Improving primary health care
Community-directed interventions double use of bednets and antimalarials | PAGE 8

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Close-up: Frank Douglas on drug discovery
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Every year has a number of new beginnings – depending on where you are in the world. In Geneva, spring has finally arrived. In Central Africa, where ivermectin is distributed via community-directed systems, this is the start of the rainy season, a time when heavy downpours can turn dirt roads to deep mud, and make travel from rural villages to health clinics difficult, if not impossible.

Both regions and seasons figure in the current issue of TDRNews. Our cover story by Communications Manager Jamie Guth, describes the experiences of rural Nigerians with a TDR co-sponsored study into community-directed interventions (CDI), a strategy based on the success of community-directed distribution of ivermectin to some 55 million people across Africa. In health districts using the broader CDI approach, the possession and utilization of insecticide-treated bednets was two times higher than in comparison districts. In addition, more than twice as many children with fever received appropriate antimalarial treatment in the CDI districts. Overall, coverage with bednets and antimalarial treatment approached or exceeded the 60% target, set in the Abuja Declaration of the African Summit on Roll Back Malaria for the year 2005. The strategy has great relevance to WHO’s attempt to promote innovative ways of getting primary health care interventions to remote communities.

Meanwhile, in Geneva, TDR hosted a series of expert meetings and consultations on new research business lines that have been created following last year’s adoption of a new Ten Year Strategy. These meetings signal the movement that has occurred over the past year from the definition of larger strategy goals to real operational activities in the restructured TDR Special Programme. Reflecting this reorganization, you will now see TDRNews meeting reports (pp. 26-30) categorized according to the new “business line” activities. For a complete rundown of TDR’s business lines refer to: http://www.who.int/tdr/about/strategy/business_lines.htm.

Another regular new feature being introduced in this issue of TDRNews is the World of TropIKA.net (pp. 23-24). This section will contain excerpts of relevant news and analysis from the new TDR-supported global research portal, www.TropIKA.net, dedicated to the sharing and review of research knowledge on infectious diseases of poverty.

Meanwhile, the newly redesigned TDR corporate website www.who.int/tdr is to be launched in June. The revamped website will provide readers and viewers with greatly enhanced capacities to access and search the full breadth of TDR’s programmatic activities, resources and grant opportunities (see TDRNews back page).

Nearly a year ago, TDR’s top governing body, the Joint Coordinating Board, met in its 30th anniversary session. That meeting launched the publication of the TDR history book, Making a Difference and a year of celebratory activities, and also marked JCB’s formal endorsement of TDR’s new Ten Year Strategy. The upcoming JCB 31 meeting, 16-18 June in Brazil, will measure and examine progress achieved so far in implementing the new strategy, and will look forward into future needs for research on neglected diseases. Meanwhile, as the 30th anniversary year draws to a close, TDR continues to make and record its history. A Nature Reviews Microbiology article summarizing TDR’s three decades of achievements, Making a Difference: 30 years of TDR, was published this month (May 2008; Vol. 6, No.5), and can be viewed both at the NRM website and on TDR’s portal: http://www.who.int/tdr/about/history_book/.

Elaine Ruth Fletcher
Editor, TDRNews
Riding a wave of interest in research

The global community is paying increased attention both to ‘upstream’ discovery research associated with technical innovation and to ‘downstream’ research concerns associated with how new interventions can be used more effectively within resource-constrained health systems of disease endemic countries. Both are key areas of focus for TDR in its new Ten Year Strategy, and TDR is thus well-positioned to contribute to ongoing and upcoming policy dialogues and actions.

Among the events shaping the ‘upstream’ environment are the recently concluded meetings of the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) in Geneva. At the 61st meeting of the World Health Assembly, 19-24 May, government delegations from all over the world will debate a draft resolution that emerged from the latest IGWG session in early May. The draft IGWG document outlines a global strategy and plan of action on essential health research to address disease conditions that disproportionately affect developing countries (see: http://www.who.int/phi).

TDR has played an active role in supporting the IGWG process, and, with its partners, also participated in some spin-off initiatives. A Geneva meeting on Priority Setting Methodologies in Health Research on 10-11 April was one such effort (see page 29). The meeting at WHO responded to an issue highlighted in the IGWG, the need to develop better research priority-setting practices. TDR also is laying plans with investigators from Africa for an African drug discovery network, in the context of TDR’s Lead Discovery for Drugs business line (BL 3). A meeting in Abuja, Nigeria in October 2008 will seek to establish that new network.

This summer, the strengthening of health systems will be high on the agenda of the 34th G-8 summit, 7-9 July in Toyako, Japan. Organizers are calling for a more “balanced” approach between disease-specific strategies and system-based solutions. While vertical disease campaigns have generated global momentum on neglected diseases, they often result in a fragmented array of donor-supported programmes at country level. In strengthening health systems in poor countries, more “empirical analysis” of what works and what does not is thus important. These were themes of a recent Lancet article written by experts and advisers to the G-8 event.

TDR has a role to play in reconciling ‘vertical disease campaigns’ and “health systems” approaches. TDR-sponsored implementation research has gone beyond both paradigms, improving delivery of specific interventions and also strengthening health systems. A recent TDR-co-sponsored study into community-directed interventions (CDI) in onchocerciasis-endemic areas illustrates this ‘responsible vertical approach.’ Results of the study, showing great strides in integrated treatment of malaria as well as onchocerciasis, were highlighted at the International Conference on Primary Health Care and Health Care Systems in Africa, 28 April in Ouagadougou, Burkina Faso (see cover story). Now, together with UNICEF, TDR is looking at how to similarly improve integrated management of fever for malaria, pneumonia and diarrhoea.

