

Global Alliance at full steam for new TB drugs

"We have a goal: getting a new drug for TB registered by 2010. It's very ambitious, to achieve that and to make the product affordable," Maria Freire, Chief Executive Officer of the Global Alliance for TB Drug Development, told the *Bulletin*.

Launched in Bangkok in October 2000, the Global Alliance was described by WHO's Director-General Gro Harlem Brundtland as "a shining example of public and private sector partnerships to bridge the gap between market opportunities and people's needs".

The Alliance aims to get improved TB drugs to those who need them — drugs which:

- shorten or simplify treatment of TB; or
- provide a more effective treatment of multidrug-resistant TB; or
- improve the treatment of latent TB infection; or some combination of these.

To get there "we have to work with compounds [molecules] as far along the development chain as possible" said Freire. "And that's why we're going out scouting companies, universities, and anyone who may have potential compounds to bring in and license... Each deal will be individual and tailored for that particular compound."

The compounds the Alliance is chasing fall into two categories. First come analogues, modifications or derivatives of existing compounds. "If we have a compound that treats patients in nine months [a typical treatment time in developing countries], and if we can modify that chemical to make it just as effective in only two months we'd have achieved one of our key goals" said Freire.

"That wouldn't be a novel compound family, but like a US Treasury Bond — a solid, safe investment" said Freire. "But we also want 'stock' — much riskier investments [as in new companies], but potentially with a much higher payoff. This means compounds that are novel and new, that the TB organism [*Mycobacterium tuberculosis*] has never seen before."

Now that scientists know the whole genome of *M. tuberculosis*, it is possible to sequence proteins in the organism and identify potential new targets. In a review last year in the *American Journal of Respiratory and Critical Care Medicine*, 2001,

163: 1055-1058, Richard J O'Brien of the Division of TB Elimination, US Centers for Disease Control and Prevention, Atlanta, and Paul P Nunn of STOP TB and WHO argued that the genome plus combinatorial chemistry and robotic screening "promises the introduction of an era of rational tuberculosis drug discovery".

According to Freire "If we had a completely novel set of compounds, since the organism will have never seen them, we would be automatically able to tackle the multidrug resistance problem. Resistance of course will arise eventually, but it will give us a very good window to attack. And hopefully we'd get a series of compounds, a family or families of compounds."

"But it's riskier because the field will not be as well known, and the toxicology will be unknown. But those kinds of compound have a possibility of high pay-off."

"We are under negotiation with compounds that fit both categories" said Freire "but the majority are analogues and derivatives".

Endemic developing countries will be central in moving these compounds forward, the Global Alliance has decided. "Our goal is to develop the drugs in

such a way that they'll be affordable in endemic countries" said Freire. "So we are choosing partners in the South, such as chemists in India to help with scaling-up. And we want to team up with service providers and institutions in the South for clinical trials."

The International AIDS Vaccine Institute (IAVI) has a similar public/private model to the Global Alliance, says Freire. "We both want to use the best both the public and the private sector can offer. There's another group for malaria, and Médecins sans Frontières is considering setting up a group for essential medicines for the most neglected diseases."

In negotiations with the private sector the Alliance argues that the TB "market" will be worth about US\$ 450–700 million by 2010. This is not negligible: companies estimate \$ 200 million to be the threshold above which it is worth making a research and development effort on new products. Western diseases such as ovarian cancer, breast cancer, and diabetes offer markets of US\$ 800 million to \$1 billion, but at US\$ 450–700 million "the pharmaceutical industry already has a real incentive to move on TB", Freire argues. ■

Charlene Crabb, Paris

New TB drugs — why do we need them?

The existing recommended TB treatment is based on two months of four drugs — isoniazid, rifampicin, pyrazinamide, and ethambutol — followed by four months of two drugs: isoniazid and rifampicin. It's a six-month treatment, costing under US\$ 10, thanks to a WHO global drug facility that handles partnerships and receives donations from different donors, and then distributes drugs free of charge to countries that need them.

