FDA launches priority vouchers for neglected-disease drugs

The US Food and Drug Administration (FDA) has launched a new program intended to encourage companies to develop treatments for so-called neglected diseases. At the same time, a team of Canadian researchers has outlined a plan for broad sharing of intellectual property (IP) to increase innovation and ensure discoveries reach those that need them in developing countries. Whether the newly devised strategies will actually galvanize new treatments for the old scourges of the poor, like malaria, leishmaniasis and African sleeping sickness, and whether biotech companies in particular will benefit, remains unclear.

The new scheme awards a priority review voucher to any company obtaining FDA approval for a product that prevents or treats a neglected disease, most of which are also tropical diseases. The program, launched in October, was enacted as part of the FDA Amendments Act (*Nat. Biotechnol.* **25**, 1061, 2007). Vouchers can be used to accelerate approval of any drug in any disease indication that would not normally qualify for priority review by placing them on the FDA's Priority Review list (**Box 1**).

Obtaining a spot on this list can cut in half the time it takes for the agency to act on a new drug application (NDA). That can translate into hundreds of millions of dollars for a company with a potential blockbuster drug, and more for a company competing to be first on the market with a new class of therapeutics, says Henry Grabowski, an economist at Duke University in Durham, North Carolina. Grabowski was part of the team that originally proposed the priority-reviews vouchers idea (*Health Affairs*, **25**, 313–324, 2006).

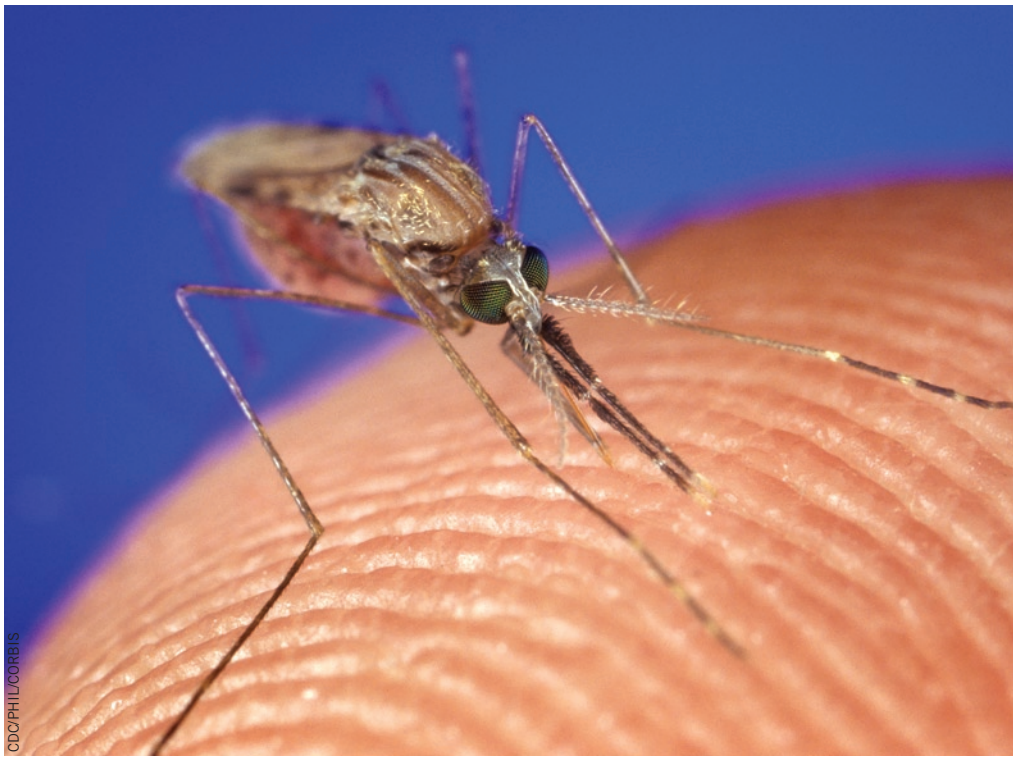
That the idea has been translated into government action so rapidly after it was first published in 2006 is impressive. But the need for greater investment in tropical disease research is clear. Conditions, such as tuberculosis, malaria, leishmaniasis and trypanosomiasis, affect 1 in 6 people globally, yet they have been off the industry's drug development radar for decades. "This incentive has captured more attention than most others we've looked at," says Wendy Taylor, founder of BIO Ventures for Global Health (BVGH), in Washington, DC. "It very creatively uses market mechanisms and doesn't require donors and governments to put up hundreds of millions of dollars to incentivize investment."

