US policy keeps drugs out of reach in clinical trials abroad

The US National Institutes of Health's (NIH) policies on clinical trials are holding up crucial research in developing countries, scientists say.

The NIH funds trials in developing countries to test the best treatment for HIV/AIDS and other diseases. But the agency will not buy drugs for these trials, leaving investigators scrambling to find funding for the drugs after their grants are approved. This has resulted in long delays, and raises concerns about how such work can continue, researchers say.

"The NIH is really crippling operational research efforts in resource-poor settings by supporting the concept, but not allowing for plans to be NIH funded," says Luis Montaner of the Wistar Institute in Philadelphia, Pennsylvania.

In July 2003, the NIH approved Montaner's plan to study a drug-dosing strategy for AIDS called structured treatment interruption in South African patients. Montaner then went looking for the $300,000 he needed to buy antiretroviral drugs for the study. He talked to drug companies, foundations and philanthropists, but nobody would buy the drugs. Foundations were not eager to play a minor role in someone else's study, and companies were not interested in providing free treatments that have already been thoroughly tested and approved.

Finally, a year after his grant was awarded, Montaner persuaded Wistar and his collaborating institute, the University of the Witwatersrand in South Africa, to provide the drugs.

Richard Chaisson, a researcher at the Johns Hopkins Bloomberg School of Public Health (*Nat. Med.* **11**, 8; 2005), has also had to deal with research delays because of NIH policy.

The NIH approved Chaisson's study of treatment strategies for AIDS in Johannesburg and Cape Town, South Africa, in 2004. Chaisson's group needed to use generic drugs for at least some of the trial participants due to South Africa's own policies.

The NIH initially balked at this request, saying it had no way to approve or review applications for the use of generic drugs in its studies. But the agency had recently decided to allow generic drugs in one international trial, the Strategies for Management of Anti-Retroviral Therapy, or SMART, trial (*Nature* **431**, 1028; 2004).

The agency asked Chaisson to submit data similar to those submitted by the SMART trial leaders, including documents certifying that the generic drugs are safe, effective and approved for use in South Africa. Then, after Chaisson had collected this information, the agency again balked, saying it had no mechanism to review the drug data. Finally, after further consultation, Chaisson says, the NIH accepted the data and allowed the study to proceed.

AFP Photo/Simon Maina

Poor choice: The National Institutes of Health will not buy drugs for trials in developing countries.

"The whole thing was ridiculous," Chaisson says. "The process was somewhat painful and delayed our study by several months."

The NIH has just approved a policy to address these and other concerns, says Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases. According to the policy, the agency will fund trials only if the investigators first show how they will obtain the necessary drugs. The policy has been in the works since 2003 (*Nat. Med.* **9**, 629; 2003), but was only recently finalized.

The agency cannot provide the drugs because, to comply with international bioethics standards, it would have to continue to provide them once the study was finished, notes Fauci. If the NIH had to foot the bills for patients' treatment after studies ended, it would not have the money to fund research trials, he says. "You have to look at what is the lesser of two evils."

But the policy leaves a huge gap for research in developing countries, says Montaner. "There's a big misconception about the reality of trying to bring research into resource-poor settings," Montaner says. "Everyone acknowledges this should be done," he says, "but there is no instrument at the moment that allows that to happen well in operational research."

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Indian law could choke cheap drug supply

The Indian government has passed a new law forbidding local companies from manufacturing copies of drugs patented elsewhere. Although last-minute changes to its wording loosened many restrictions, critics say the law will eventually raise the cost of generic drugs for millions of people in developing countries.

Companies in India, the world's leading supplier of generic medicines, were required to fall in line with World Trade Organization (WTO) rules by 1 January 2005. The government initially proposed a bill that was widely seen as favoring multinational pharmaceutical companies even beyond the WTO's mandate. But following widespread protests from groups such as Médecins Sans Frontières and left-wing political parties, the ministry of commerce amended the wording.

According to the revised version, generics manufacturers can oppose patents before and after approval and export patented medicines to countries facing a public health crisis. Patents can also be revoked in the event of "public interest." The new version also forbids 'evergreening,' meaning that patents would be granted only to new products and not for the new use of a known product.

The law only affects patents filed after 1 January 2005. It has no effect on generics introduced before 1995, and companies can continue to copy drugs discovered between 1995 and 2005—for which patents are pending—after paying a "reasonable royalty."

AIDS activists say the ruling will cut the supply of second-generation generic drugs to poor patients. "If half of the 700,000 HIV-positive people in developing countries are able to afford antiretroviral treatment it is because of the Indian industry's ability to churn out copycats," says Anand Grover, a lawyer with the Mumbai-based Affordable Medicines and Treatment Campaign.

But some generics manufacturers say the new law will in the long run be good for Indian science—and for business. "The amendments will encourage innovations," says Satish Reddy, managing director of the Hyderabad-based Dr. Reddy's Laboratories.

In anticipation of the rule, several Indian companies have ramped up their research operations (*Nat. Med.* 11, 3; 2005). The expiry of patents on several drugs is expected to open up a multibillion dollar market in six years for Indian generic companies.

Still, some companies such as Cipla, a leading manufacturer of generic AIDS drugs, are unhappy about the new regulations. "The new law will lead to monopoly and India cannot afford monopoly," says Yusuf Hamied, Cipla's managing director.

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