But why all this effort to create new drugs? Mario Raviglione of STOP TB and WHO told the *Bulletin* "the present treatment is 98–99% effective, if the TB is not multidrug resistant". "With multidrug-resistant TB (MDR-TB), which is resistant to at least the two most powerful of the four drugs — isoniazid and rifampicin — the efficacy drops to 50%" says Raviglione. But in the majority of cases — i.e. non-resistant TB — there are no serious side-effects, except a possible liver toxicity for isoniazid and rifampicin, a tingling numbness in the feet or hands for isoniazid, and temporary visual problems with ethambutol, "but generally they're rare and tolerable".

So if the existing drugs are good, why is it so important to develop new ones? First because the existing regimen is too long, says Raviglione. The recommended DOTS strategy, which is based on short-course chemotherapy, is called "short-course" only because it is shorter than the 12–24 months used 20–30 years ago.

The great discovery in clinical trials in the 1970s and 1980s was the synergy amongst the various different TB drugs, shortening the course to six months. However, six months is still not short enough, and causes difficulties for both patients and care programmes. "If we could get to three months, two, or even one, that would be a dream, that would be a major, major achievement that would allow us to treat TB much more easily than today" said Raviglione.

The second reason new drugs are needed is because the existing ones have to be taken so often. Currently in the first two months all four drugs must be taken every day or every other day, and in the last four months the final two drugs must be taken three times a week. "If we could have a drug that could be administered once a month for six months, by injection for example, that would make treatment much easier" said Raviglione.

The third reason is multidrug resistance. Existing "second-line" drugs to attack MDR-TB are expensive, have toxic side-effects, and have to be taken for two years because their effect is fairly weak compared to first-line drugs. "If we had better, safer and cheaper second-line drugs the treatment of MDR-TB would be a lot easier" said Raviglione.

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A new TB drug by 2010 — or sooner?



WHO/TDR

Buenos Aires: a doctor explains about DOTS and shows the tablets to a young woman with TB. The patient began DOTS but then stopped, remained infected, and has come back for further treatment. She may now have drug-resistant TB.

The last drug developed for TB was rifampicin, which first came into wide use in 1971–72. But the 30-year intermission may soon be over: on the starting blocks are fluororoquinolones, a class of drugs that are effective against several mycobacteria. TB is caused by *Mycobacterium tuberculosis*. “Fluoroquinolones might be quite strong for TB” says Mario Raviglione of Stop TB and WHO.

Earlier this year, researchers led by P. R. Narayanan at the Tuberculosis Research Centre in Chennai, India, reported in the *Indian Journal of Tuberculosis*, 2002; 49: 27-38 that they had successfully treated patients in just four months by replacing one of the four standard anti-TB drugs, ethambutol, with a fluoroquinolone called ofloxacin. The researchers treated patients with daily doses of isoniazid, rifampicin, pyrazinamide, and ofloxacin for three months, followed up with twice-weekly doses of isoniazid and rifampicin for an additional one or two months. Not only were the cure rates greater than 98%, but relapse rates were less than 5% in the two years following treatment.

“If this study can be confirmed, perhaps with better, more powerful fluoroquinolones, it would already be a major advantage to TB control,” says Raviglione. “This could come in three to five years.”

“Ofloxacin is just a launching pad as replacement for ethambutol” in the

standard DOTS therapy, says Bernard Fourie, Director of the Tuberculosis Research Lead Programme in South Africa. “Ofloxacin is essentially setting the scene for bigger work on more exciting fluoroquinolones such as moxifloxacin, gatifloxacin and levofloxacin.”

Rifamycins are another class of antibiotics that TB experts have their eyes on. One of the compounds, rifampicin, has been a cornerstone of TB treatment for decades. Now researchers are interested in some of its molecular relatives including rifabutin from Pharmacia Corporation, and rifapentine, which is manufactured by Aventis Pharmaceuticals and approved for TB in the United States.

The newest class of broad-spectrum antibiotics, oxazolidinones, also show “very interesting activity against *M. tuberculosis*,” says Giorgio Roscigno, Director of Strategic Development for the Global Alliance for TB Drug Development. Pharmacia Corporation recently received approval for linezolid, an oxazolidinone, for treating specific acute bacterial infections. Roscigno and other experts hope related compounds will be studied for TB as well.