TDR is also helping to support countries to undertake such research themselves. At a meeting in Geneva, 3-5 April, TDR and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) developed a framework for implementation and operations research in the context of health control programmes (see page 26). The draft framework is now open for comment on the TDR and GFATM websites, and for use by countries in the preparation of Round 8 of the GFATM requests for proposals: http://www.who.int/tdr/topmenu/news/default.htm.

Research on infectious diseases of poverty benefits from the wave of global interest in innovation and implementation. Our new TDR strategy leaves us in a position where we can respond to both ‘discovery’ and ‘delivery’ ends of the research continuum. However, we are in a fast-changing environment, and we have to be ready for new challenges. TDR’s Joint Coordinating Board (JCB), meeting 16-18 June in Brazil, will examine TDR’s progress to date, and assess how TDR might further respond to the renewed interest in research for health.

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Dr Robert Ridley, TDR Director

31st session of the JCB

TDR’s Joint Coordinating Board meets in Rio de Janeiro

The Joint Coordinating Board (JCB), TDR’s top governing body, will hold its 31st session in Rio de Janeiro, the first time the Board has met in the Americas. Hosting the event, 16-18 June, will be the Government of Brazil, whose links to TDR extend back to the early days of the Programme.

In addition to the JCB sessions, focusing on progress in TDR’s Ten Year Strategy implementation and future challenges, JCB members will visit research laboratories and vaccine and pharmaceutical production facilities at the headquarters of the Oswaldo Cruz Foundation (FIOCRUZ), a global leader in health research and one of the early recipients of TDR capacity-strengthening support. Members also will visit sites of TDR-supported research on visceral leishmaniasis and other parasitic diseases in Belo Horizonte, and syphilis diagnostics and antimalarial drug research sites in Amazonas State.

Bamako Ministerial Forum

‘Research for health’

It’s been called the Olympics of Research. The 2008 Global Ministerial Forum on Research for Health will bring together over 600 researchers and decision-makers in Bamako, Mali, 17-19 November. Underlining the breadth of the theme “research for health”, the forum will focus on linkages between health, science and technology, as well as education, food, water, agriculture, the social sciences and community action research.

Participants will include ministers of health, science and technology, agriculture, social development and finance, as well as UN agencies, multilateral institutions, NGOs, donors and research councils. Bamako 2008 is co-organized by six partners – the Global Forum for Health Research, the Council on Health Research for Development (COHRED), the Government of Mali, the United Nations Educational, Scientific and Cultural Organization (UNESCO), the World Bank and the World Health Organization, with TDR playing a key role in planning.

Bamako 2008 has three key objectives:

• Strengthening leadership in the management of research for health, equity and development
• Engaging all relevant constituencies in the process and conduct of research and innovation for health
• Increasing the accountability of research systems

Calls for proposals for papers and presentations were issued in the spring. A series of regional meetings also have been held in preparation for the event. Those included a High Level Ministerial Meeting on Health Research in Tehran, Islamic Republic of Iran, 7-19 November 2007, and the European Regional Preparatory Meeting for Bamako 2008, in Copenhagen, Denmark, 29-30 April 2008. Additional meetings are scheduled as follows:

• Pan-American Interministerial Round Table on Research for Health 18 May, Geneva, Switzerland
• Asia-Pacific Preparatory Meeting for the 2008 Global Ministerial Forum on Research for Health 10-12 June, Bangkok, Thailand
• Ministerial Conference on Research for Health in the African Region 23-26 June, Algiers, Algeria.

For more information, see: www.bamako2008.org

TDR launches TB study

Goal: making diagnosis more accessible

TDR has launched a major study to determine if the number of patient visits required for a standard TB diagnosis can be reduced, and the delay involved in diagnosis can be cut from three days to just one. The multi-centre study of a new “front-loaded” sputum smear microscopy approach will take place in Nepal, Nigeria, Ethiopia, Brazil and Yemen, in collaboration with the Liverpool School of Tropical Medicine. Currently, in most disease-endemic countries, three sputum samples are examined over the course of two days, with a laboratory report generally being issued on the third day. The first specimen is collected on day 1 when the patient presents to the health centre, a second is collected...
the following morning (day 2) by the patient at home and brought to the health centre, at which point a third specimen is collected. The “front-loading” method involves collection of two sputum specimens on day 1, with an examination to determine if they are positive. If the initial specimens are negative, there remains the option, however, of collecting a morning specimen on day 2.

“A recent systematic literature review commissioned by TDR has reported that under the current system, the first smear identifies around 80% of smear-positive TB patients, the second a further 15% and the third the remaining 2-5%,” said Andy Ramsay, the TDR manager leading the study.

“So what we are aiming to find out is whether we can diagnose around 95% of the smear-positive cases by examining two specimens, both collected on the first day.”

Of the eight million people who develop active TB every year, most do not receive a laboratory confirmed diagnosis. Tuberculosis is a disease of poverty. Patients being investigated for tuberculosis in developing countries are currently required to make repeated visits to health facilities. The costs for the visits incurred by patients, particularly by poor patients, are often prohibitive, and other TDR-funded studies in India, Thailand, Peru and Zambia have shown that the proportion of patients dropping out of the diagnostic process can be considerable.

Briefing on Capitol Hill
TDR has growing presence in the US

TDR is showcasing the importance of implementation research in the global battle against infectious disease in a briefing to congressional staff and lawmakers on Capitol Hill in Washington DC. The 23 June briefing, co-sponsored by two US-based NGOs, the Global Health Council and Research!America, is to include presentations by TDR Director, Dr Robert Ridley, and Dr Oladele Akogun, one of the primary investigators in

**Director General, Bangladesh Health Services**

**Professor Abul M Faiz**

Professor Abul M Faiz, a longtime collaborator with TDR in malaria research and a current member of the WHO Malaria Treatment Guidelines Committee, has been appointed as the Director General of Health Services for the Government of Bangladesh.