Novartis' anti-malarial drug Coartem (an oral combination of artemether and lumefantrine) may be first to obtain a voucher. In September, the FDA granted the Basel-based company priority review for its NDA submission, and a decision is expected in the coming months. Coartem was developed before the voucher scheme arose, and Novartis would not speculate on how it might use a voucher offered by the agency.

An important aspect of the vouchers is that they can also be bartered: a company may not only transfer the voucher for a drug candidate in its own pipeline but can also sell it to another company. The latter option is likely to be more valuable to small biotechs that are looking for new sources of cash to finance internal programs.

For larger biotech companies that already have approved products on Western markets, one option may be to repurpose these drugs for diseases rife in developing countries, thereby gaining access to priority vouchers to be used for more lucrative programs. Indeed, a report, *Closing the Global Health Innovation Gap* published by BVGH in November 2007 indicated that many established biotech companies have, for example, kinase drug discovery programs that could be repurposed and tested against agents of neglected diseases.

But for most early-stage biotech companies, the carrot of a priority voucher is unlikely to be sufficient to drive work on neglected diseases,



Novartis could be the first company to win a priority review voucher for its artemisinin-based drug Coartem, which targets *Plasmodium* parasites transmitted by mosquitos (pictured).

Box 1 Priority review explained

The FDA assigns priority review status to drugs that address urgent unmet health issues. A priority review should reduce the time the agency takes to review the drug application from ten months to just six months. But with limited resources, the agency can't always meet those goals. The voucher scheme will add drugs to the priority review list—drugs that may not be urgently needed—and lobby groups are concerned that the scheme will slow down the approval process for more important drugs on the list. "The general public might become disenchanted if this mechanism meant that life-threatening conditions were displaced out of the queue," says Roy Widdus, a consultant with Global Health Futures Network in New York. "I think most people have concluded that this is a public relations nonstarter." On the other hand, much of the value of priority review vouchers will depend on how the FDA evaluates those drugs that previously would not have been eligible for such review. Drug developers are wondering if a priority review voucher for, say, a cholesterol drug will get bumped to the bottom of the priority review list when drugs for more urgent, unmet medical needs are also in line. If this happens regularly, it may greatly diminish the value of the voucher. *—Emily Waltz, New York*

particularly if relevant drug candidates are not already present in pipelines. "The legislation is skewed to favor big pharma," says Michael Becker, CEO of VioQuest Pharmaceuticals in Basking Ridge, New Jersey. "If you're a startup company just entering phase 1 or preclinical studies with a product that treats neglected diseases, you're talking about five to ten years of development and investment to maybe get a priority review voucher. That's a hard sell to venture capitalists," he says. "What is somebody going to pay today for a voucher that you don't have in hand?"

But some small biotech companies are still viewing the prospect of a voucher as a negotiating tool. Joel Bellenson, CEO of Vancouver-based Upstream Biosciences, an early-stage biotech developing treatments for tropical diseases trypanosomiasis and leishmaniasis, says the possibility of achieving a priority voucher is helpful in positioning his company as a target for acquisition or partnering. "Our ability to culminate the deal will be in part because of the vouchers," he says.

