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Unapproved tests on a chip

Prenatal genetic tests can now check for abnormalities in developing fetuses, but there is still no regulatory framework for them in the United States.

For more than a decade, genetic tests have been on the way that would tell patients about genetic variations that might increase their susceptibility to disease. And all the while, bioethicists have been warning the US government of the impending need to regulate such tests when they arrive. Now hundreds of these tests are available, including powerful prenatal tests that use microarrays to scan hundreds of genes in unborn children. Yet despite the warnings, the tests remain effectively unregulated.

Last December, Affymetrix of Santa Clara, California, became the first company to get approval from the US Food and Drug Administration (FDA) for a microarray chip for use as such a diagnostic device. The chip can check for genetic differences that might predict a patient's tolerance to drug treatment. Now, researchers at Baylor College of Medicine in Houston, Texas, are offering pregnant women a genome-scanning test that checks for abnormalities in developing fetuses (see page 733). But because of the way this test was developed, it is not currently subject to FDA review — and neither are tests made by private companies that can do prenatal screening but haven't yet been used to do so. The FDA has declined to say whether it intends to review these sorts of tests.

One major point of confusion is whether the FDA has the power to regulate tests that are developed within a particular laboratory and are then used only in that lab, without being sold to outsiders. In 1997, the agency said that it would regulate these 'home brew' tests under the same rules that it uses to regulate other medical devices. But in 2003, when it issued further guidance on the ingredients that are used to make home brews, it decided that it didn't have the power to regulate them after all. Instead, the FDA said it would regulate only the 'analyte-specific reagents' — the ingredients, such as antibodies or nucleotide sequences, that make up the test. And it will only regulate the analyte-specific reagents if they are sold to the maker of the test; if the reagents are developed in-house, neither the reagents nor the test are subject to regulation by the FDA.

Companies that sell microarrays for others to use in genetic tests do have to register with the FDA, and must submit information supporting their ability to make the arrays properly to the regulator for approval. These rules also hold for companies or labs that make key components of genetic tests, such as gene probes. However, private labs that make and use their own microarrays for genetic testing are not subject to FDA scrutiny.

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Additionally, some companies are stretching the interpretation of the rules by marketing genetic tests that may be of dubious value (see *Nature* 426, 107; 2003). Because the companies make and use their own testing materials, they don't have to register under the regulations governing companies that sell microarrays to others. The unfortunate end result is a free-for-all in the marketing of genetic tests to the public, as well as widespread confusion among researchers and laboratories about their regulatory obligations.

The introduction of prenatal microarray tests into this picture creates additional urgency for the regulators to act. If misdiagnoses occur, children may be born with an unexpected disease, or fetuses may be terminated on the basis of false information. Let's hope that such episodes don't have to be documented before the FDA acts to clarify its role as a regulator of genetic testing. If the agency finds that it lacks the authority to properly supervise the makers and users of home-brew genetic tests, then Congress should intervene to grant it that authority. ■

Launching a business

There's little evidence that commercial approaches can radically reduce the cost of getting into space.

It has long been an item of faith among some space aficionados in the United States that private enterprise can, if given the chance, sharply reduce the cost of rocket launches. For this vocal group, the government — and NASA in particular — has always been the enemy. What's necessary, they believe, is a commercial launch business unfettered by bureaucratic oversight.

The emergence of such a business has been hampered by its limited range of customers. A few operators of commercial telecommunication satellites aside, the only reliable customers for would-be rocket makers in the United States are government agencies, primarily NASA and the Department of Defense. In the 1990s, it looked for a while as though the satellite business might rapidly expand, as plans were laid to have swarms of small communications satellites circling the Earth. A number of would-be rocket builders opened offices, hoping to capture some of that business. But when the new satellite businesses failed to materialize, the rocket companies disappeared.

Today, the most prominent player in the private rocket business is Internet tycoon Elon Musk, whose California-based company SpaceX has pledged to bring down the cost of launching materials into orbit by an order of magnitude (see page 736).

Musk starts with several advantages. His rocket, Falcon 1, which is sitting on the Kwajalein atoll in the Pacific awaiting its first launch, was produced by a small design team. It doesn't have the overheads of the large corporations such as Boeing or Lockheed Martin that build existing US rockets. The rocket project is financed by Musk himself, and if it works as advertised, there's a real chance that SpaceX could offer to launch payloads at a lower cost than existing options.