Faiz began working with TDR in 1996, when he received support from the Research Capacity Strengthening (RCS) unit, for malaria research he was conducting at the University of Chittagong, Bangladesh. The research resulted in a very detailed clinical assessment of the severity of malaria cases in Bangladesh. Then in 1998, Faiz was awarded a grant by the TDR Task Force on Severe Malaria to carry out a large scale, randomized controlled trial in Bangladesh on rectal artesunate as emergency treatment for malaria. The study, which was also conducted in Ghana and Tanzania, and completed in 2006, was a significant achievement for TDR, as it demonstrated the survival benefits of using rectal artesunate for children.

Until his appointment as Director General in January 2008, Faiz was: Professor of Medicine, Principle and Acting Dean of Dhaka Medical College, Bangladesh; Director of the new Bangladesh Institute for Tropical Diseases; and also a member of the committee supporting the Adviser for Health and Family Welfare of the caretaker government.

Dr Melba Gomes of TDR, who worked with Professor Faiz on the rectal artesunate assessment project, among other collaborations, said of the Professor, “He is a man of noticeable integrity and huge presence, who speaks only when he has something to say. I went with him to the field and was struck by how his former patients remembered him years later, from the time when he was a young medical officer. I think he has been, and will continue to be, successful because he has such great integrity.”

Dr Oladele Akogun.
the recently-completed TDR study on community-directed interventions in Africa (see cover story).

The event is one among a number of recent and planned events aimed at raising the profile of TDR’s mission and activities among US-based institutions and audiences.

Among those, a 30-31 March meeting of TDR’s Standing Committee also was held in Washington, DC, including representatives of TDR’s four co-sponsoring agencies, UNDP, UNICEF, the World Bank, and WHO. The Standing Committee meeting coincided with a special WHO 60th anniversary exhibition at the United Nations in New York City, which included a display profiling TDR’s foundation in 1975 (see below).

Meanwhile on World Malaria Day, 25 April, television viewers worldwide had the opportunity to view a news story describing how TDR implementation research is increasing use of insecticide-treated bednets and antimalarials. The news story was distributed by the New York City-based UN broadcast news services, with which TDR has begun to collaborate.

Stockholm, Sweden: Location of the conference on Alignment and Harmonization in Cooperation on Research for Health.

The UN news story documented the recent research into community-directed interventions in Africa, undertaken by TDR and co-sponsored by the African Programme for Onchocerciasis Control. Also on World Malaria Day, New York University’s School of Medicine screened to the public a recent production from the BBC’s Kill or Cure series that profiles TDR home management of malaria research.

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TDR can play facilitating role

Funders’ conference aims to harmonize activities

The relative weakness of health research systems and institutions in poor countries remains a conspicuous barrier to health advances. But to improve research systems, donors and disease endemic countries must agree upon strategies for strengthening research capacity. Harmonization of such strategies was the focus of a recent meeting in Stockholm, on 3–4 April. The Donor Alignment and Harmonization in Cooperation on Research for Health: Meeting Barriers was organized by the Swedish Government’s aid agency (SIDA), involving over a dozen donor as well as recipient institutions. The stated goal of the conference was to ‘increase and improve impact of investments into structures and institutions in poor countries to ensure that knowledge and research capacities are built on a sustained basis.’ Conference participants agreed that five issues had to be addressed in order to achieve this goal:

- enhanced understanding of systems
- enhanced Code of Conduct regarding the ethics in collaborative work
- enhanced information sharing
- enhanced strategy development in country
- enhanced direct support for capacity development.

The meeting specifically noted that TDR has an important role to play in this process, through consolidating activities, facilitating synergies, and information sharing.

Funding agencies participating in the Stockholm meeting included: Sweden (SIDA), Norway (NORAD), the Netherlands (MFA, the Research Council, Science for Global Development, NWO/WOTRO and the Netherlands Platform for Global Health Policy and Health Systems Research), Denmark (MFA and the Danish Research Network for International Health), Canada (IDRC, CGCHR and the Global Health Research Initiative), UK (DFID), the World Bank, WHO/TDR, Howard Hughes Medical Institute, the Bill & Melinda Gates Foundation, EDCTP, and the Wellcome Trust. In addition, the Bamako 2008 Secretariat was represented.

African representatives included: WHO/Africa, ISHReCA (Initiative for Strengthening Health Research Capacity in Africa); Kenya Medical Research Institute (KEMRI) in Kilifi and Nairobi.

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Compiled with contributions from Camilla Dalla-Favera
30th session

STAC reviews new TDR business lines

In its 30th session, 25-28 February, TDR’s Scientific and Technical Advisory Committee (STAC) received a comprehensive report on the implementation of TDR’s Ten Year Strategy, particularly activities in the ’Stewardship’, ’Empowerment’ and nine research business lines. These business lines provide the operational focus of the Programme’s new strategy, endorsed last year by TDR’s Joint Coordinating Board.

At the meeting in Geneva, TDR staff presented plans and progress for each business line to STAC working groups, which reviewed and evaluated each plan, and then presented comments and feedback to the STAC plenary session. The “peer-reviewed” style format of the meeting was an innovation of STAC Chair Professor Peter Ndumbe. Overall, STAC members were positive about progress made so far. Recommendations included:

• TDR should further develop targets and impact indicators to reflect the pivotal role of disease endemic countries (DECs) in planning and priority setting.
• TDR should assist in the development of the WHO Research Strategy, utilizing expertise from formulating its own vision and strategy.
• Delivery of strategy objectives should reflect the importance of partnership.
• STAC welcomed the increased interactions with disease control groups and regions.
• TDR should consider equity in terms of socio-economic groups which benefit from interventions.

