

Dangling a Carrot for Vaccines

Drug companies do not see much of a market in treating diseases of developing nations. Michael Kremer hopes to change that—with a plan that taps the profit motive By JR MINKEL

It's a gray, drizzly March day at Harvard University. Economist Michael Kremer is recalling his postcollegiate year, 1985, spent teaching high school in Kenya, contracting malaria, recovering and watching sick Kenyans fare worse than he. Melancholy enters his voice. "The burden of disease is just very clear," he nearly sighs. "This is a terrible crisis. It seems vital to put the same sorts of entrepreneurial spirit and effort, and creativity, unleashed by the market sector"—he laughs

dryly, as if in disbelief—"to work on these diseases as is being done for the diseases in rich countries."

Poor nations labor under the weight of malaria, AIDS, tuberculosis and a score of diseases lesser known in rich countries, but they cannot afford to pay the prices companies want for drugs. Whereas some might denounce the pharmaceutical industry's profit seeking, Kremer wants to harness it. He has championed the idea that governments and other donors should try to make a malaria or tuberculosis vaccine as attractive to industry as the average drug market is. "I want them to do the same thing for malaria they would do for breast cancer," he says.

Right now research and development for neglected vaccines occurs primarily through public-private partnerships, which have invigorated the field in the past half a decade. Nonprofit groups such as the International AIDS Vaccine Initiative channel money from donors into deals with biotech and pharma companies. Industry involvement is growing, says Michel Zaffran, deputy executive secretary of the Global Alliance for Vaccines and Immunization, "but it's still not at the level one would like to see." Aid groups negotiate with drugmakers to procure vaccines for poor nations, but industry remains wary it will be haggled down to an unwelcome price.

Kremer advocates constructing a kind of artificial market for a vaccine. A donor would commit to paying a certain sum, a few hundred million dollars up to perhaps \$5 billion, on delivery of a viable vaccine. Once a vaccine is manufactured, the donor would purchase it at a high price per dose until the sum is exhausted; thereafter, the company would be obligated to supply the vaccine to poor countries at a low price. "The idea is quite simple, and it really gets at the heart of the problem—that there are insufficient markets in the developing world to attract industry," remarks Wendy Taylor, founder of BIO Ventures for Global Health.

The recipient of a MacArthur fellowship in 1997,



MICHAEL KREMER: DRUGS TO THE POOR

- Advocates the use of advanced market commitments (AMCs), in which donors agree to pay high prices for vaccines on condition that they later be sold cheaply to poor nations.
- On whether companies can be coaxed into making vaccines for neglected diseases: "If you make it attractive enough, they will."

the 41-year-old Kremer is adept at sketching out institutional fixes for problems in developing countries. To ease these nations' debt, he has argued that the international community should regard loans to odious regimes as loans to the ruling despots themselves, perhaps dissuading banks and other private lenders. To break up black markets surrounding the antiquities of poor countries, he proposes leasing the artifacts to museums.

His first foray into financial incentives for disease treatment was in 1998, when he studied the idea that the public sector could buy out the patents of working vaccines. A year later Kremer had an inspirational conversation with Jeffrey D. Sachs, a development economist at Columbia University. The concept evolved into a vaccine purchase fund, in which a donor would commit to buying doses of an already manufactured vaccine—something the World Bank had also recommended. “We were both quite enthusiastic about the idea of buying out the product,” Kremer says. At a colloquium, Sachs and Kremer outlined the idea in front of attendees from international aid groups and industry, who were not immediately persuaded.

Undaunted, Kremer published a pair of subsequent papers laying out the rationale, design challenges and trade-offs. He envisioned the purchase commitment as a long-term contract specifying clinical criteria, setting up an independent adjudicating committee and requiring poor countries that wanted the vaccine to make a small co-payment.

“The details of how this is done will make a big difference,” Kremer acknowledges. One trade-off hinges on the commitment's payment structure, which could range from a competition that awards a sum to the first company that develops a vaccine to a more marketlike approach, in which any product meeting the clinical requirements is eligible for purchase. By judiciously selecting the price and quantity of doses that they commit to, donors can choose to reward the fast development of an initial vaccine or the introduction of subsequent, possibly superior products, Kremer says.

One criticism leveled at advanced market commitments (AMCs), as the purchase commitments are now called, is that they would encourage industry to dust off abandoned, mediocre vaccine candidates. To Kremer, that is the whole point: “If they have something they think has a 10 percent chance, I want them to take that off the shelf.”

To succeed, the commitment has to minimize industry's risk of supplying vaccines to a single buyer, the donor, who might decide to pay the lowest price possible once a vaccine was developed. The U.S. government's Project BioShield illustrates the danger. Enacted in 2004, it allocated \$5.6 billion over 10 years to stimulate development of vaccines and drugs for potential

terrorist threats. The government has purchased drugs from a few biotech firms. But BioShield's original rules, now modified, gave administrators discretion in whether, how much and at what price to buy, and some companies that sunk millions into drug development were left without a customer.

The Center for Global Development, where Kremer is a nonresident fellow, convened a working group in 2003 to study the feasibility of purchase commitments. Made up of economists, lawyers, public health experts and representatives from industry, the group published its recommendations last year, including sample contracts. It advocated allowing multiple companies to share in an AMC, in part to attract more industry participation, and letting poor countries refuse a vaccine, in case circumstances changed. These efforts caught the

attention of the Group of Seven nations. In its December meeting last year, the G7 called for a pilot proposal from the World Bank for one of six diseases: malaria, HIV, tuberculosis, rotavirus, pneumococcus or human papillomavirus.

The concern persists that AMCs might compete with public-private partnerships. A commitment would have to be designed to tie up funds only on completion of a vaccine, Kremer emphasizes. “There was a tendency earlier on to present this as an alternative to up-front funding,” he admits. “We're not trying to take the public sector out of this.”

Indeed, getting industry, donors and the public sector working together seems key to making an AMC work. Industry still faces uncertainty about how much vaccine poor countries would want to buy and how to set a long-term price in advance. The G7 has asked the World Bank and the Global Alliance for Vaccines and Immunizations to help improve demand forecasting and other implementation issues. Robert Hecht of the International AIDS Vaccine Initiative notes that the international vaccine procurement system and laws governing liability and intellectual property also need further development. “There are many people who doubt it will actually work, and there are many who hope it will,” Zaffran says.

If Kremer errs on the side of overexuberance, it stems partly from his desire to help those sharing the lot of the Kenyans he knew and partly from his belief as an economist in the power of institutions to shape incentives. “There's a tendency for this whole debate over pricing of drugs in the developing world to be framed in terms of access versus incentives,” he says—poverty versus profit. “Both sides in that debate are taking the existing institutions as given. I'm trying to think about ways to make the market work to the advantage of people.”

Malaria or tuberculosis vaccines should be as attractive to industry as the average drug market is.

JR Minkel is a frequent contributor.