Pink or blue? The need for regulation is black and white

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A new direct-to-consumer genetic test purports to detect fetal gender as early as five weeks of pregnancy. The availability of this test highlights the consequences of the current system of oversight for genetic tests and underscores the need for an enhanced regulatory framework to ensure the accuracy, reliability, and validity of genetic tests. (Fertil Steril® 2006;86:13–5. ©2006 by American Society for Reproductive Medicine.)

Imagine that a new patient walks into your office for her first prenatal visit. Like most parents-to-be, she is excited about the pregnancy and tells you that she is certain she is having a boy. You ask how she knows, expecting to hear that her grandmother predicted it or that boys "run in the family." Instead, she tells you that she purchased a genetic test that claimed to predict the sex of a fetus "as early as 5 weeks of pregnancy," with "greater than 99.9 percent accuracy." You ask why she wanted to know, and she says she was curious and now she can begin painting the nursery blue.

Or perhaps the patient arrives more anxious. She tells you she knows she carries a genetic mutation for hemophilia, which causes disease only in a boy, and took the test to ease her mind, or, as it turned out, prepare herself for a potentially affected child. Perhaps she says that based on the test results she has been thinking about terminating the pregnancy.

You are skeptical about the validity of the test results, but your patient is convinced they are right. After all, she tells you, DNA doesn't lie, and the government wouldn't allow a company to sell a genetic test unless it worked, right?

Wrong. Recent media reports have disclosed that some women who purchased the Baby Gender Mentor test kit from an online vendor and submitted their blood samples to a Massachusetts-based commercial testing laboratory have gotten the wrong answer: The company said "it's a boy," and the baby was in fact a girl (or vice versa) (1, 2). Even more troubling, according to media reports in one case the company called a pregnant woman and informed her that her fetus had a genetic abnormality, although the product makes no claims regarding the test's ability to detect abnormalities and the woman had not consented to such testing (3).

Putting aside the profound ethical implications of unauthorized medical testing, does the test work? Maybe, maybe not. Experts are skeptical, and the company has not published any data, citing proprietary concerns (4). This alone should have set off warning bells among federal regulators. Sadly, it hasn't.

According to media reports, the company claims the Food and Drug Administration (FDA) does not regulate the product because it is not being used in "medical diagnosis" (5). The FDA has not publicly confirmed or denied this assertion. While clearly the FDA is not currently regulating it, the claim that it can not is puzzling and disturbing. The FDA has the legal authority to regulate medical devices used "in the diagnosis of disease or other conditions" (6). Tellingly, the word "condition" was added to the law so that FDA could regulate the accuracy of pregnancy tests, pregnancy being a medical condition but clearly not a disease. Because of that change in the law, FDA now regulates as medical devices a variety of pregnancy-related diagnostic products, including pregnancy tests and ovulation prediction kits. Although some may quibble whether gender is a "condition" rather than an immutable biologic characteristic, knowing the gender can yield information about fetal health—hemophilia, for example, affects males almost exclusively. Moreover, if the company indeed is reporting back information about chromosomal abnormalities, then an intended use of the product includes the diagnosis of medical disease in the fetus, a use that may lead to invasive medical testing by the mother.

Thus, a fetal gender test is quite plausibly a device within the definition of the FDA's governing statute. The problem from the FDA's perspective appears to lie elsewhere. Unlike pregnancy and ovulation tests that are sold as "kits," i.e.,

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free-standing products, the Baby Gender Mentor test, like the vast majority of genetic tests, is produced in-house by a laboratory. Although in past years the FDA has asserted that it has jurisdiction over so-called "home brew" tests, it currently appears disinclined to directly regulate laboratory-produced tests, leaving most genetic tests outside its review of safety and effectiveness.

