VIEWPOINT

Genetic Testing and FDA Regulation
Overregulation Threatens the Emergence of Genomic Medicine

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Counter Viewpoint

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Should the FDA regulate laboratory-developed diagnostic tests? —No.

In November 2014, the US Food and Drug Administration (FDA) revealed its intent to regulate thousands of medical diagnostic tests being performed in as many as 11 000 clinical laboratories throughout the United States, focusing especially on genomic medicine.[1] Although the FDA is well intentioned, the current plan for regulation is unnecessary and, if carried out, could result in the closure of many laboratories, undermine innovation, and potentially limit patient choice. Moreover, the proposed regulation, if unchanged, is likely to lead to thousands of laboratory submissions to the FDA, for which its own staffing capacity is tenuous at best. If implemented, the requirements may have the unintended effect of derailing the long-awaited emergence of genomic medicine.

The last several years have seen substantial expansion in genetic testing, resulting from advances in technology that allow rapid and accurate sequencing of large fractions of an individual's DNA. Such analyses have begun to inform patient care in spheres ranging from carrier screening and the diagnosis of birth defects to individualized diagnosis and treatment of cancer.[2,3] These developments have occurred in the span of just a few years, in large part because of the nimbleness of relatively small clinical and academic laboratories that can quickly respond to new medical findings and patient needs by rapidly and safely developing and improving laboratory-developed tests. The resulting landscape is one of vibrant competition in which laboratories that offer genetic testing now compete on the basis of quality, service, innovation, and cost.

The FDA now proposes to regulate laboratory-developed tests as "medical devices," mandating that laboratories be treated as manufacturers that must meet formal FDA manufacturer requirements for each test developed—a costly and time-consuming process. However, this approach has little valid or even apparent justification. The FDA has failed to cite more than a few anecdotal examples of patient harm to justify its proposed actions. During a congressional hearing on the draft regulation,[4] the director of the FDA's Center for Devices and Radiological Health cited insufficient evidentiary support in the case of a test designed to assess heart disease risk and another test targeting ovarian cancer detection. He also cited a case involving overt falsification of data in a test claimed to guide breast cancer treatment. The FDA's inability to document any consistent or systematic harm is highlighted by the center director's own statement during that hearing in which he said, "Absence of evidence doesn't mean there is an absence of a problem."[4]

Implementing sweeping regulation of a system that is likely producing considerable benefit, based only on a curious presumption of harm and isolated anecdote, could be damaging. It is unrealistic to imagine that any degree of regulation will foreclose all possible harm, especially when faced with overt fraud and falsification. Rather, when formulating regulatory policy it is important to consider current benefits as well as evidence of harm, exercising caution lest net harm be caused through unwarranted regulation.

If serious quality or reliability problems existed in the realm of genetic testing, increased scrutiny by the appropriate government agencies would be appropriate. However, clinical laboratories that perform laboratory-developed tests already must meet multiple and rigorous demands by federal and state agencies that include professional organizations such as the College of American Pathologists or the Joint Commission. In amending the Federal Clinical Laboratory Improvement Act (CLIA) in 1988, the intent of Congress was to provide for the regulation of clinical laboratory testing under a single comprehensive statutory framework. Although it is reasonable to contemplate further accreditation requirements for genetic laboratories, such as expansion of oversight standards in CLIA to more robustly address genomic testing, the proposed regulation by the FDA is incompatible with CLIA and not what Congress likely envisioned with that legislation.

The proposed actions of the FDA could have important negative consequences. As the American Medical Association has stated in its formal comment on the FDA's plans,[5] "The FDA proposal adds an additional layer of regulatory requirements which may result in patients losing access to timely life-saving diagnostic services and hinder advancements in the practice of medicine." Academic laboratories, from which much of the innovation in genetic testing derives, have insufficient resources to meet the proposed requirements of the FDA and would essentially be precluded from developing (or even improving) tests in response to patient needs, clinician demands, and changing technology. All that remain may be a few very large laboratories and commercial manufacturers who have the resources necessary to meet the new FDA requirements on each test they perform and pay the inevitable user fees associated with FDA oversight. Such a situation would be particularly difficult for

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patients with rare genetic diseases, for whom laboratory-developed tests are the only testing option because of insufficient financial incentives to sustain a commercial market.

In this current debate, small laboratories, academics, and professional organizations are arguing against increased, restrictive regulation, whereas large commercial entities that generally oppose regulation are in favor of the FDA's action because it is likely to be financially beneficial for them. However, monopolies and limited choice are rarely good for the public. For example, it is both instructive and unsettling to examine the state of genetic testing for breast cancer susceptibility before and after the Supreme Court largely invalidated Myriad Genetics' patents on the *BRCA1* and *BRCA2* genes last year.[6] Prior to that decision, only a single laboratory was permitted to offer sequencing of those clinically important genes, leading to a situation in which improvements in testing were stifled, women and their physicians had no options to obtain independent second opinions, and patient access to testing was limited.[7] Immediately following elimination of this monopoly, numerous laboratories began offering testing. The ensuing year has been beneficial for patients, with multiple laboratories now offering expanded, high-quality, and less costly testing for breast cancer susceptibility. Should the FDA's current intent regarding regulation be realized, monopolies in laboratory medicine may reappear, affecting not just genetic testing but diagnostic testing more broadly.

Another serious issue involves whether the FDA has the required statutory authority to regulate laboratory-developed tests.[8] These tests are not "articles" manufactured in large quantities to meet specific manufacturing and labeling standards and thus subject to regulation under the Medical Device Amendments to the Federal Food and Drug Act. Rather, they are procedures—procedures for performing diagnostic tests that will vary with the expertise of the laboratory developing them and the clinical needs of patients. The individual nature of laboratory-developed tests requires flexible regulation, not the costly, burdensome, and uncompromising standards the FDA applies to commercial device manufacturers. Given the questionable legitimacy of the FDA's proposed action, if these changes are implemented they will most certainly trigger expensive and time-consuming legal challenges.[9]

Too much regulation can be as harmful as too little. A nuanced middle ground must be found that protects the public and allows for innovation. Patients and the public are just beginning to benefit from the long-awaited genomic revolution in medicine. Overly zealous regulation should not impede progress by those who are best prepared to develop the next generation of genetic tests and deliver on the promise of genomic medicine.

ARTICLE INFORMATION

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