

The Federal Food, Drug, and Cosmetic Act (FD&C Act) grants FDA authority to regulate medical devices. A medical device is defined to include an "article" that is "intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease."

Test Kits

FDA regulates devices used in laboratory analysis of human specimens for diagnosis, treatment, or prevention of disease as "in vitro diagnostic devices" or IVDs. IVDs are defined as "reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae."

Currently, FDA regulates genetic tests as IVDs, also called "test kits," if the components of the test are bundled together, labeled for a particular use, and sold to a laboratory as a unit. Such kits must undergo successful premarket review before they may be commercially distributed. In order to receive FDA authorization to sell the kits, companies must submit information to FDA demonstrating that the test is safe and effective.

FDA has, to date, reviewed about a dozen genetic test kits. These include tests for mutations causing the blood clotting disorders Factor II and factor V Leiden, some of the mutations that cause cystic fibrosis, two genes within the cytochrome P450 family of enzymes, which are involved in drug metabolism, and variants in the UGT1A1 gene, which is also involved in metabolism of certain drugs,

FDA's review of test kits, like other products the agency regulates, is limited to the manufacturer's "intended use," as evidenced by the claims the manufacturer makes about the product in labeling. A manufacturer may not promote a test kit for an "off-label" use, i.e., one not approved by FDA. However, FDA does not regulate claims made by laboratories using FDA-regulated test kits that go beyond the approved labeling.

ASRs

Certain components of genetic tests performed by laboratories that are not sold as kits also are regulated by FDA. These components, known as "analytic specific reagents" or ASRs, serve as the "active ingredient" of laboratory-developed tests (LDTs). ASRs can be manufactured for sale or made in-house by the laboratory. FDA's oversight of ASRs is fairly narrow; ASRs may be sold only to laboratories certified to perform high complexity tests and must be labeled in accordance with FDA requirements. FDA regulations state that LDTs that are developed using commercially distributed ASRs must be ordered by a health professional or "other persons authorized by state law," but the agency does not appear to have ever enforced this provision. Additionally, the regulation does not distinguish between a patient's personal physician and a physician-employee of a testing laboratory. Nor does FDA regulate the claims that laboratories make about the tests developed using ASRs.

In September 2006 FDA issued a draft guidance document clarifying the scope of the agency's ASR regulations. The guidance states that multiple reagents bundled together, or reagents that are sold with specific indications for use, cannot be sold as ASRs. FDA finalized this guidance document in September 2007.

Laboratory-Developed Genetic Tests

Genetic tests for more than 1200 conditions clinically are available today; most are not available as test kits but only as LDTs. Laboratories develop these tests in-house using purchased individual components - such as ASRs - and/or individual components they make themselves. With one exception, described below, FDA exercises "enforcement discretion" with respect to LDTs, which are therefore not subject to any prior review to assess their clinical validity. Instead, individual laboratory directors make determinations regarding the their laboratories' ability to perform specific tests, and whether the tests yields clinically relevant information. Genetic testing laboratories must comply with the Clinical Laboratory Improvement Amendments (CLIA), but this law focuses on the laboratory's operations and does not assess whether the tests performed by the laboratory provide clinically relevant information. Additionally, in contrast to other types of laboratories performing medical tests, CLIA does not require genetic testing laboratories to enroll in programs designed to assess their analytic validity (meaning whether the laboratory can get the correct answer when performing the test).

In September 2006 FDA released a draft guidance document addressing a subset of LDTs that the agency termed in vitro diagnostic multivariate index assays (IVDMIAAs). These tests use laboratory data and an algorithm (analytical tool) to generate a result for the purpose of diagnosing, treating, or preventing disease. Examples of IVDMIA tests include those used to diagnose and guide treatment decisions for breast cancer, prostate cancer recurrence, cardiovascular disease, and Alzheimer disease. The draft guidance stated that FDA considered IVDMIAAs to be medical devices and that FDA would require them to undergo premarket review before being marketed. FDA issued a revised draft guidance document in July 2007.

Current Oversight Gaps and Consequences

For most genetic tests, there is no government agency currently assessing whether genetic tests provide clinically relevant information to physicians and patients. Those few manufacturers who do choose to devote the resources necessary to obtain FDA approval for a test kit face competition from clinical laboratories that can develop and perform the tests on their own with no FDA scrutiny. Recent years have seen the rise of genetic testing companies making dubious claims about genetic tests and selling their tests directly to consumers. The current regulatory system is both inequitable and inadequate to protect the public's health.

*Compiled by Audrey Huang
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