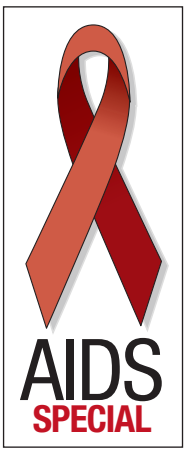
Out of Thailand, into Africa

Can African nations produce their own affordable AIDS drugs? Yes, says the woman behind Thailand's successful HIV treatment programme. Julie Clayton talks to a driven individual who won't take no for an answer.

AIDS warrior: Krisana Kraisintu is determined to bring anti-HIV drugs to everyone who needs them.



Krisana Kraisintu soon realized the magnitude of the task facing her when she made her first trip to the Democratic Republic of Congo (DRC) in December 2002. The instigator of Thailand's successful effort to produce cheap drugs to combat HIV, Kraisintu is attempting a repeat performance where it is needed most: in sub-Saharan Africa.

"I didn't feel any danger until I heard gunfire — there were gunshots and fighting all around us," says Kraisintu. "But I was not afraid to die, because I am a Buddhist, and if I die it is a new beginning."

Despite the continuing civil war, Kraisintu has since returned to the DRC three times. "I will not stop until I've finished," she says. "But it's very slow because of the war." Indeed, a trip planned for March this year had to be postponed because the border with Rwanda was closed.

Kraisintu's goal is to help the DRC, Eritrea and Tanzania to produce generic copies of branded antiretroviral drugs. Only this, she believes, will ensure affordable supplies to support lifelong treatment for impoverished patients. As examples of what can be achieved, Kraisintu points to Brazil and her own country, which have both established free national AIDS treatment programmes, thanks to local production of generics.

But Brazil and Thailand are among the most industrially advanced nations in the developing world, and many experts don't believe that poor African states are in a position to emulate their achievement. "I don't know how they can, because pharmaceutical production is so technology intensive," says Warren Kaplan, a consultant in public-health and drug policy, currently with the World Health Organization (WHO) in Geneva. "Where are they going to get the people from for the quality control?"

For Kraisintu, such comments echo the scepticism she encountered when she first proposed establishing generic production in Thailand. Her quest was sparked in 1992 by an argument with a prominent Thai politician, who revealed his prejudice against HIV-infected individuals. "He said that all people who contracted AIDS were bad people," Kraisintu recalls. "I quarrelled with him for three hours. I was a member of his political party, so I quit and said that I had to do something."

Fortunately, Kraisintu was in a position to turn her words into action. As director of the Research and Development Institute of Thailand's Government Pharmaceutical Organization (GPO), Kraisintu was well aware of the life-extending and life-enhancing properties of newly emerging cocktails of antiretroviral drugs. But in Thailand they were only within the reach of the wealthy. Many people with HIV were simply left to die in the care of monks at the nearest Buddhist temple.

Kraisintu began trying to persuade colleagues and government officials that Thailand could produce its own generic versions of antiretrovirals at a fraction of the cost of brand-named originals. "My colleagues didn't want to do it," she says. "The finance department said it would bankrupt the GPO because production would be so expensive."

Winning formula

So Kraisintu had to divert her own precious research funds to purchase the raw materials to produce her first generic AIDS drug, zidovudine, in 1995 — which the GPO sold to the Ministry of Public Health to prevent mother-to-child transmission of HIV.

Over the next four years, Kraisintu developed the formulae for other antiretroviral drugs. Progress was slow, but in 1999 the medical charity Médecins Sans Frontières placed orders for GPO antiretrovirals, attracted by their low prices. This made doctors throughout Thailand realize that the GPO's drugs were safe and effective. Kraisintu was then producing enough drugs to treat only 5,000 patients, still using research funds. But when a Ministry of Finance audit in 2000 showed that the drugs were selling at a profit, the GPO agreed to invest in full-scale production for the treatment of 20,000 patients.

In April 2002, Kraisintu launched a three-

S. TORFINN/PANOS

Conflict in Africa is slowing the fight against HIV.

in-one drug cocktail of lamivudine, stavudine and nevirapine, dubbed 'GPOvir'. The single-pill combination made it easier for patients to stick to their treatment. Since then, production has grown even further. By the end of this year, Thai officials plan to expand the national treatment programme to 70,000 people — and are also offering to supply drugs to 30,000 patients in Cambodia, Laos and Vietnam.

These successes are directly attributable to Kraisintu's leadership, says Suwit Wibulpoprasert, deputy secretary at the Thai Ministry of Public Health. "We owe a lot to her." Kraisintu's boundless energy was also a factor. "One week with her is OK, but two or three weeks together is very exhausting," says Christoph Bonsmann of Action Medeor, the German medical charity that is sponsoring Kraisintu's work in Africa.