A compound dubbed PA-824 is also stirring up excitement. A member of a novel class of substances known as nitroimidazopyrans, PA-824 attacks *M. tuberculosis* on two fronts. It disrupts protein synthesis and cripples the ability

of the pathogen to make a fatty acid needed for building the cell wall.

In laboratory tests, the compound’s one-two punch appears to be lethal to most versions of the microbe. “Its mechanism of action is sufficiently different from that of any other anti-TB drug that PA-824 kills drug-resistant cells, even strains resistant to six or seven anti-TB medications, at exactly the same level as it kills sensitive strains,” says Bryan Walser, vice-president of corporate strategy at Chiron Corporation, a California-based pharmaceutical company. “And it kills fast because it also targets non-growing bacteria unlike some other antibiotics that require the *M. tuberculosis* to be growing. While other drugs must be used for six months, PA-824 is likely to act more quickly than that.”

Its ability to kill both the active and the inactive forms of the pathogen, as well as multidrug-resistant strains, suggests that PA-824 could be the all-in-one drug every one is looking for. But despite its potential, further development of PA-824 was “on ice” until last February, says Craig Wheeler, president of Chiron’s biopharmaceuticals division.

That’s when the Global Alliance and Chiron announced they were joining forces to push PA-824 further along the development pipeline. Under the agreement, the Global Alliance will complete preclinical testing and move the compound through phase II trials, which will test PA-824 on a small number of TB patients. If the results are good at that point, Chiron can “opt back in” to the development, reimburse the Global Alliance for the development costs, and negotiate for rights to the potential drug in developed countries. Regardless of Chiron’s decision, the Global Alliance would keep full rights to the drug in developing countries to ensure that the compound will be affordable and available where it is needed most.

The agreement keeps a potential “gold medal” compound in development. Only one in 10 molecules ever makes it to the market, and the cost of getting it there is an estimated US\$ 300–500 million. So relieving a pharmaceutical company of some of the financial risk, while keeping a promising molecule in development is a “win/win,” says

Wheeler. "Chiron would not have taken PA-824 forward on its own."

Meanwhile, some pharmaceutical companies are scouring their chemical compound collections for molecules with anti-TB activity. For example, the AstraZeneca research facility in Bangalore, India, is in the second year of a five-year programme to find a lead compound for further development. "We have screened one million compounds and have many 'hits'," says Anand Kumar, director of the AstraZeneca Research Foundation. "By the end of this year, we will have selected them down to the few compounds that we feel are most suitable for developing further."

Other researchers are turning to nature for novel anti-TB molecules. Botanists and biochemists at the University of Durban in South Africa have isolated three compounds from native plants that show "significant" anti-TB activity. The identity of the compounds is still under wraps, but they have survived major steps in early drug development, says Fourie. "We're very confident this work is not going to be futile."

The mood itself is infectious. "What you're sensing with the scientists is not only an excitement about the field," says Maria Freire, Chief Executive Officer of the Global Alliance for TB Drug Development, "but the sense that a new therapeutic drug, by 2010, actually can happen." ■

Charlene Crabb, *Paris*

Estonia races to halt multi-drug-resistant TB before HIV takes hold

"When they said I had TB I didn't even know what it was. All I knew was that if you get it, you die. It was just a disease of the lungs. I'm 21. This summer I'll be 22", said Pia, a patient at Tartu Lung clinic, Estonia, in a television interview in 1995. Pia died of multidrug-resistant (MDR) TB two days before her 22nd birthday.

Another patient in Estonia, Kairit, was interviewed in 1997, and said: "After four months of treatment they said I had a dangerous microbe which didn't react to the TB drugs. I felt really frightened. I'd heard of resistant bacteria. I knew they didn't give you much hope". She

was being treated for MDR-TB, and her seven-year-old son lived with his grandmother. "Sometimes I go to see him. I creep away early in the morning because I don't want him to know I've got to go back to the hospital. I've been taking pills for two-and-a-half years but the disease just keeps growing." Not long after that, Kairit died too.

The stories of Pia and Kairit and their losing battle with MDR-TB were told in a short video to an audience of 150 national TB programme managers from 32 countries. They were attending a meeting of the DOTS-Plus working group in the fight against MDR-TB, held from 10 to 12 April 2002 in Tallinn, Estonia's capital city.