• Climate change should be factored into Stewardship and a watching brief should be kept on emerging and re-emerging diseases.
• Disease endemic countries should play a key role in TDR’s communication strategy.
• A strategy to deliver on innovation for product development in DECs should be further developed.
• TDR should explore the development of a policy under which research funded by the Programme be published for open and unrestricted access.

STAC members also emphasized that the sharing of information and efforts across business lines, and within networks and partner organizations, would be important to the overall success of the strategy.

For more information:
on the new TDR business lines and strategy: www.who.int/tdr.

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STAC visits Swiss Tropical Institute

TDR STAC members visited the Swiss Tropical Institute (STI) in Basel, 24 February, to view its facilities and learn of its research and services in tropical diseases, at the invitation of Professor Marcel Tanner, STI Director and outgoing member of STAC. The Swiss Tropical Institute has connections to TDR extending back to the 1970s. However, an even closer interaction with TDR developed following the arrival of Professor Tanner in the mid-1990s. While STI’s mandate extends to all tropical diseases, collaborations with TDR have related largely to malaria, schistosomiasis and human African trypanosomiasis. Collaborations also exist in social sciences, particularly gender research, and extend to GIS applications and spatial statistics, population-based and molecular epidemiology, and basic laboratory sciences. Over the years, STI has participated with TDR in numerous multi-lateral partnerships. STI faculty frequently serve on TDR committees and supervise TDR-supported doctoral students, many of whom have become internationally recognized scientists.

Professor Tanner has been a STAC member since 2001, and prior to that served on a number of other TDR committees. During the visit to the Institute, Professor Tanner was warmly thanked by STAC members and TDR Director Robert Ridley for his and STI’s contributions to TDR. “We will miss Marcel on STAC – his scientific wisdom and his good humour. But we know TDR and STI will continue to be linked through his efforts and those of his staff and students,” Ridley said. Ridley also thanked two other outgoing members for their longtime service to TDR, Dr Niels Ornbjerg, Director of DfI Centre for Health Research and Development in Copenhagen, and Dr Gill Samuels, formerly of Pfizer Inc. and currently Chair of the Foundation Council of the Global Forum for Health Research. “We look forward to continued engagement with both,” Ridley said.
A recently-published, three-year, multi-country study demonstrates how community delivery of under-utilized health interventions in an integrated manner can dramatically improve access to vital drugs and preventive treatments, particularly for malaria, in remote African communities.

The study of community-directed interventions (CDI) tested whether the strategy developed to deliver ivermectin for onchocerciasis (river blindness) in remote communities could be used to deliver a broader package of interventions – in this case, Vitamin A, insecticide-treated bednets, antimalarial medications, and tuberculosis treatment. The study was remarkable in size, covering some 2.35 million people in three countries. Results were released at the International Conference on Primary Health Care and Health Care Systems in Africa on 28 April. The study has also been the focus of a BBC World documentary. Jamie Guth, TDR’s communications manager, accompanied researchers to Garbachede, in northern Nigeria, to report on the CDI innovation.

ABUJA, NIGERIA – The sun has only recently climbed over the horizon as our crew assembles for the start of our journey. It is already hot and humid on this July day in Abuja, Nigeria. Ahead of us is a long day’s drive over rough roads of dusty red potholes weaving through small markets. We are on a journey with a BBC television crew to see how a very remote, northern Nigeria community has been able to double appropriate malaria treatment among children (the documentary is available on the TDR website at www.who.int/tdr).

Our destination is Garbachede, a remote village in northeastern Nigeria, almost a 15 hour drive from the capital city, Abuja. Here evidence is emerging that rural Africans can dramatically reduce the burden of disease from malaria through community-directed programmes of treatment. How and why did such a programme begin?

How it began

The concept of community-directed treatment with ivermectin first took root in this area about 12 years ago, at a time when onchocerciasis was still an omnipresent disease across large swathes of west, central and eastern Africa. The parasitic infection by *Onchocerca volvulus* causes people’s legs to look like mottled tree trunks, bringing on severe itching and disfiguring skin lesions, and in many cases, eventual blindness (thus the popular name for the disease – “river blindness”).

The parasitic worm is carried by the blackfly *Simulium damnosum*. The blackfly vectors breed mostly in fast-flowing water, and so the disease is most common in communities near rivers. Flies bite people, transmitting the parasite into the skin of their human victims. Each female worm produces millions of larvae that migrate throughout the body, and it is easy to see nodules of these worms just under the skin.

When ivermectin was registered as a treatment for onchocerciasis by Merck & Co. in 1987, TDR began working to find a means of assuring annual ivermectin treatments in the remote rural areas of Africa where the disease is endemic. Research was undertaken first with
Community-directed interventions’

Community drug distributor Cleophas Bakari distributing ivermectin to a family in the village of Garbechede, Nigeria.

The main steps in the CDI process

- Advocacy/Planning Meetings with Stakeholders
- Training of District/FLHF Staff
- Health Staff Hold Introductory Meetings with Community Leaders
- Planning Meetings with Entire Community
  - Community decides how to implement
  - Community selects implementers
- Training of Volunteer Community Implementers by Health Staff
- Community Implementation of the Interventions
- Monitoring by FLHF Staff
- Community Reports back to Health System

the Onchocerciasis Control Programme, then operating in West Africa (OCP), and later with the African Programme on Onchocerciasis Control (APOC), created in 1995 to address the disease in eastern and central areas of Africa.

In the mid-1990s, an innovative programme in which communities direct ivermectin distribution and treatment, was modeled and tested successfully. Since then, in coordination with APOC, the community-directed approach has been extended to more than 55 million Africans. By 2010, the programme will reach nearly one-sixth of the population of sub-Saharan Africa, moving the region significantly towards elimination of onchocerciasis as a public health problem.

