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Congress vouches for priority review of childhood disease

A recently introduced piece of legislation in the US aims to foster new treatments for rare pediatric diseases by extending an existing voucher program offered by the country's Food and Drug Administration, but some critics say the approach is fundamentally flawed.

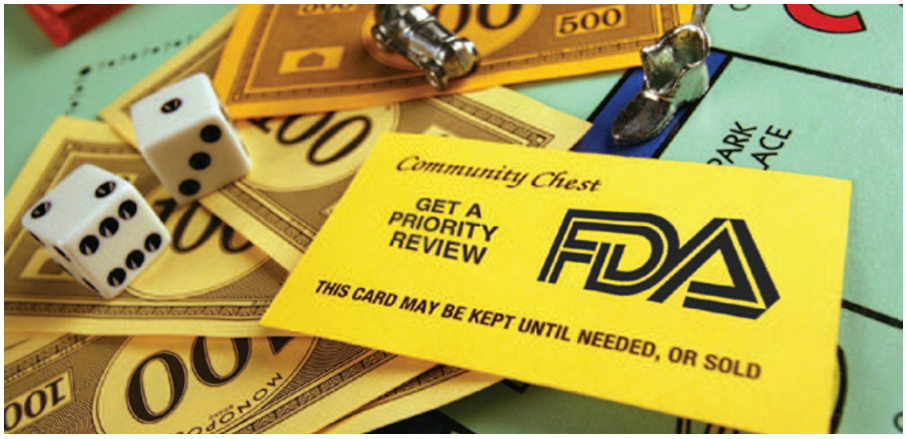
Priority review vouchers, or PRVs, were originally passed by the US Congress in 2007 to encourage pharmaceutical companies to develop new treatments for neglected tropical diseases such as tuberculosis and malaria. Under the scheme, when a drug company's qualifying neglected disease treatment is approved, it can receive a PRV redeemable for an accelerated review of another new drug application for any condition. The company must also pay a user fee to the FDA to redeem the PRV—for the 2012 fiscal year, the fee is nearly $5.3 million. Ideally, using the PRV reduces the usual ten-month approval process to six months.

"Providing reasonable incentives can help the drug industry enter a market where market forces haven't provided enough of an incentive" by themselves, says Peter Adamson, chief of clinical pharmacology and therapeutics at the Children's Hospital of Philadelphia, who specializes in new drugs for childhood cancer.

Both the Senate and the House of Representatives last year introduced versions of the Creating Hope Act, which would allow companies to also earn PRVs for new drugs aimed at rare diseases affecting children, such as pediatric cancers and cystic fibrosis. Both bills are still being reviewed by congressional committees.

However, the impact of the program remains debatable for some. "PRVs would be a questionable policy even if they did work," says Aaron Kesselheim, who studies pharmacoeconomics at the Harvard School of Public Health in Boston. "But it turns out they don't even seem to work."

Thus far, the FDA has granted only one PRV voucher: in April 2009 to the Swiss drug giant Novartis for its malaria treatment Coartem (artemether/lumefantrine). The company then used the PRV to speed up the review for an expanded use of its anti-inflammatory antibody Ilaris (canakinumab) for the treatment of gouty arthritis, but an FDA advisory committee voted 11-1 against approving the drug for this indication last June.



Alan Crosthwaite

Vouched for: Congress backs priority review vouchers to spur drug development.

Kesselheim points out that Coartem is hardly a novel malaria treatment, having been on the market outside the US for more than a decade. "This didn't actually incentivize any new research," he says.

David Ridley, a health economist at Duke University in Durham, North Carolina and one of the authors of a report that served as the outline for the PRV system, says that it is too early to pronounce the program a failure (*Health Aff.* **25**, 313–324, 2006). Since it takes around seven years to get a new treatment to phase 3 clinical trials, he's hardly surprised that there hasn't been a bumper crop of PRVs nearly four years since it began.

Ridley says he's already seen evidence that PRVs have spurred interest in new research. He pointed to NanoViricides of West Haven, Connecticut, which has identified a new molecule to combat dengue fever—a tropical disease that currently has no treatment beyond fluid replacement and acetaminophen—in part thanks to the possibility of attaining a voucher, he claims.

Ridley acknowledges that the voucher system, as described in his original paper and in its original implementation by Congress, is far from perfect. "Some of those deficiencies reflect my naiveté as an academic," he says.

But the Creating Hope Act, Ridley says, corrects several flaws in the PRV mechanism. The legislation adds language specifying that companies can earn PRVs for tropical disease treatments already available outside the US only if they've been on the market for two years or less—making sure that it engenders new research.

Kesselheim says that although this reform, which he dubbed "the Coartem corollary," is a good step in addressing problems with PRVs, it doesn't change his critique of the overall mechanism. There is research to suggest that accelerated FDA reviews are linked to a higher risk of safety problems down the road, according to Kesselheim.

A better way to encourage drug development for rare and neglected tropical diseases is to enhance the US National Institutes of Health's (NIH's) funding for basic research science, Kesselheim says. However, with austerity on the lips of every Washington pundit, advocating for even maintaining existing funding levels for research is not likely to earn points for any politician.

Adamson says that although increasing funding for NIH research is obviously desirable, it's difficult to develop therapeutics without collaborating with the pharmaceutical industry. He says incentives are the most effective solution to bring drug companies aboard, though PRVs do need some fine-tuning, admittedly.

"They're still something of an experiment," Adamson says.

Roxanne Palmer