The global burden of MDR-TB is notoriously difficult to estimate. But the number of *previously untreated* cases of TB that were multidrug resistant in the year 2000 has been calculated recently to be between 185 000 and 414 000 (95% confidence intervals), about 3% of all new TB cases. Particularly hard hit are the Baltic states, Russian Federation, Eastern Europe and parts of China. According to these estimates Estonia is the MDR-TB capital of the world, with 14% of all new TB cases being multidrug resistant (Christopher Dye et al., *Journal of Infectious Diseases*, 2002,185: 1197-1202 (15 April)).

One of the prime causes of MDR-TB is patients defaulting on the basic treatment for TB — a daily dose of medication for six to nine months. Irregular dosage or stopping part of the way through the course lets drug-resistant organisms multiply. In order to avoid this, national TB programmes around the world are attempting to implement DOTS, the WHO-recommended strategy to control TB, which requires supervision by health or community workers during the first two months of daily TB medication.

For the TB patient, taking medication every day is time-consuming, costly and often unpleasant. After a couple of months of treatment, the patient begins to feel better and is tempted to stop taking the pills.

"They interrupt their treatment, and within one or two years develop multidrug-resistant disease" says Manfred Danilovits of the Estonia National Tuberculosis Programme. "After that, they spread the infection to others."

In Estonia MDR-TB has made its way into the general population. At least one fifth of the MDR-TB patients have full-time jobs — and a frequent reason for defaulting is that patients feel too busy to come to the clinic.

The homeless and the poor are at high risk, and half of Estonia's MDR-TB cases are alcoholics. In the cobbled streets of Tallinn's old town, a homeless alcoholic in his mid-30s, Sergei, says he is afraid that he will be infected as his living conditions are precarious, sleeping 'underground' as he does, with other homeless alcoholics, often drinking from the same cup. On the other hand, Sergei says that if he were infected, he could look forward to a hospital stay "in a clean bed and being fed decent food."

In Kose, an hour away from the Estonian capital, there is a specialized MDR-TB hospital with 72 beds. They are all occupied. Once admitted, the patient passes through showers before taking the elevator up to his room in the infectious disease wards. As MDR-TB is contagious, control is particularly strict in the Kose hospital. Double-glazed sliding doors protect the health-care workers and ultraviolet air purifiers are on every wall. The patients receive intensive treatment with second-line drugs, the cost of which can amount to as much as US\$ 19 000 for one person. But efforts of the Green Light Committee, led by WHO, Médecins Sans Frontières and Harvard Medical School, have enabled Estonia and other countries to save as much as 94% on these costs.

"Currently at least half our MDR cases are being treated, and transmission of the disease to the population has been reduced," claims Kai Vink, of Estonia's National TB Control Programme. "We think that we can have this infection under control before HIV/AIDS begins to make its own negative impact on TB rates". ■

Marion Lindsay, *WHO*

Raju has TB and AIDS and lives on the street

While Mumbai prepares to sleep, Raju the masseur goes out to look for work. He is a pavement dweller, 40 years old and emaciated, partly from alcohol and drug addiction. He also has tuber-

culosis and AIDS. Despite the pain of his condition, Raju has to work in order to eat well enough to go through another day of heavy medication. If taken on an empty stomach, the high-potency TB drugs — which are provided free of charge by the municipal corporation — could produce side-effects of weakness, giddiness, nausea or fever. Raju looks for clients every night in the hope that he can earn the 60 rupees that would just about get him two meals.

Raju came to Mumbai, like thousands of others from rural India, in search of a job. He worked as a domestic servant, a bootlegger and a vegetable chopper before becoming a masseur. In the 25 years since he came, he has never visited his home in Katni, a village in the central state of Madhya Pradesh.

“With what face can I go back? How can I explain to my parents what I have been doing all these years? I want to go back with something to show for the years I have been away,” says Raju with visible pain. “I have fallen in my own eyes,” he says.

