDA 510K-cleared non-variola orthopoxvirus test.

## 3. Can a monkeypox virus test be developed and validated by a laboratory and used for patient testing without going through the FDA approval or clearance process?

Yes, if a laboratory develops and validates a test for its own use, it would be called a laboratory developed test (LDT), in-house developed test, or "home brew" test. An LDT is a type of *in vitro* diagnostic test that is designed, manufactured and used within a single laboratory. When a laboratory develops a test system in-house without receiving FDA clearance or approval, the Clinical Laboratory Improvement Amendments (CLIA) prohibit the release of any test results prior to the laboratory verifying the test's analytical validity by establishing certain defined performance characteristics for when that test system is used in the laboratory's own environment. Furthermore, the laboratory's analytical validation of LDTs is reviewed during its routine biennial survey—after the laboratory has already started testing.[4]

## 4. Why can't the FDA use the EUA process for monkeypox virus tests?

The Emergency Use and Authorization (EUA) process is enabled under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), when the Secretary of the US Department of Health and Human Services declares that a public health emergency exists in the US. The purpose of the EUA is to help strengthen the nation's public health protections against chemical, biological, radiological and nuclear threats. The EUA process was authorized for both the Zika outbreak (2016) and the current coronavirus pandemic (2020) but not, at this time, for the monkeypox virus outbreak as it has not yet been declared a national public health emergency.

## 5. Do both CMS and FDA regulate laboratory testing?

Yes, the US Center for Medicare and Medicaid Services (CMS) and the FDA regulate the quality of laboratory testing in different ways. CMS, through the CLIA program, regulates laboratories that perform testing onhuman specimens to ensure accurate and reliable test results. The FDA regulates manufacturers and devices under the FD&C Act to ensure that devices—including those intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease or other conditions—are reasonably safe and effective. Thus, the two agencies' regulatory schemes are different in focus, scope and purpose, but they are intended to be complementary.

## References


1. Levin, Papantonio Rafferty Law. The FDA's 510(k) Clearance Process. Website accessed August 2, 2022: https://www.levinlaw.com/fda-510k
2. Le, K (2021) FDA Clearance vs. FDA Approval Process for Medical Devices. Website accessed August 2, 2022: https://www.goodrx.com/healthcare-access/medication-education/fda-approval-vs-fda-clearance
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4. CMS (2013). LDT and CLIA Frequently Asked Questions. Accessed from: https://www.cms.gov/regulations-and-guidance/legislation/clia/downloads/ldt-and-clia_faqs.pdf