In view of this success, APOC’s governing board, the Joint Action Forum, asked TDR in 2003 to investigate how the same approach could be used to deliver other critical primary health care interventions in the same communities. The community-directed approach with one treatment – ivermectin – was expanded to add other interventions, thus called ‘community-directed interventions’ (CDI). In 2005, trials of CDI were undertaken in 33 health districts in Cameroon, Uganda and Nigeria covering 2.35 million people.

And that is how we arrived here, at the conclusion of the three-year study that tested how the community-directed approach could be used to deliver other primary health care interventions of importance to the communities. Specifically tested in this study were four new interventions: distribution of Vitamin A, insecticide-treated bednets, and drug treatment for malaria and tuberculosis.
One community’s experience

On a rainy afternoon at the community health centre in Garbachede – a low concrete structure with no windows – we met Haruna Adamu Kirim, the local health worker, who has run the clinic for the past five years. In one area, about 20 young pregnant women were singing songs to help them learn how to have a healthy pregnancy. Elsewhere, a local family was getting their leprosy care. And a young herder had come in for emergency stitches of a gash in his finger from a cow horn. This is mainly a farming and cattle raising community, with nomads moving in and out with their herds.

Kirim was involved in the initial community discussions about what kinds of health issues should be included in the multi-country study. “I always come across lots of malaria, it’s the commonest problem,” he told us. “Then there is typhoid and gastroenteritis. TB is common as well. But the most common is malaria.”

“In fact, malaria was the most frequently identified problem across the 35 research sites here in Nigeria and also Uganda and Cameroon,” notes TDR’s Dr Hans Remme, who oversaw both the study design and its overall execution. “Thus, malaria prevention and treatment were two important interventions tested in the TDR study.” And indeed, final data from the trials showed that of the interventions tested, home management of malaria treatment had made what was perhaps the biggest impact in terms of disease control. “The final study survey indicated that treatment with appropriate drugs within 24 hours of the onset of fever had more than doubled coverage – from under 30% in the control sites to nearly 70% – higher than the Roll Back Malaria Programme targets for 2005,” said Remme.

But at the start of the programme, not everyone was optimistic that the study would yield such positive results.

“When I started I had my doubts as a scientist,” said Oladele Akogun, the primary investigator for this site. “These are not scientists, they are villagers. But when you give them broad initiatives, they come up with the answers for the community. For example, giving Coartem® (Artemether lumefantrin) when someone comes down with malaria, any time of the day or night, I never had thought we could get someone to do that. I just thought about getting a community drug distributor. But they decided to incorporate women into the system, who were indeed willing to do this. They didn’t tell me. I only found out about it later during monitoring.”

Esther Bokawurkum is one of the mothers who was selected by the community to be a drug distributor for malaria. She maintains a stock of Coartem® in her home, keeps records on who is treated and checks to make sure that the full dose is taken.

She told us, “I think my neighbours prefer coming to me because I monitor the dosage they have to give to their children, unlike at the health clinic where they are just
given the drugs and some instructions and left to do it on their own. I am nearby and they can easily rush to my house, even in the middle of the night, and I will attend to them.”

Over the course of the study, the researchers found that more women attended community meetings, spoke out and demanded responsibilities, and were selected as CDI implementers, particularly as a result of the growing awareness of their potential role in malaria treatment.

Haruna Adamu Kirim, who has overseen the training for the drug distributors in his role as head of the community health centre, became convinced by his own experience with community-directed treatment. “I can see that they can definitely do it,” he said.

Cleophas Bakari, another one of the community drug distributors recruited by the village, wasn’t sure in fact that he could. “At first I had doubts,” he recalled. “But later, I went for the training, and as the training went on, I learned that I could do the job well.” Cleophas now makes sure that all of his family members and others who turn to him have their annual dose of ivermectin, and he also distributes bednets and shows neighbors how to treat them with insecticides. Bednets were the second intervention whose use increased very significantly in the CDI study districts, as compared to the control districts where distribution continued through traditional channels. At the conclusion of the third year of the study, the proportion of households possessing at least one insecticide-treated bednet approached the Abuja Roll Back Malaria target of 60% for 2005, despite a continuing shortage of nets.

Along with looking at coverage, the study also examined what made the CDI strategy work. What motivates drug distributors such as Cleophas, and how they are reimbursed, was one issue examined since the community drug distributors essentially work as volunteers, and communities decide if and what kind of reimbursement they can offer. In most cases, while small tokens of food, transportation, cash or in-kind farm labor were often preferred, the study found that there were also powerful motivators of community recognition and status, the feeling of making a contribution or learning something new and valuable.

Cleophas told us, “My community members are happy whenever I help them. Since I don’t get paid, some of them will give me some money, they might give me about 10 or 15 cents (10 or 20 naira). And some of them will help me by informing other people who are not around when I visit. They tell them that the drugs are available and that the community drug distributor has arrived.”

Community empowerment

The core of the CDI research concept is to support community empowerment. Decisions are made in the open at community meetings where everyone is invited. Garbachede, for instance, is a mixed community of half Christians, half Muslims. The Muslim cleric is also the village chief, and he himself was blinded by onchocerciasis. When we visited, he sat on a woven mat under a tree in the middle of a group of about 250 people clustered closely around him. A local researcher translated the proceedings from the local Hausa language for our film director. One man complained that households near him had not received their annual ivermectin treatment to prevent river blindness. A representative from the health clinic asks him to be more specific. Who missed out and where? Other people then began to list names and places. Soon, the health worker proposed that the community update the census, to establish exactly how many people live in the area. The idea was met with en-

Investigator (center, left) interviews a community members in a village in West Province, Cameroon.
The results

The CDI approach was shown to be much more effective than currently used delivery approaches for all studied interventions except DOTS treatment for TB.

- **Malaria treatment:** More than twice as many children with fever received appropriate antimalarial treatment in CDI study districts. The percentage receiving appropriate treatment, on average, exceeded the 60% target set by the Abuja Declaration of the African Summit on Roll Back Malaria for the year 2005.