A year ago, Raju realized that his persistent cough and rapid loss of weight could mean serious problems. So he turned to the state-run J J Hospital, which provides free or subsidized treatment for poor patients. He had to stand in a queue for two hours to register as a patient. An X-ray and blood test later, he was diagnosed as having TB and AIDS. “The doctor told me that I would die, that the drugs are very expensive, that if I have more difficulty I could come back. They gave me two types of pills for four days and nothing more,” he recalls.

Raju turned to the corporation-run Nair Hospital for help. Here he had to wait three hours. They did some tests, gave him a packet of biscuits, the same message, and a month’s supply of medicines. “I did not eat those yellow and white capsules because I got fever after a couple of doses. Moreover, a friend, who is partly educated, said these were not TB medicines, so I threw them away,” says Raju.

Miserable and debilitated, Raju then heard about Sankalp, a non-governmental organization (NGO) that helped poor patients overcome drug addiction. Raju enrolled for Sankalp’s de-addiction programme. He was sent to the Seewri TB Hospital, the main TB

referral centre in Mumbai, where he got some relief.

After his discharge, Raju was referred to the government-run TB dispensary for the DOTS programme in his locality, a facility he had not known about before. The treatment included a course of 60 injections, but the dispensary did not have syringes. Raju now had the additional expense of a disposable syringe every day.

“I stopped going to that centre for a combination of reasons... the long queues, the indifferent staff, their irregular hours. But, also I could not afford to buy those syringes. And, although they never said anything, I felt the staff did not like me because I had AIDS, and because I was poor and lived on the pavement,” said Raju.

However, the doctor at Sankalp persuaded him to resume treatment at another DOTS centre closer to the NGO’s office. The one-month break in treatment meant that it had to be started from the beginning again. Sankalp monitors his treatment, counsels him daily, and lets him use its day-care centre. But the indifference of the staff at the TB centre continues to bother Raju.

However, thanks to the support of Sankalp, Raju’s craving for alcohol has subsided. All his energy is focused on earning money to buy food so that the medicines can flush the TB out of his system. Unfortunately, the only food he sure of getting is sub-standard grain and rotting vegetables. The only encouraging thing about his case is that he wants to survive and is trying to. ■

Rupa Chinai, *Mumbai*

Reading the rice genome starts a new chapter in food science

The world’s rice growers, who cover 11% of the world’s arable land surface with their crop, giving half of the world’s population 80% of their diets, have struck lucky with a fluke of nature. The genome of rice is the smallest of all those of the cereal crops, less than 1% of the wheat genome, for example, but it is similar enough to wheat and other rich-world crops that companies and research institutes have been racing to sequence it. Some scientists have called it the “Rosetta stone” for cereals, after the ancient stone inscribed in three

languages that allowed historians to read Egyptian hieroglyphics for the first time. And in April separate publications in *Science* by the Swiss-based company Syngenta, and the Beijing Genomics Institute (BGI) and others, read out most of the rice Rosetta stone.

The result: the draft sequence of most of rice’s 430 million base pairs along its 12 chromosomes. Monsanto had produced an earlier draft of 60% of the rice genome, but these results — using a quicker, rough draft technique called “whole genome shotgun” leave those data standing, along with those of the International Rice Genome Sequencing Project (IRGSP).

Syngenta have sequenced *Oryza japonica*, and the BGI has sequenced *Oryza indica*, which together cover most Asian rices, and are similar to the rices of Africa and America.

Not only that: although a private company, Syngenta has promised to collaborate with the International Rice Research Institute (IRRI) in Manila during the crucial 10-year process of “functional mapping” of the genome. During this time the raw data are turned into a sequence of clearly identified functional genes. The BGI has already made its data freely available worldwide.

Ron Cantrell, Director of IRRI, told the *Bulletin* “we would like to encourage Syngenta to share their data freely with as many public researchers working in the developing world as possible. While their genomic data may not be merged with our own genome database, it should still be able to be accessed independently by rice scientists in resource-poor countries. It will then be up to researchers to make sense of all the rice genome databases that now exist — Syngenta’s, BGI’s, Monsanto’s, and IRGSP’s.”