But that would be only half the battle. The main things constraining the development of new launch options are the low number of customers and the emphasis that these customers place on reliability, as opposed to cost.

Government agencies are by far the largest customers for rocket launches, and they would like to bring costs down. But reliability remains a greater priority. Take a high-value payload such as the $4.5-billion James Webb Space Telescope planned for launch sometime in the next decade, or the $500-million New Horizons Pluto probe scheduled to take off from Cape Canaveral on an Atlas V rocket next month. When the satellite costs far more than the rocket ride, the project manager will pay extra to make sure the spacecraft is delivered safely to orbit. A few tens of millions of dollars in savings wouldn't matter much considering the cost of failure. Similar considerations influence operators of telecoms satellites, who can seldom afford to lose them or delay their arrival into space.

The only remaining customer potential lies with space tourism. But even assuming that a few dozen millionaires visit Earth orbit each year by 2020, the market will remain commercially insignificant. In any case, the space tourists — or at least their insurance companies — may also favour proven reliability over a cheap ticket.

Openings will still arise for the development of more space-launch options on the margins. NASA, for example, is now considering relaxing its traditional insistence on several layers of oversight and inspection for flights that will take food and water to the space station. The agency would instead pay for a delivery service and let the launch provider assume responsibility for the success of the launch.

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Such approaches will help to spur on people such as Musk and establish whether they can indeed build a reliable track record in the space-launch business. Until they have done so, the suggestion that entrepreneurial activity can make a substantial difference to the cost of space travel should still be considered pie in the sky. ■

Enough, already

No convincing case has been made for increasing the amount of plutonium held at a Californian lab.

The US Department of Energy is planning to double the amount of plutonium that can be stored at the Lawrence Livermore National Laboratory in California. Under new rules announced last week, the nuclear-weapons lab can keep up to 1,400 kilograms, or enough for around 300 bombs.

Not surprisingly, antinuclear activists are up in arms about having so much bomb-grade metal in such a heavily populated area. But researchers who want the US nuclear-weapons laboratories to set a good example for the rest of the world should be equally dismayed at the plan.

Since 1992, the United States has maintained a moratorium on the testing and development of new nuclear weapons. There's no real need for this research lab, which accommodates an outstanding civilian research programme next to its weapons-related activity, to be playing with this quantity of plutonium.

Livermore is expected to use some of the expanded inventory in nuclear-weapons research, including experiments at the National Ignition Facility (NIF), a massive laser facility that will recreate some of the conditions inside nuclear weapons at detonation. The facility's original function was to perform such experiments on hydrogen isotopes, rather than plutonium. Officials at the Department of Energy never formally excluded the option of using plutonium in the NIF, but a 1995 report prepared by scientists in the department's non-proliferation office warned that its use at the facility could be seen as provocative by other nations.

The other main reason why Livermore wants to hold more plutonium, according to energy-department documents, is that it will start to lay the groundwork for the renewed mass production of plutonium pits, used in US nuclear weapons. Livermore will be charged with developing new technologies for manufacturing the pits, for use at a proposed industrial-sized production facility. But questions remain over whether this facility is either necessary or appropriate, and this year Congress declined to appropriate the money needed to begin planning for its construction.

Most of Livermore's new plutonium stocks would be shipped there from the Los Alamos National Laboratory in New Mexico, where the Department of Energy's track record in handling plutonium does not inspire much confidence. According to a report released on 29 November by the Institute for Energy and Environmental Research, a watchdog group based near Washington DC, Los Alamos has managed to lose between 300 kg and 600 kg of the material over the years. The group suggests that much of it was dumped indiscriminately in the desert during the early days of the nuclear age, or was mislabelled when shipped off elsewhere for long-term storage.

"The laboratory is wasting its time researching pit production for a facility that may never actually be built."

And Livermore has had its own problems with plutonium. In January, its plutonium facility, where scientists work with the metal under heavily controlled conditions, was shut down amid safety concerns. Problems cited at the time included cracks in the building's ventilation systems and poorly constructed 'hot boxes' for handling the metal. The facility was allowed to reopen at a reduced capacity last month.

In light of all this, Livermore's plan to double its inventory of plutonium is ill-advised. A case for plutonium experiments at the NIF has not been made, even to review groups that have the security clearance needed to assess it. And the laboratory is wasting its time researching pit production for a facility that may never actually be built. For a mixed-use scientific facility in a residential area, 700 kg of plutonium is enough, already. ■