- **ITNs for malaria prevention:** Possession and utilization of insecticide-treated nets (ITNs) was two times higher in the CDI districts, despite shortages of ITNs in most research sites. In the CDI study districts, the proportion of households possessing at least one ITN approached the 60% target set by the Abuja Declaration of the African Summit on Roll Back Malaria for the year 2005.

- **Vitamin A:** Vitamin A coverage was significantly higher in the CDI districts than in the comparison districts, with 90%, on average, of eligible children receiving the supplements in the CDI districts.

- **DOTS treatment for TB:** Only in the case of DOTS were no significant differences noted in coverage for CDI districts and comparison districts; satisfactory completion of DOTS treatment was around 90% in both cases.

- **Ivermectin for onchocerciasis:** The addition of multiple interventions to the CDI package did not have any negative effect on treatment for onchocerciasis, but in fact boosted ivermectin treatment by an additional 10%.

- **Integrated delivery of interventions:** At least four to five interventions could effectively be implemented through CDI strategies. The coverage with the different interventions generally increased over time in the CDI districts, reflecting “maturation” of the CDI process.

With respect to costs to the health system, CDI was also more efficient than conventional delivery systems. Without any increase in implementation costs at the health district and first line health facility (PLHF) level, the CDI process achieved higher coverage for different interventions. At the community level, there was an increase in ‘opportunity costs’ with CDI, reflecting greater time commitment from community implementers who generally volunteered their time, thus forgoing other remunerative activities. Intrinsic incentives, such as recognition, status, knowledge and skills gain, were generally perceived as more powerful motivators in the process than material incentives.

There were no specific technical limitations that prevented community implementation of any of the interventions. When given the necessary training and support, community implementers demonstrated that they could effectively implement each of the five study interventions, irrespective of their level of complexity, and were indeed eager to use the approach and sustain it over a period of time. However, the major observed constraints were social constraints (acceptability and appropriateness of the intervention) and health system constraints (e.g. shortage of supplies; reluctance of health workers to empower community implementers to manage TB drug administration; and, in some isolated cases, health policies restricting distribution of antimalarials by anyone other than certified health services staff).
WHO Nigeria malaria programme officer Bayo Fatunmbi (on left) and other local, regional and national officials, meeting with the Governor of Taraba State, His Excellency Damboda D. Suntai (on right) to discuss scaling up the programme.

“I will try to meet with our traditional healers and other officials here in Bali to discuss this,” Otsemobor replies, “This can start immediately. Don’t wait until August. There are drugs and nets from the federal government and the Global Fund, you just need to keep this going now that the research is ending.”

Following their exchange, we made a visit to the community’s spiritual chief to see where he stood on the matter at hand. We removed our shoes before entering his chambers, passing through sheer white curtains into a sanctuary carpeted with dark, red wool. The chief, while not an official government figure, is a traditional leader who plays an important role in community affairs, as an advisor and opinion-maker.

Visits like this one underline how important stakeholder involvement have been to the success of the process, principal investigator Akogun later emphasized to us. “TDR has made stakeholder engagement very important. I believe this approach should be a component of any research funding,” he said. “From the start, the users of the research products are brought in. Everyone sees that WHO is playing a role, the federal ministry and state governments play a role, as do local governments and NGOs. So when the research results are published, there is pressure at all levels, on the NGOs, local government, the state government, etc. to act upon the findings. This has already made a huge difference.”

Most fundamentally, stakeholder involvement has been critical to CDI’s widespread acceptance by communities – along with the concrete health gains achieved. Esther Bokawurkum, a volunteer community drug distributor, is among those who hopes the programme will expand: “I will be very happy if more interventions are introduced into the community. We live in a very remote, rural area and there are so many diseases here which affect us. So if more interventions are introduced, we will have fewer sick people in the community. Everyone will be at peace and the number of people dying will fall.”

From research to scaling up

Results of this ground-breaking research were publicly released at the International Conference on Primary Health Care and Health Care Systems in Africa, in Ouagadougou, Burkina Faso, on 28 April. Prior to that, findings and conclusions of the study were presented at the 13th session of the Joint Action Forum (JAF), the governing board of the African Programme for Onchocerciasis Control (APOC), in December 2007. The JAF endorsed the key recommendations emerging from the study – namely that CDI systems used for distribution of ivermectin should now be used more widely to deliver a broader package of health treatments. The JAF also called upon TDR to spearhead new research on practical guidance and tools for the use and scale-up of the approach.

APOC will be using this research evidence to expand its model through all the African countries that have successfully used the community-directed approach for ivermectin. The potential is great – reaching Roll Back Malaria targets so that vulnerable children and pregnant women sleep under bednets, and doubling malaria treatments.

For more information:

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Public health initiative involves rural entrepreneurs

TDR evaluates free antimalarial distribution through CFW franchises

In central Kenya, where water-sodden rice fields thick with mosquitoes make malaria a daily fact of life, a new and innovative model of small franchise health clinics and drug distribution shops is offering poor people new possibilities to access good quality drugs and treatments at affordable prices.

NJUKA, KENYA – The model of Child, Family and Wellness (CFW) shops now is being evaluated by TDR to see how effective it may be in getting needed drugs to poor, rural families, and lowering rates of serious illness.

The shops operate under a unique formula of a public-private partnership at the local level. Trained nurses or shop operators run their own businesses. But they operate under a franchise arrangement with a Kenyan-based NGO, Sustainable Healthcare Foundation (SHEF), which provides quality-assured drugs and other much-needed health products (e.g. water purification tablets and insecticide-treated bednets) to the outlets. SHEF, moreover, sets uniform, affordable prices for tests and procedures – and in the case of ACTs, provides them for free in conformity with Kenyan government guidelines. SHEF also provides training and supervision to shop owners and health care providers.