Cantrell said that while Syngenta’s willingness to share at least some of its data should be recognized, he was keen to encourage the company to go further, adding that the firm was continuing to develop its approach to sharing the results of its rice research. He had been worried when he had first heard that the inventors of vitamin-A rich, genetically modified (GM) “golden rice” (Ingo Potrykus of the Institute for Plant Sciences, Swiss Federal Institute of Technology, Zurich, Switzerland, and Peter Beyer of the Centre for Applied Biosciences, University of Freiburg,

Germany) had decided to involve Syngenta, in their quest to get this rice made available. "I thought, boy, that's going to really slow things down. At IRRI we had found that as we tried to deal with private companies, they didn't understand what we were trying to do. So I wasn't thrilled."

"But as the old story goes", Cantrell said, "I've come away with a different point of view. We've found Syngenta helpful in trying to work out all of the intellectual property issues in negotiating with this golden rice technology; they clearly understood the need for new technology to address issues of poverty, and I thought they were really trying to be helpful. So we have had a quite a positive experience with the company."

In fact, Syngenta can well afford to be generous with rice. It will make its profits from the application of the understanding — and genes — that it finds in rice to more profitable crops such as wheat, barley, and maize. All the cereal genomes, according to *Science*, "have the same genes in the same order", but the profitable ones seem to have more DNA, making their genomes so large it would have been impractical to sequence them. Wheat alone has a genome 16 billion base pairs long, an extraordinary five times the size of the human genome.

Scientists say a "Green Gene" revolution is now possible and needed to feed the world, but others are more sceptical. The last Green Revolution produced more food, but much of it

didn't reach the people who most needed it.

According to a survey of the differences in nutrition during childhood — the most sensitive age — in 63 developing countries between 1970 and 1995 by the independent International Food Policy Research Institute, the following factors caused most of the improvements:

- level of women's education (caused 43% of the improvements);
- national per capita food availability (26%);
- health and environmental factors (19%);
- women's status in society (12%).

According to these figures, if improving rice productivity affected food availability it would contribute to 26% of the causes of improvement in child nutrition, whereas improving the status and education of women would more than double that effect (43% + 12% = 55%).

Understanding the genome may also make it easier to modify rice genetically to produce more micronutrients, but WHO's micronutrient specialist Bruno de Benoist points out that the first modified rice, golden rice, which produces vitamin A, still has a long way to go.

"It's still only available experimentally, and it produces far too little vitamin A" says de Benoist. Shortages of micronutrients are most important in pregnancy and very early childhood. But according to de Benoist a child would

need to eat 1 kg of golden rice a day to meet its vitamin A requirement, or 300 g for a third of it. "And they should be eating vegetables as well — golden rice is unrealistic at the moment, compared to food supplements."

De Benoist also raises concerns about the potential allergenic effects of GM foods, and about the dangers of high-technology seeds causing poor farmers to become dependent on international seed companies.

But if all the potential problems with GM foods were solved, what should be the top health targets for molecular geneticists? "It depends on the region of the world" said Graeme Clugston, director of WHO's department of nutrition for health and development, "but top of the list must come vitamin A, lysine, iron and zinc". ■

Robert Walgate, *Bulletin*

South Africa breaks through to realism on antiretrovirals for AIDS

The South African government has tripled its HIV/AIDS Budget to 1 billion rand (about US\$ 90 million) in a single year. In doing this it hopes to keep the promise it made in April to provide free antiretroviral drugs to rape survivors. The government also promises to make nevirapine universally available to all pregnant HIV-positive women by December. Official sources say that the government has been trying to move away from the controversies that have dogged its position on HIV/AIDS for a considerable time.

Meanwhile a range of South African women's organizations, including People Opposing Women's Abuse and Rape Crisis, have launched a campaign to put pressure on pharmaceutical companies to reduce their drug prices so that the government can keep its promise.

South Africa has one of the highest rates of rape in the world, and the largest HIV-positive population in the world.

Antiretrovirals (ARVs) are expected to be available to rape survivors by late this year, once the Department of Health has finalized its national protocol on the treatment of victims of sexual assault, according to the Health Minister, Manto Tshabalala-Msimang.

The Cabinet's decision to make antiretroviral drugs available to rape

New rice for Africa to increase farmers' yields 50% — without fertilizer

Even without the new genetic knowledge, traditional rice crossing and back-crossing plus the biotechnological technique of "anther culture" has just produced a dramatic advance for Africa, according to the West African Rice Development Association (WARDA), based in Côte d'Ivoire.

