

to catastrophes,” according to the report, which was published by the Center for Health and Global Environment at the Harvard Medical School and sponsored by reinsurance company Swiss Re and the United Nations Development Programme.

While it is important to encourage people, governments and companies to buy insurance, not everyone can afford it or see the need.

Microfinancing is another avenue, giving poor people the means to improve their economic situation so that a disaster does not hit them as hard as it would otherwise, and also by lending them money to use in recovering from it.

Many countries are working to improve their disaster preparedness, but more needs to be done, Ugarte said.

“Countries are now better prepared in comparison to 1970,” he said. “But now the level of preparation and risk reduction that you need is huge in comparison to that year.”

The Michoacan earthquake in Mexico in 1985 showed that being well prepared was not enough because hospitals in the disaster zone were destroyed.

Likewise, in Grenada Hurricane Ivan damaged and disrupted much of the Caribbean island’s health system, making it difficult for health workers to respond to the needs generated by the hurricane.

PAHO has expanded its programmes to focus not only on preparedness but also on mitigation. This involves reducing secondary deaths and destruction that can occur in the aftermath of a disaster, and implementing building codes that require hospitals, schools, military bases other vital structures to be built to withstand such disasters.

Many countries say they can’t afford more preparation, but some measures are simple and can be inexpensive, such as a tsunami warning system, Ugarte said. “But from there to Banda Aceh, that is another step,” Ugarte said, referring to the capital of the Indonesian province that was worst hit by the earthquake and tsunami of December

2004. “And from Banda Aceh to all the little communities on the coast, that’s another issue. That last link of the chain is not in place. And that is the system that we need to build.”

Disaster experts say early warning systems and education are essential to prevent and mitigate against the effects of natural disasters. In its *World disasters report 2005*, the International Federation of Red Cross and Red Crescent Societies notes that a simple phone call saved thousands of lives when the giant tsunami waves hit India in 2004. A fisherman’s son named Vijayakumar Gunasekaran, who lives in Singapore, heard about the tsunami early on the radio and phoned relatives living on the east coast of India. Following his warning, all 3630 residents evacuated their village there before the waves arrived. ■

Theresa Braine, *Mexico City*

“There’s a huge relationship between this kind of damage and poverty.”

Dr. Ciro Ugarte, Regional Advisor for Emergency Preparedness and Disaster Relief with the Pan American Health Organization.

New type of R&D cooperation spawns malaria drugs

Artemisinin-based combination therapy drugs (ACTs) are the most effective malaria medicines to date, but many of the world’s poorest countries can not afford them. Two ACTs that are due to go on the market this year may help to fill the gap.

Artemisinin-based combination therapy drugs (ACTs) drugs are seen as a new way forward to treat malaria. But combining these medicines into a single tablet is often a challenge, and like most innovations is rarely tackled by scientists in developing countries.

Recently, however, a team from Brazil’s Farmanguinhos, an institute of the Oswaldo Cruz Foundation (FIOCRUZ), solved the scientific puzzle of how to combine two anti-malarials, artesunate and mefloquine, into one tablet.

“Artesunate is a very tricky substance to work with,” said Solange Wardell, coordinator of the Brazilian team, adding: “a slight increase in humidity could make artesunate decompose, thereby ceasing to be active.”

Wardell said it was essential that the combined drug be stable in tropical,



Members of the Brazilian team at Farmanguinhos.

Farmanguinhos

humid climates where malaria is prevalent. It took a year of experiments to achieve that stability.

Brazil is one of several countries involved in a project run by a non-profit group Drugs for Neglected Diseases Initiative (DNDi) to develop fixed-dose artesunate-based combination medicines. Brazil's state-owned laboratory Farmanguinhos is perhaps best known for manufacturing generic versions of antiretroviral drugs that have helped to cut treatment costs for AIDS in developing countries.

As striking as Brazil's role was the participation of other unusual players in the project. Traditionally, research and development (R&D) in the pharmaceutical sector is done in developed countries; little innovation comes out of developing countries due to lack of funds, know-how and research-based pharmaceutical industries. This project based mainly on cooperation between developing countries marks a change. In addition to Brazil, Burkina Faso, Malaysia and Thailand were key players.

When Jean-René Kiechel, who held senior R&D management positions in the pharmaceutical industry, left the industry after three decades, he certainly broke the mould. "I heard about DNDi and was interested in the fact that it was trying to develop new drugs for neglected diseases. I felt I could contribute," said Kiechel, who subsequently became the project manager for the malaria medicines initiative.

Drug resistance is a major problem for treating malaria. In many parts of Africa single treatments for malaria, such as chloroquine, have lost their effectiveness because malaria parasites in humans' blood have become resistant to drugs designed to kill them. As a result, there is a huge demand for ACTs, drugs based on derivatives of artemisinin, a potent extract of the *Artemisia annua* plant.

