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Home-brew tests need regulation

A US proposal to regulate medical diagnostics from individual labs reflects the tests' growing complexity. Such guidance should be welcomed, not resisted.

On 18 April, the US Centers for Disease Control and Prevention (CDC) published an alert. The agency had learned of a new test being used to diagnose Lyme disease, a tick-borne bacterial infection that can cause fatigue, joint pain and nervous-system problems. The test, like many others for the disease, had not been formally evaluated and approved by governmental regulators, and agency scientists worried that the method would churn out too many false positives. But because of a regulatory loophole, there was little the CDC could do except ask consumers to avoid the tests and urge people to seek out the few diagnostics that had been approved by the US Food and Drug Administration (FDA).

The problem extends well beyond Lyme disease. Thousands of other 'home-brew' medical tests — those developed in individual laboratories and used to guide the diagnosis and treatment of everything from cancer to *Candida* — have largely escaped federal oversight.

That is now likely to change. On 31 July, the FDA unveiled its plans to regulate the field. In doing so, the agency is risking the wrath of industry and academic labs alike, which have argued that regulation of home-brew tests will slow the development of diagnostics unnecessarily. Yet expanded oversight is warranted, and researchers would do well to learn from the FDA's example. As medical diagnostics become more elaborate and more important in health-care decisions, they need to be treated with more gravity.

In 1976, the US Congress declared that most diagnostic tests could be considered medical devices and therefore fell under the FDA's regulatory purview. But at the time, laboratory tests tended to be simple, familiar assays performed using components that had been approved for clinical use. Typically, physicians and pathologists — often at the same institution that carried out the test — interpreted the results. Given this relatively safe environment, the FDA exercised its discretion and declared that it would not regulate home-brew tests. (The FDA does, however, regulate commercial tests that are developed and then sold as kits to be used in other labs.)

A COMPLEX BREW

Today, the medical-diagnostics field is very different. Tests are used more frequently, and in higher-risk settings, to select therapies for critically ill patients. Although some familiar tests remain, home-brew tests are increasingly carried out using cutting-edge science and technologies, and yield results so complex that they require proprietary algorithms to parse the data. Genome-wide surveys of gene-expression patterns and genomic abnormalities, for example, have emerged as attractive ways to select treatments for people with cancer. But they present challenges for standardization across labs.

The business of laboratory testing has also changed, with many tests now provided by large companies that mass-market their products. The well-known test for cancer-associated mutations in the genes *BRCA1* and *BRCA2*, for example — provided by Myriad Genetics of Salt Lake City, Utah — is a home-brew assay because its results are not independently analysed outside the company. Although that test has a substantial body of research backing its veracity, many other tests do not. And whereas regulators inspect general techniques and equipment at some of these labs, they generally do not ascertain the validity of the particular tests the labs deploy.

The FDA announced its intentions to change this policy at least as early as 2010. Opposition was swift and fierce, and came from both industry and academia. The long delay in the release of the FDA's new policy prompted rumours of political interference. In July, five US senators wrote a letter to the Office of Management and Budget, which has to review proposed regulations, to question the delay in releasing the FDA's guidance.

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But in another letter sent last month, a host of academic testing labs decried efforts to regulate the field, saying that the tests should be considered services rather than devices. It is easy to understand some of their concerns. The FDA is famously overcommitted and under-resourced, and adding to its remit raises fears that the agency will be slow to issue approvals, becoming a roadblock to innovation just as the technologies are beginning to build up speed.

Fortunately, the plans unveiled by the FDA may sidestep such concerns. The regulations will be phased in gradually, to avoid abrupt interruptions of important medical services. And the agency intends to focus first on tests that bear the most risk for patients. Low-risk tests and those for rare diseases are likely to be excluded from regulation.

Properly executed, the proposals could bring welcome scientific rigour to a field that has become unruly. Some FDA staff say that they have struggled to combat the outdated sense of complacency with respect to medical tests — and not only in clinical pathology labs. Researchers, too, have had to be persuaded that diagnostics deserve heightened scrutiny. Too many scientists are still not aware that the agency needs to review trials involving medical tests — for example, clinical trials that select cancer therapies on the basis of mutations found in a participant's tumour. If such a trial is considered sufficiently risky, the FDA may require further evidence that the test is valid.

Researchers sometimes chafe at these rules. But in 2010, Duke University in Durham, North Carolina, ended three clinical trials designed to determine whether gene-expression profiles could predict patient responses to lung-cancer therapies. The trials were based on results from cancer researcher Anil Potti, and were terminated well after other scientists reported flaws in his analyses. Those flaws might have been acknowledged earlier if the FDA had been consulted before the trials started.

With its proposal to regulate home-brew tests, the FDA is responding to a changing medical climate. Researchers must be willing to do the same. ■