With recent activity by both the US Food and Drug Administration (FDA) and the US Government Accountability Office (GAO), a new era of government-regulated genetic testing is upon us. In the past 10 years, the scope and volume of genetic tests [most falling into the category of laboratory-developed tests (LDTs)] being offered has increased dramatically. Traditionally, genetic tests have been for single-gene disorders, such as cystic fibrosis and Marfan syndrome. In recent years, the scope and complexity of genetic testing has increased, and there has been a shift in emphasis toward predicting disease, especially complex disease. This shift has been mainly due to the arrival of direct-to-consumer (DTC) testing to the genetic-testing market.

DTC genetic tests, which have not been under the review of the FDA, are traditionally offered via the Internet and are performed in the manufacturers’ accredited laboratories as LDTs. The FDA’s first public foray into oversight of DTC genetic testing was in May 2010, after Pathway Genomics, a DTC-genetic-testing company based in San Diego, announced the upcoming availability of their personal genetic-testing kits at Walgreens drugstores nationwide. After Pathway’s announcement, the FDA promptly sent an enforcement letter to Pathway, in which they declared Pathway’s testing kit a medical device, and asked them to respond within 15 days to explain why their test should not require premarket review (1). The FDA followed suit by sending similar letters to 19 additional genetic-testing companies in the following months. In July, the FDA held its 2-day “Public Meeting on Oversight of Laboratory Developed Tests,” at which many genetic-testing companies and genetics organizations participated (2). During this meeting, FDA representatives stated that CLIA oversight of laboratories was no longer sufficient to protect the public. Although the FDA stated that it would invoke its right to oversee LDTs, how this would be done and when it would happen were not specified.

In addition to the FDA’s activities, the US Congress held a public hearing in July 2010, “Direct-to-Consumer Genetic Testing and the Consequences to Public Health” (3). A focus of this hearing was the GAO report, “Direct-To-Consumer Genetic Tests: Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices” (4). This report was a product of a yearlong investigation by the GAO into the scientific validity, safety, and utility of DTC genetic tests.

The GAO report, combined with the recent activity by the FDA, has left a state of uncertainty in and has resulted in variable action by the genetic-testing industry. Several DTC genetic-testing companies have been openly critical about tactics used by the GAO and the FDA. Most of the DTC companies have also expressed a willingness to work with the government to help with the regulatory processes. Some companies (including Pathway Genomics) have modified how their products are being offered in the DTC market; however, it is not only the DTC genetic-testing companies that the impending government regulations are affecting. Now, all genetic testing companies, including those that provide LDTs through healthcare professionals, are in a state of uncertainty regarding when and how the FDA regulatory overhaul will commence.

A recent issue of Nature highlighted 2 opinion pieces on the topic of FDA regulation of LDTs (5, 6). Both authors Beaudet and Javitt concede that some level of FDA regulation of genetic tests is necessary. Where and how this regulation is administered is where their opinions diverge. Beaudet argues that given the complex nature of genetic testing, both in terms of the evolving technologies and the complex biology, a highly detailed approach to FDA regulation would require an unnecessarily major expenditure of government time and money and could be detrimental to patient care by impeding the current state of genetic testing. He instead proposes that government regulation focus more on the integrity of analytical processes and data storage, and less on the results interpretation provided by board-certified healthcare professionals. The basis of the reasoning for the latter point is that

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1 Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN.

* Address correspondence to this author at: Department of Laboratory Medicine and Pathology, Mayo Clinic, 200 First St. S.W., Rochester, MN 55905. Fax 507-266-4176; e-mail baudhuin.linnea@mayo.edu.

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2 Nonstandard abbreviations: FDA, Food and Drug Administration; GAO, Government Accountability Office; LDT, laboratory-developed test; DTC, direct-to-consumer; SACGHS, Secretary’s Advisory Committee on Genetics, Health, and Society.
board-certified practitioners are specifically trained to optimally interpret the clinical utility of genetic results, whereas DTC genetic-test results are not mediated through a healthcare professional and thus require further scrutiny regarding their clinical utility and implications. Javitt takes a different approach and states that making a distinction between DTC genetic tests and those offered through healthcare professionals is likely to become complicated and misleading. She also points out that a federal shut down of DTC testing (a potential action that has been implied by FDA representatives) would be difficult to justify. She instead proposes a model whereby each test, regardless of who offers the test, is regulated according to its level of risk. She also states that oversight of the newer, more complex tests offered by both DTC and clinical laboratories is likely needed. Javitt suggests that a first step for regulators would be to enforce existing laws pertaining to false advertising.

The extent of validation data that require government review before offering a genetic test is an important concern. Beaudet questions the appropriateness of genetic tests needing to meet certain requirements for clinical sensitivity, specificity, and utility as proposed in the 2008 report by the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) (7). Genetic testing is becoming increasingly complex, both in terms of technology and results interpretation. Because of these and other factors, Beaudet suggests that providing to regulators the type of validation information proposed by SACGHS could bring genetic testing to a standstill. Javitt likewise agrees that resources would be wasted if the FDA required all laboratories to submit clinical validation data for all tests. She does, however, go on to say that proper validation should be proved for tests that use novel methods or have results that may have important impacts on therapeutic decisions and clinical care. Javitt concedes that the state of knowledge regarding the clinical importance of markers is increasing at a rapid pace, and this growth will create challenges for determining which tests/markers require increased scrutiny and at what level.

Overall, these 2 authors agree that some degree of governmental oversight of genetic testing is important and even essential. They also agree that regulating every aspect of genetic testing for all genetic tests would be wasteful, especially from the clinical validation standpoint. Whereas Beaudet more or less supports a distinction between genetic tests provided by DTC companies and healthcare professions, Javitt does not agree that an authentic line can be drawn. Javitt instead proposes that each test be individually determined to have a specific level of oversight, regardless of which type of genetic-testing company is performing the analysis.

Although a reasonable approach to government oversight of genetic testing will ensure that specific standards are met, especially in those areas with questionable clinical utility, it is not clear how a reasonable approach can or will be achieved. The complex nature of genetic testing is going to likewise lead to complexities in the management and delivery of its oversight. Nonetheless, government oversight of genetic testing is just around the corner. While the genetic-testing industry is in its current state of uncertainty, it can maintain hope that its past and future testimony at FDA-sponsored public meetings and elsewhere will be taken into consideration for the benefit of all.

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References