Kraisintu had first tried to launch a GPO 'Mission to Africa', involving the transfer of technology to make antiretrovirals, in 1999. But her colleagues showed little enthusiasm for the project. Then, in 2002, the German director of the DRC-based company Pharmakina read about the launch of GPOvir in the popular magazine *Der Spiegel*. He invited Kraisintu to the DRC, initially to help produce antiretrovirals for the treatment of infected company employees.

At about the same time, a contact at the WHO recommended Kraisintu to Ramadhan Madabida, director of the drug-manufacturing company Tanzania Pharmaceutical Industries, who was looking for help in setting up local production of drugs for another devastating disease, malaria. In April this year, with Kraisintu's help, Madabida's firm launched its version of artesunate, an antimalarial drug derived from a Chinese herb.

Kraisintu decided to make a complete break with the Thai GPO in December last year. In the end, it was an easy decision, as her goals in Thailand had been met. "If I remained in the GPO I would never be able to do anything for African countries," she says.

Now she and Madabida are working to produce cheap antiretrovirals in Tanzania. There is a huge need: more than 2 million of Tanzania's 34 million population are infected with HIV; about 200,000 urgently need drug treatment, yet only some 2,000 are receiving it.

Beating the brands

Kraisintu and Madabida plan to produce the three drugs used in GPOvir. Initially, these will be made as individual pills, and later as a three-in-one combination. Kraisintu expects the locally made generics to cost around 25 times less than the branded drugs on which they are based, allowing each patient to receive combination therapy for as little as US$140 per year. By September this year, Kraisintu hopes to be producing enough drugs to treat 5,000 Tanzanians, and then to expand over the subsequent few months by between six- and tenfold.

P. VIROT/WHO

But formidable hurdles lie ahead, including the difficulty of establishing a suitably trained workforce. Kraisintu has set about the task of working in Africa with her customary vigour. On her first visit to Madabida's factory in Arusha, in April 2003, Kraisintu arrived straight from the airport at mid-morning and immediately set about producing antimalarials. "She refused to eat until she got the first result," says Madabida. "By 5 p.m. we had our first tablet. It had a very positive impact."

But getting Tanzanian drug manufacture up to international standards won't be achieved through sheer energy alone. "I'm not sure Krisana is always patient enough," Bonsmann observes.

Kraisintu accepts that she may have to modify the relentlessly energetic approach that underpinned her success in Thailand. "You have to understand the culture," she says. Kraisintu is now learning Swahili, and feels that she is gradually gaining the Tanzanians' confidence — but not without difficulty. For example, she initially faced scepticism when she suggested making artesunate by mixing dry powdered ingredients and compressing them directly into tablets — avoiding the usual 'wet granulation' step.

Perhaps the biggest obstacle may come from WHO standards for drug safety and quality. Manufacturers can volunteer for WHO inspection, with the incentive that, from 2005 onwards, countries depending on international aid to buy drugs will only be permitted to purchase those that are approved by the WHO.

Tanzania Pharmaceutical Industries' 40-year-old plant will never make the grade — which means that the Tanzanian government will have to fund local production until the facilities can be upgraded. To do so, Kraisintu and Action Medeor have applied for a €5-million (US$6.1-million) grant from the European Union, to purchase a ready-to-assemble modular production plant designed to internationally acceptable specifications.

The facilities in the DRC and Eritrea are new, and would meet WHO standards, but production of antiretrovirals has not yet begun because of conflict in both countries. Pharmakina has ceased all production and evacuated its staff. But Kraisintu hopes that they will be back by the autumn to start ordering raw materials.

African generic manufacturers may also face legal challenges. In theory, developing countries are protected from patent-infringement suits by amendments agreed to the World Trade Organization's trade-related aspects of intellectual property rights agreement. But in practice, the protective clauses may prove to be unwieldy.

Kraisintu is willing to do battle in the courts if necessary. She was recently preparing to testify against the drugs giant Bristol-Myers Squibb over a Thai patent for the antiretroviral didanosine (also known as ddI). Kraisintu and others contended that the company had merely licensed the drug from its inventors at the US National Institutes of Health and had made an obvious addition of an agent that enhances absorption into the body.

In January, the case came to a halt when Bristol-Myers Squibb announced that it would "dedicate the patent to the people of Thailand". Kraisintu regrets not having her day in court. "I wanted to fight to the end," she says.

Kraisintu's admirers believe that she will apply the same determination to her work in Africa. "People who are fighting for affordable medicines see her as a warrior," says Onanong Bunjumnong, formerly a member of the Thai branch of Médecins Sans Frontières. In squaring up against AIDS in Africa, this warrior has taken on the ultimate fight. ■

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