

On 4 March, the WNU, established by sex workers in Phnom Penh, sent a letter to Cambodian Prime Minister Hun Sen, reaffirming support for his decision in August 2004 to prohibit a planned trial of the drug tenofovir. The drug is produced and marketed under the name Viread by a US company, Gilead Sciences. It is currently used to treat patients who are already HIV positive. The company hopes that it will also prove effective in preventing infection with HIV, and US and Australian organisations have been enlisted to test this possibility in countries in Africa and Asia.

The 4 March letter was prompted by reports that would-be sponsors of the tenofovir test and some NGOs are lobbying the Cambodian government in the hope of reversing the prime minister's August decision and allowing a trial go ahead. This information sheet is produced by the Womyn's Agenda for Change in support of the Phnom Penh sex workers.

### **What is wrong with the proposal to test tenofovir? Don't new medicines have to be tested on people to find out if they are safe and effective?**

New treatments do eventually have to be tested on human beings; everyone recognises that. But such tests always involve potential dangers for the participants, so it is important that the dangers be minimised as much as possible and that participants who are injured in any way be guaranteed appropriate treatment for any problem that is a result of the test.

The Cambodian sex workers are not objecting to drug testing in general. They call the proposed tenofovir test "unethical" because it fails to meet these and other necessary conditions.

The risks and benefits of clinical trials should be equitably distributed. While Cambodian sex workers are to take all the risk, benefits from the trial are unlikely to reach them.

Participation in clinical trial must be based on fully informed consent. It appears that the researchers have not taken adequate steps to inform all the potential participants about the exact nature of the trial. The researchers have not even disclosed the details of protocol of the proposed trial.

### **What potential dangers are there for participants if the tenofovir test goes ahead?**

Supporters of the trial have been quoted as saying that it involves "little risk" for the participants. But they have so far not bothered to be precise about the risk, nor to explain how they calculate it. Normally for a scientific study such as this, risks are calculated, in much the same way that insurance companies calculate the risk of someone having a serious illness or crashing their car.

There are a number of different dangers that can be identified. One is contracting HIV. Tenofovir is not likely to increase this danger directly (although several years ago tests of an anti-HIV cream called nonoxynol-9 were stopped when it was discovered that it significantly increased the chances of HIV infection).

However, the risk of HIV infection could be increased if participants in the test think that tenofovir gives them protection that makes condom use unnecessary. And the people

conducting the test would have reason not to stress condom use: if all the participants in the test always used condoms, there would be no real test of the effectiveness of tenofovir.

The government of Cameroon suspended a test of tenofovir for several weeks in February because of concern that participating sex workers were not properly informed and protected. "There's an obvious conflict of interest between enforcing prevention measures and carrying out the clinical trial of a drug that could help prevent HIV infection", Fabrice Pilorgé, an officer of the AIDS activist group ACT UP-Paris, said about the Cameroon test.

"A friend who agreed to take part [in the test] told me she was vaccinated now and couldn't catch AIDS", a young sex worker in Cameroon told a French TV station.

### **What about side effects from use of tenofovir?**

Because tenofovir has been used as a treatment for AIDS for several years, some possible side effects are already known. Gilead, the company that manufactures tenofovir, warns users:

"Lactic acidosis (the build up of lactic acid in the body) and severe liver problems, including fatal cases, have been reported with the use of reverse transcriptase inhibitors similar to tenofovir, alone or in combination. Contact your doctor immediately if you experience nausea, vomiting, or unusual or unexpected stomach discomfort; weakness and tiredness; shortness of breath; weakness in the arms and legs; yellowing of the skin or eyes; or pain in the upper stomach area. These may be early symptoms of lactic acidosis or liver problems."

Common side effects of tenofovir are headache, sore muscles, nausea, vomiting and loss of appetite. There is also evidence that the drug may cause kidney damage, and may reduce bone mineral density, leading to osteoporosis.

There are no reliable data on possible side effects in people who are not infected with HIV.

### **Would participants in a test of tenofovir in Cambodia receive treatment for medical problems?**

It appears that there is no intention to provide *adequate* treatment. One reason that sex workers refused to join the trial last year was that the sponsors refused to promise them free medical care for problems that might emerge at any later time. Osteoporosis or damage to internal organs might not be evident for many years.

It is not even certain that test participants who contract HIV will receive free treatment for that. In Cameroon, in the consent letter signed by sex workers participating in the trial, the sponsors state: "In case of infection ... we will not procure treatment against AIDS. We will be able to direct you to clinics where you will have to pay."

There is a need to monitor the long-term side effects of the trial. The known side effects are based on the experience of people living with HIV/AIDS. There is not adequate information on the possible side effects of tenofovir on non- HIV-infected people.

### **But if participants receive regular medical check-ups as part of the trial, wouldn't**

### **those check-ups find any early signs of side effects?**

They might, but they might not. The trial is being conducted by epidemiologists—that is, by doctors who specialise in studying epidemics. You don't go to an epidemiologist if you have a pain in your stomach; you go to a clinical doctor, whose training and experience are in noticing and interpreting symptoms that are often vague or unclear. And even skilled clinical doctors may not observe signs of a problem that is not going to appear for several years.

The senior investigators for the trial should be experienced HIV/AIDS clinicians.

### **What are the benefits of conducting a tenofovir trial?**

There are certainly potential benefits for Gilead, the manufacturer. "Treatment Insider", an on-line newsletter of the American Foundation for AIDS Research, reported in October 2002:

"The value of tenofovir to Gilead is inarguable. In the second quarter of 2001, the firm posted a net loss of \$32.4 million. Losses have been continual for the 15-year-old company. This spring, with tenofovir accounting for nearly half of Gilead's sales, it announced a second quarter profit of \$19.7 million."

Remember that this profit is based on using tenofovir as a treatment for people who are HIV positive. If tenofovir were to prove useful in preventing HIV transmission, Gilead's profits would undoubtedly soar.

Obviously, there is a benefit to anyone whom tenofovir prevents from being infected with HIV, if it proves able to do that. But it is not likely that many ordinary Cambodians would be able to use it. In the United States, the wholesale price of Viread is \$360 per month. Gilead has said that if tenofovir proves useful in preventing HIV transmission, it will sell it to poor countries at "cost". Only Gilead knows for certain what its costs are. However, the company already has an "access program" to provide tenofovir to poor countries at a price of \$39 a month. (Haiti is the only country in Latin America or the Caribbean to qualify under Gilead's definition of "poor"). If that were the price here, the drug would still be beyond the reach of most Cambodians.

### **Are there any other problems with the proposed trial?**

It seems clear that tenofovir is being tested mainly in poor countries because that is cheaper than doing it in rich countries. In effect, this means that Cambodians would be used for the experiment because they are poor, and this makes it easier to deprive them of the protections that would be normal for such a test conducted in a rich country.

For example, the tenofovir trial involves only five counsellors and one doctor for 400 sex workers. And all of the counselling is offered in English, a language little used in Cameroon.

It is normal in developed countries that tests involving human beings are overseen by an ethical review committee that is independent of the test sponsors. Communitybased ethics review committees are also increasingly a norm in many situations. There has been no mention of such a committee for any Cambodian test.