When the voucher scheme arose, Becker's team at VioQuest already had a development program for Lenocta (sodium stibogluconate) an inhibitor of certain protein tyrosine phosphatases as a treatment for leishmaniasis, and was also looking at applications in oncology. Now the company is facing financial trouble and has turned to vouchers as leverage for investment. "We've been trying to turn our expected voucher into money today to save the company," says Becker.

Priority vouchers are one of several 'pull' mechanisms established to encourage innovation in the treatment of developing-world diseases, including advanced market commitments, in which governments or organizations commit to buying a certain amount of a drug once approved (*Nat. Biotechnol.* **22,** 1061, 2004). Vouchers will also need to work in concert with 'push' mechanisms, such as much larger investments in R&D (*Nat. Biotechnol.* **26,** 357, 2008) and R&D tax credits aimed at early-stage development. For instance, companies that successfully register treatments or vaccines for any of the 16 problematic diseases that qualify for vouchers might also be entitled to provisions under the Orphan Drug Act, which grants a 10-year market exclusivity to drugs for rare diseases or those with no economic viability.

Vouchers may also be valuable to public-private product development partnerships (PDPs) focused on diseases of the poor. Getting drug companies involved in these partnerships can be difficult and, according to Duke's Grabowski, a voucher may offer an incentive for a private partner.

In fact, a report released in September by a group of Canadian researchers finds that mega-collaborations along the lines of PDPs are critical for innovation, particularly for diseases that affect the developing world. "Innovation occurs better when it is networked," says Richard Gold, a law professor at McGill University in Montreal and the lead author on the report. "It's hard to predict when the breakthrough will come and which combinations of knowledge will lead to that," he says.

The report *Toward a New Era in Intellectual Property: From Confrontation to Negotiation* (http://www.theinnovationpartnership.org/ieg/documents/report/TIP_Report_E.pdf), a culmination of seven years of research by The Innovation Partnership, a nonprofit based in Montreal, takes an in-depth look at the world's IP system and the business models that have developed around it. Existing IP rules are hindering innovation, the authors conclude, because they lead to patent hoarding and distrust of other research groups while failing to prevent competitors from copying inventions. As an example, the researchers point to Salt Lake City–based Myriad Genetics, whose aggressive enforcement of patent rights were simply ignored by Canadian provincial governments, undermining the company's ability to fully capitalize its *BRCA1*/*BRCA2* breast cancer genetic screening test.

Gold and his co-authors also urge the health industry to rethink drug development business models in a way that does not revolve around hoarding IP. Companies, nonprofits and governments with common drug development interests should group together to share expertise and IP, the authors say. Several initiatives have already set out with pieces of this strategy in mind. In July, Geneva-based UNITAID, a drug purchasing organization hosted by the World Health Organization, announced it would move to establish a patent pool to address the lack of pediatric anti-retrovirals in formulations suitable for developing countries.

Lois Muraguri, a research fellow at Innogen in Edinburgh, UK, remains circumspect about the Innovation Partnership's report, however; many of the report's lofty recommendations have been proposed or discussed in the past, she says. "The problem is how to implement them. We're talking about different personalities and working cultures and perspectives," she says.

Structuring such collaborations in a way that benefits industry, particularly small biotechs, is particularly difficult, industry experts point out. Small biotechs depend on the strength of their patent portfolios to attract venture capital. Sharing IP goes against the basis of their business models.

But Gold and his colleagues say these business models must be changed. "I understand it's scary to develop new mechanisms to partner and share your knowledge," says Gold. "But not doing so hasn't been particularly beneficial." Key is getting venture capitalists (VCs) to evaluate companies based on the quality of their technology, rather than the extent of their patents, he says. "We have to educate VCs that patents aren't that valuable."

The FDA's vouchers may be an alternative way for biotechs to get investment, but they still don't break the mold of the existing model for innovation, says Gold. "The voucher initiative doesn't change the way innovation occurs," he says. "Entrenching an old model of innovation, rather than finding mechanisms to encourage the development of new ones, will be a band-aid solution at best."

Emily Waltz *New York*