The CFW model was created in the year 2000 by HealthStore Foundation, a US non-profit organization that operates SHEF. It aims to fill the gaps that exist between the overloaded public systems, the unregulated private sector, and donor-funded initiatives that may provide solutions for a brief period but are not sustainable over time.

Of the 65 CFW outlets that have opened in central and western Kenya over the past several years, 48 have a dual role as a shop and clinic staffed by nurses and offering basic tests and health services, while the remaining outlets operate as shops only. The model, if shown to be effective, could provide a way forward for getting rapid malaria diagnosis and life saving treatment with artemisinin-combination therapy (ACT) to remote rural communities in parts of Africa in a sustainable manner, says TDR’s Dr Franco Pagnoni, acting leader of the ‘Evidence for antimalarial policy and access’ business line (BL 9).

TDR is currently evaluating a pilot project whereby 18 SHEF outlets are distributing free ACTs alongside their other for-pay drugs and services, to see if this can improve rates of ACT use in poor, rural parts of Kenya.

The pilot project was initiated in response to a 2006 Kenyan government recommendation that older antimalarial treatments, to which malaria parasites have become resistant, be replaced with the new ACT, particularly artemether lumefantrine (AL), Coartem®.

SHEF began to introduce ACTs into the CFW franchises in late 2007. Since AL is only given in Kenya following a positive diagnosis of malaria with a rapid test, it can only be offered in those SHEF clinics or shops that are staffed by a qualified nurse or other health worker. TDR was asked by SHEF to evaluate the extent to which the ACT distribution through the CFW system improved access for children in rural populations to appropriate antimalarial treatment. Appropriate treatment, as defined by Roll Back Malaria, means access to ACT treatment within 24 hours of onset of fever and/or a positive rapid test diagnosis of malaria.

The TDR field assessment of ACT distribution through the outlets began last year. A Nairobi-based research firm, the Steadman Group, performed a baseline household survey prior to the introduction of ACTs into the network...
and determined that in targeted communities, only about 15% of the children with malaria received appropriate antimalarial treatment. A follow-up survey is now in the final phases, after being delayed due to the unrest that followed the Kenyan elections.

This study is a good example of implementation research, an area in which TDR is expanding its focus, where the use of practical tools is examined scientifically in the field to see how they perform and how they may be improved or applied to other health interventions.

“We set out to define how much the distribution of ACT through the CFW network could increase access of the population to this good-quality treatment,” says Pagnoni. TDR’s BL 9 is engaged in a range of research efforts examining ways to scale up home and community-based management of malaria. “If the results from our study are positive, this may provide an incentive for stakeholders to expand the CFW model both in Kenya and elsewhere.”

On a recent TDR tour of CFW shops in central Kenya, Regina Nyaga, a Kenya-enrolled Community Health Nurse at the Nzuka CFW clinic, said that indeed, the proportion of children becoming seriously ill from malaria seems to have dropped significantly since she started prescribing the new ACTs. Most of her clients are the families of farmers growing rice in the water-logged fields that chronically harbour mosquitoes carrying the *Plasmodium falciparum* parasite. Nyaga notes, however, that patients often distrust the rapid malaria diagnosis, and demand treatment even when the test is negative.

It thus remains a challenge to nurses like herself to convince clients that the fever might be the result of another condition. “We encourage them to be tested for typhoid [for instance],” Nyaga says.

Her comments offer an example of how the CFW franchises, operating under the technical supervision of an NGO umbrella, can ensure more appropriate treatment through adequate training of staff. NGO supervision also provides for strict quality-control of the drugs provided through its outlets to avoid the problems encountered when counterfeit or inappropriate drugs are sold in poor communities at exorbitant prices.

SHEF obtains its drugs in bulk at a discount rate from reputable suppliers, and ships directly to franchises. Apart from ACTs, which are being provided free of charge in the pilot, all the other drugs and tests are sold to franchisees at cost with a maximum 10% additional charge to cover distribution costs. This ensures sustainability of the system while providing poor people with access to health products for a minimal cost.

While services and drugs at conventional private clinics can be prohibitively expensive and vary greatly according to locale, the CFW shop prices are the same across all retail drug outlets both for drugs as well as for nurse consultations and tests. “You will see exactly the same price if you walk into any franchise,” says Athuman Chiguzo, Malaria Project Coordinator for SHEF. Despite the set prices, SHEF says franchisees are making sustainable incomes from outlets by using economies of scale. For instance, they may buy medicinal syrups in bulk from SHEF at a reduced cost, and then sell individual 100 ml doses to patients. Says Chiguzo, “We have control in terms of drugs and prices but the income is sustainable.”

SHEF also assesses the business case for an outlet in any given area before it agrees to a franchise. It sends field-workers to analyse the incomes of people living in that area, and the position of the premises. Once given the go-ahead, the franchisee is responsible for renting and maintaining the premises, and recruiting and paying staff. SHEF supplies shop-front signs and other branding materials.

But there is still much work to do in terms of improving access to ACTs in the CFW network. Preliminary results from the survey suggest that some CFW outlets are perceived merely as pharmacies rather than health facilities because of the very basic services on offer. Others do not have enough testing kits. However, the survey found that many patients welcomed the convenience of a nearby healthcare source, services provided on credit and subsidized insecticide-treated nets (ITNs).

At the same time, due to its own difficulties accessing ACTs, SHEF is still offering the drugs in only a few of its clinics. Some initial support for the pilot ACT project and TDR evaluation came from ExxonMobil while the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) provided the ACTs free of charge. However, GFATM has yet to release funds that will pay for antimalarial treatments across the entire SHEF network, says Chiguzo.