Most clinical laboratories, however, are at least subject to basic minimum standards under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (7). This law requires the government to certify laboratories performing testing to provide "information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings." Because the company offering the Baby Gender Mentor test performs laboratory testing on maternal blood samples, it would also seem to fall under CLIA. However, the Centers for Medicare and Medicaid Services (CMS), which enforces CLIA, apparently has concluded that the company does not meet this definition and requires no certification. Interestingly, New York State, which is exempt from CLIA because it has a more rigorous program, has informed the company that it is unlawful to market the test in New York State, but it is unclear whether the company has made any changes in response.

At the very least, one would expect the Federal Trade Commission (FTC), which has an explicit statutory mandate to prevent advertising that is false or misleading (8), to step in. Indeed, the FTC has asserted its authority to take action against fraudulent genetic tests (9) and has announced it would undertake a joint effort with the Food and Drug Administration (FDA) and the National Institutes of Health to identify appropriate targets for legal action (10), but the agency has not taken any regulatory action with respect to fraudulent claims for genetic tests, even though customers have filed complaints with the agency about the Baby Gender Mentor test (11).

Despite the federal government's inaction, there are justifiable legal bases for government action to oversee the Baby Gender Mentor test. The failure to act is consistent with a more widespread and disturbing impasse regarding genetic testing oversight. Unfortunately, Baby Gender Mentor is not alone in the world of commercial actors hawking genetic tests directly to consumers. Another, for example, provides a "DNA, diet, and lifestyle assessment" that it claims can help consumers manage risks associated with heart health, bone health, and insulin resistance, among other conditions. Still others purport to tell consumers whether their genes explain their infertility or put them at increased risk for depression, cardiovascular disease, or Alzheimer's disease.

Beyond direct-to-consumer tests, genetic testing has become part of mainstream medicine: Tests for than 900 genetic diseases are clinically available (12). These tests have serious consequences, from what breast cancer treatment regimen to follow to what antidepressant will afford optimum safety and efficacy. Although the majority of these tests are currently mediated by a health care provider, any of them could, in theory, be offered directly to consumers in a manner similar to the Baby Gender Mentor test. State laws vary with respect to whether tests can be offered directly to consumers, and many states allow it (13). Moreover, even those tests that are currently physician mediated for the most part lack formal assurance from any of the traditional regulators that they are safe, accurate, or provide information useful to health-care decision making.

The lax oversight of genetic testing is not new, nor has it gone unnoticed. For more than ten years, federal government officials have been discussing the need for improved oversight of genetic testing. Ten years and two Secretary-level advisory committees later, not a single piece of legislation—and little regulation—has been promulgated (14).

As early as 1995, the National Institutes of Health and the Department of Energy together convened a government task force to review genetic testing in the United States and make recommendations to ensure the development of safe and effective genetic tests (15). The task force recommended, among other things, that genetic tests not become clinically available unless they had been demonstrated, through independent external review, to be clinically valid. In 2000, the Secretary's Advisory Committee on Genetic Testing (SACGT) issued a report in which it concluded that the current oversight of genetic tests was insufficient to ensure their safety, accuracy, and clinical validity (16).

Among its recommendations, the SACGT proposed that CMS develop a specialty area for genetic testing under CLIA, and that the FDA should review all new genetic tests. Neither of these recommendations has been implemented. In 2000, the government announced its intent to develop a specialty area under CLIA (17). Five years later, no proposal has been forthcoming. Political life dictates that government change often is motivated by human injury; both thalidomide and the Dalkon Shield impelled stronger FDA oversight of drugs and devices, and faulty interpretation of Pap smears led to increased government oversight of clinical laboratories. Although government advisory committees have been urging the government to strengthen genetic testing oversight for more than a decade, none of their myriad recommendations has resulted in regulatory change.

How many Baby Gender Mentors—and the associated anxiety, unwarranted medical procedures, and potential adverse consequences—will it take to provoke action on genetic testing? By fostering an environment in which bad actors can thrive and good ones are tarnished by association, and in which the public may lose trust in the "power of DNA" to improve their health, the status quo imperils the promise of genetic testing to bring about truly "personalized medicine."

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