In mid-April, amid the furore about the genetic sequencing of rice, WARDA announced that it had crossed the Asian *Oryza japonica* with African upland *Oryza glaberrima* rice varieties to produce a new rice that is yielding "up to 50% greater yield without fertilizer", Guy Manners of WARDA told the *Bulletin*, and at least double that "under improved management". Called NERICA (New Rice for Africa), the new variety also matures 30–50 days earlier than the currently grown varieties, he says.

According to *The Independent* newspaper of Banjul the new rice is also substantially richer in protein, more tolerant to disease, drought and acid soils, resists some of the most damaging insect pests in West Africa, and can out-compete weeds. "Because the rice was designed for resource-poor farmers, it can help farmers reduce poverty and save developing countries millions of dollars in rice imports" said *The Independent*.

Kanayo F. Nwanze, Director-General of WARDA, says "Ironically, rice was considered a luxury food in West Africa only two decades ago. Today, it's the staple." WARDA says rice now contributes more calories and protein than any other cereal in humid West Africa, and about the same as all roots and tubers combined. Moreover, demand for rice is growing faster in this region than anywhere in the world, with rice imports increasing eightfold over three decades, to over three million tonnes a year, at a cost of almost US\$ 1 billion, says WARDA.

Will the new genomic knowledge help WARDA's future research? "A lot!" said Manners.

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survivors took many AIDS activists by surprise. A month prior to this, the ruling ANC's National Executive Committee had announced the opposite: that antiretroviral drugs to prevent HIV transmission following sexual assault or needle-stick injury "could not be provided in public health institutions" as their efficacy was "unproven".

The new decision represents a victory for a number of key government officials who have been working for months behind the scenes to improve the government's stance on HIV/AIDS. These officials include Ayanda Ntsaluba and Nono Simelela in the health department, Joel Netshitenzhe who is in charge of government communication, and three Cabinet Ministers: Tshabalala-Msimang, Essop Pahad, and Ben Ngubane.

At the Cabinet's annual retreat in January, ministers and top officials had voiced dissatisfaction with the government's handling of HIV/AIDS. Several ministers were given the task of preparing a document that could revitalize the national HIV/AIDS campaign. In February, President Thabo Mbeki told Parliament in his state of the nation address that his government was committed to "intensifying its comprehensive programme against AIDS", and was in discussions with some of the pharmaceutical companies to find new ways of making drugs more affordable.

While Simelela and Ntsaluba were drawn into preparing the new document on HIV/AIDS control, a court case instituted by the Treatment Action Campaign put the government under intense pressure to provide nevirapine to all pregnant HIV-positive women. Condemnation of the government's refusal to expand access to nevirapine came from several sources, including former President Nelson Mandela, old anti-apartheid ally Danny Glover, heads of South African missions abroad, members of parliament, trade unions, and ordinary citizens.

The new HIV/AIDS proposals gave the Cabinet a golden opportunity to send a message of hope to the nation. Some of its more important points are the following:

- Acceptance that ARVs can "help improve the conditions of people living with AIDS if administered at certain stages in the progression of AIDS".

- Commitment to continue efforts to reduce the cost of ARVs including discussions with drug companies, applying to the Global Fund to Fight HIV/AIDS, TB and Malaria for help, and investigating the production of generics. (According to the health department, the treatment of one million people would cost the government in the region of 7000 million rand — about US\$ 630 million. The Actuarial Society of South Africa estimates that the country will have 6.5 million HIV-positive people by the end of 2002).
- The establishment of a Presidential HIV/AIDS Task Team consisting of Deputy President Jacob Zuma and Ministers Tshabalala-Msimang, Pahad and Ngubane.
- Revamping the South African National AIDS Council (SANAC), the multisectoral body charged with leading the national HIV/AIDS campaign. The Treatment Action Campaign's Nathan Geffen said his organization would give "serious consideration" to becoming part of a genuinely representative SANAC.
- A call to people living with HIV/AIDS to "partner with government" in monitoring the availability of drugs at health institutions to treat opportunistic infections. ■

Kerry Cullinan, *Durban*