No resistance to ACTs has been reported to date, but there is currently only one fixed-dose ACT combination on the market, Coartem, produced by Novartis. This product is on the WHO prequalification list of products recommended for purchase by UN and other agencies. WHO and UNICEF are making it available at US\$ 2.4 per adult course of treatment, but for some countries even this is too expensive.

Every year Africa accounts for more than 60% of an estimated 350–500 million clinical cases of malaria globally, while children in Africa account for 80% of nearly one million malaria-related deaths worldwide according to WHO's Rollback Malaria department.

Many African countries have changed their national malaria treatment policy, switching from single to combination treatment. But the problem is that countries can not afford the new combination drugs, which are much more expensive than the old medicines.

Another problem is the laborious way medicines must be taken to treat malaria. Failure to stick to the exact dosages, taking one drug without the other or, as, often happens, not completing the course can reduce the effectiveness of the treatment.

Seeing the urgent need to develop a more effective and more affordable form of malaria treatment, Geneva-based DNDi sought to develop two fixed-dose combinations each containing two drugs in one tablet. "The idea was that instead of having to take a different number of drugs each day you would take one or two fixed-dose combination tablets once a day for three days," Kiechel said.

While the Brazilian team combined artesunate and mefloquine into a medicine known as AS/MQ, a team at the University of Bordeaux 2, France, combined artesunate and amodiaquine to produce a second antimalarial, AS/AQ.

The UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical



Malaria kills more children aged under five years old in sub-Saharan Africa than any other infection.

WHO/Stephanie Hollyman

Diseases (TDR) provided scientific advice for the project, and helped coordinate clinical trials. Funding came from different sources. DNDi provided US\$ 4.4 million for both the clinical research and registration application scheduled for this year; INCODEV, a European Union programme that promotes cooperation between developing countries provided US\$ 1.39 million; Farmanguinhos contributed US\$ 614 000. In addition, TDR provided US\$ 538 000 and Médecins Sans Frontières (MSF) provided US\$ 180 000.

In parallel with the Brazilians, the French team was coordinated by Pascal Millet of the Bordeaux University 2 School of Medicine. He set up a public–private partnership with the university's laboratories and French start-up, Ellipse Pharmaceuticals, to develop AS/AQ. Like the Brazilians, this team also succeeded in developing a stable combination.

The next step was the clinical trials. The Sains University in Malaysia did some of the studies, including Phase 1 trials of AS/AQ in healthy human volunteers, prepared technical reports for the drug registration files for both projects, and provided analytical support for other studies required for registration. Dr Visweswaran Navaratnam, Professor of Tropical Clinical Pharmacology at Sains, was the Scientific Programme Leader supervising this part of the project.

The team from Burkina Faso's Centre National de Recherche et de Formation sur le Paludisme did the safety and efficacy field trial of AS/AQ. Their contribution was also crucial, explained Kiechel, because they conducted trials among small children there. Children aged under one year are one of the most vulnerable groups to malaria.

The third phase of clinical trials of AS/MQ were done by a team from Mahidol University in Thailand, further testimony to the project's cooperation between developing countries.



WHO/Stephanie Hollyman

Malaria causes untold human misery as well as economic and social devastation in much of Africa. Children in Africa account for 80% of nearly one million malaria-related deaths worldwide.

Sornchai Looareesuwan, Director of Emerging and Re-emerging Diseases Research Programme and his team did studies to compare the efficacy and tolerability of the combined AS/MQ drug with that of the two component drugs taken separately.

DNDi has a contract with French pharmaceutical group, Sanofi-Aventis, to manufacture AS/AQ. The first marketing authorization applications were expected to have been submitted at the end of 2005. The French group has indicated that it will make AS/AQ available at cost price to the national health services of countries that have registered it, as well as to NGOs and international organizations, according to Clive Ondari, Coordinator at WHO's department of Medicines Policy and Standards. Farmanguinhos is in discussions with possible partners in Asia to manufacture AS/MQ.

Once AS/AQ and AS/AM are approved by regulators and prequalified by WHO, developing countries will be eligible for grants from the Global Fund to fight HIV/AIDS, Tuberculosis and Malaria to purchase the new products.

“The biggest challenge for us will be to obtain all the requirements needed for exporting the drug,” said Wardell, explaining that registering AS/MQ in Brazil and other countries was a new activity for Farmanguinhos. To help them, DNDi has provided a consultant.

Like the Brazilians, other teams from developing countries involved in the project took on unfamiliar tasks. Navaratnam said the need to supplement and integrate varying levels of knowledge and skills between partners in developed and developing countries had been a challenge. “Additional time was needed to ensure new methodologies transferred were properly adapted and realized,” he said.

The challenge, from Millet's point of view, was uniting scientists and private entities towards the same goal of providing a stable pharmaceutical product that was transferable to an industrial partner. Nevertheless Millet, like other players, echoed how pleased he was to “work on an international project with so many different and complementary people at the international level”. ■

Clare Davidson, *Sao Paulo*