FEDERAL REGULATION

Gene Tests Get Tested

If any company is the coal miners' canary of genomics, it is Myriad Genetics Inc. of Salt Lake City. Last fall, Myriad became one of the first companies to bring a genomics invention to market—a diagnostic called BRCAnalysis that spots mutations in the breast cancer susceptibility genes *BRCA1* and *BRCA2*. It looked like a sure winner: a test that would give women from families in which breast cancer is rife a chance to know whether they carry the genetic defect. But instead of reeling in the cash, Myriad has run into a series of obstacles—including concern about the need for federal regulation of the field—that suggest genetic testing may not lead to the quick commercial payoff some had predicted.

Myriad's apparent difficulties reflect uncertainties facing any company hoping to strike it rich in diagnostics. Many tests will involve genes like *BRCA1* and *BRCA2* which are associated with disease in certain families but whose function is poorly understood, so patients—and most physicians—will have trouble interpreting test results. Indeed, some professional groups, including the American College of Medical Genetics, have recommended that genetic tests be used only in research projects until their accuracy and validity are proved. For patients who test positive, these uncertainties may be compounded by fears of discrimination.

When Myriad launched a national campaign to market BRCAnalysis with a price tag of $2400 last October, it was putting these issues to the test for the first time. Many stockbrokers were upbeat. Matthew Murray of Lehman Brothers in New York commented in September that the breast cancer test would be "the most immediate pathway to cash flow from genomics. ... We believe that there will be strong demand for this test." Myriad appeared to be brimming with optimism, too: As it began marketing its test, the company unveiled plans to raise cash by selling $43 million in new stock.

On 25 November, however, Myriad pulled the stock offering off the market with a terse statement: "The company has decided to withdraw [the stock] ... because it believes that [market] conditions are not favorable to going forward at this time." Myriad has not released data on sales of BRCAnalysis, but company spokesperson William Hockett claims the turnabout on the stock was unrelated to any problems with the test; it was just a matter of waiting for a better time to sell stock.

But some investment experts believe that Myriad's decision also reflects the inherent problem of trying to move rapidly when so many issues are unresolved. For instance, Reijer Lenstra of the Smith Barney firm in New York says "There are concerns about what the test means and who should be getting it. ... This is not an easy thing to market; forget a quick launch."

If Lenstra is right, Myriad's experience adds urgency to a major goal of the biotech industry: clearing away a thicket of social and regulatory issues that may undermine confidence in genetic testing. Just how—or who—should deal with these issues is, however, a matter of some debate.

So far, the Food and Drug Administration (FDA) has indicated that it has authority only to regulate the safety and efficacy of tests that are sold as prepackaged "medical devices," such as test kits for HIV. In-house laboratory testing of the kind offered by Myriad and OncorMed of Gaithersburg, Maryland, doesn't fall within its purview.

MYRIAD GENETICS

Slow start. Myriad's $2400 diagnostic faces potential regulatory hurdles.

And as Patricia Murphy, vice president of OncorMed, made clear last July when she testified before the Senate Labor and Human Resources Committee, industry leaders are happy to keep FDA out of the picture. Instead, Murphy recommended that testing be monitored by the states and by the federal agency that upholds the Clinical Laboratory Improvement Act (CLIA)—the Health Care Financing Administration of the Department of Health and Human Services.

But some independent experts are not convinced that the CLIA system can do the job. Pediatrician N. Anthony Holtzman of Johns Hopkins University in Baltimore and geneticist Michael Watson of Washington University in St. Louis, who co-chair an independent government advisory group called the Task Force on Genetic Testing (TFGT), both point to the same weakness: CLIA checks only for lab quality; it does not address the important question of "validity"—whether a test result actually makes a valid prediction about what is likely to happen to the patient. Risk estimates derived from studies of large families with a high cancer incidence, for example, may not hold up in the general population. Watson argues that it would be best to restrict use of genetic tests until their validity is well established.

The TFGT, which reports to Francis Collins, director of the National Center for Human Genome Research, has drawn up draft guidelines including a suggestion that the federal government create a committee to monitor the quality and validity of genetic tests. The group's final report, due in February, is likely to have a lasting impact.

Even more important to the future of the genetic testing business is finding ways to ensure the privacy of people who test positive for a high-risk gene. Congress passed a law in 1996 that makes it illegal for companies to deny health-insurance coverage to workers just because they have medical risks—including genetic risks. But Collins says much broader protections are needed to ensure that people aren't discriminated against by employers and insurance companies.

Collins is not alone: Industry insiders say that genetic testing will remain under a cloud until protections are firmly in place. They point to preliminary data from cancer researchers at Georgetown University in Washington, D.C., and the University of Pennsylvania, Philadelphia, showing that fewer than half the women who were offered a *BRCA* test last year accepted it.

The biotech industry is now pushing for stronger privacy laws. In September, the board of directors of the Biotechnology Industry Organization (BIO), a Washington, D.C.–based lobby, adopted a statement saying that "Congress should enact a comprehensive bill" guarding the confidentiality of medical records. BIO argued that "privacy standards should be national in scope."

When the 104th Congress ended in 1996, nearly a dozen bills designed to prevent genetic discrimination were left on the agenda. Many of these proposals are now being reintroduced for what's shaping up to be a critical year for genomics companies and genetic testing.

–Eliot Marshall