Observes Pagnoni, “Once we have the results from this project, and if they are positive, we would naturally like to see the initiative expanded and then test the approach across the broader selection of SHEF outlets.”

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“With reporting by Tatum Anderson in Kenya

**Baseline survey of malaria medications**

<table>
<thead>
<tr>
<th>Medicines taken</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroquine</td>
<td>2%</td>
</tr>
<tr>
<td>Quinine</td>
<td>17%</td>
</tr>
<tr>
<td>Amodiquine</td>
<td>27%</td>
</tr>
<tr>
<td>AL 15%</td>
<td></td>
</tr>
<tr>
<td>Other antimalaria</td>
<td>14%</td>
</tr>
<tr>
<td>SP 32%</td>
<td></td>
</tr>
</tbody>
</table>

Medicines taken, 410 patients interviewed.
A baby with severe malaria who was given rectal artesunate at home to stabilize his condition until his mother could carry him for several hours to the nearest hospital. Local mothers were trained to give the artesunate as part of a study of the TDR-fostered drug formulation to see if this could increase the number of children treated early and effectively. (Tanzania • 2006 • WHO/TDR/Cragg)
As TDR celebrates the 30th anniversary of its Joint Coordinating Board (JCB), we share excerpts from TDR’s new history of the ‘people, products and partnerships’ that made a difference to public health.


Phase III

TDR’s third decade was one of expansion — new diseases, a new sponsor (UNICEF), and expanded outreach and collaborations. Dengue and TB were added to the portfolio, as well as diagnostics for TB and sexually transmitted diseases. TDR helped incubate and launch several new public-private partnerships for drug and diagnostics development, and led a major initiative in global drug discovery research networks. The Programme also stimulated global collaborations in genomics, including sequencing of the A. gambiae genome. Field research was extended to help scale up interventions, and social, economic and behavioural research played an enhanced role. TDR moved into broader spheres of capacity-strengthening, including good research practices, ethical review, South-South collaborations, and international research networks linked by new technologies.

WHO Directors-General
Dr LEE Jong-Wook (2003–2006)
Dr Margaret Chan (2007–present)

TDR Directors
Dr Robert G. Ridley (2004–present)

Highlights
Incubation and foundation of MMV and FIND • Support for creation of TB Alliance and DNDi • Establishment and transition of several anti-malarial drug development projects to MMV and DNDi • New drug discovery networks • Miltefosine for visceral leishmaniasis • Tools and field research supporting visceral leishmaniasis/lymphatic filariasis elimination campaigns • Validation of syphilis diagnostics for elimination efforts • Validity of ACT use in home management of malaria • Rapid assessment (RAPLOA) of onchocerciasis/Loa loa co-endemicity • Extension of community-directed interventions beyond onchocerciasis • Anopheles gambiae and Tritryps genome collaborations • Partnering MIM • Establishment of SIDCER • Thousands of people trained in new RCS short courses • 70% of R&D partners engaged are from developing countries.
Catalyzing partnerships and collaborations

A third external review in 1997/98, as well as the arrival of new TDR director Dr Carlos Morel, a former president of FIOCRUZ with a background in biotechnology and national policy-making, heralded yet another shift in the tenor and tone of TDR. Indeed, if the foundation decade was focused on disease portfolios, and the second decade increased emphasis on field research, the third decade of the programme would re-focus on product development and partnerships for new research efforts. Although TDR had always operated as a network-based organization, the programme would assume a greater role as a catalyst and leader of initiatives in drug development, diagnostics, genomics and research capacity strengthening that would, in many cases, go on to be formally developed by other entities. In recognition of TDR’s impact on health and its vital contribution to attaining the MDGs, a new UN co-sponsor, the United Nations Children’s Fund (UNICEF), committed its support in 2003.

A ‘trans-disease’ approach was introduced, with activities organized in business-like managerial structures, with reference to both a matrix of diseases and functional areas of research (Morel, 2000). Priority setting was driven both by identifiable research opportunities and the needs posed by the burden of disease. One immediate issue was the global re-emergence of both TB and dengue in epidemic proportions; both dengue and TB were added to TDR’s portfolio of diseases by the JCB, as well as a pilot project on diagnostics for sexually transmitted infections. Later in the decade, still more changes would be introduced by the departure of Morel and the arrival of present-day TDR Director, Dr Robert Ridley, a biochemist with experience in Africa, academia and industry, who would preside over a fourth external review and development of a new TDR Ten Year Strategy.

Promoting new partnerships for drugs, diagnostics and innovation

One of the remarkable aspects of TDR since its early days has been the pioneering collaborations the programme fostered between the public and private sectors, perhaps unparalleled in other global public health institutions (TDR, 1986). However, as the volume of research activity increased, along with cost and complexity, more formal partnerships became necessary. TDR began to shift successful, but relatively expensive, product R&D projects into new or existing PPPs.

In 1999, TDR finalized the launch of the Medicines for Malaria Venture (MMV). A year later, TDR played a significant role in creating the Global Alliance for TB Drug Development (TB Alliance), which had the director of TDR as its first chairman of its board. And in 2003, TDR helped create yet two more PPPs, the Drugs for Neglected Diseases initiative (DNDi) and the Foundation for Innovative New Diagnostics (FIND).

TDR has continued to play a role in development of drugs where needs and gaps exist. For instance, Miltefosine for visceral leishmaniasis was developed as a direct collaboration between TDR, the pharmaceutical firm Zentaris and the Government of India. TDR also has carried rectal artesunate through with

Eco-bio-social research — linking health and environment to dengue disease control

"Eco-bio-social" research has been another emergent sub-theme in social research at TDR. This identifies links between health, environmental and social factors that might be harnessed more effectively for disease control, particularly vector control. TDR-sponsored eco-bio-social research has focused so far on dengue. As there is no effective drug cure, integrated vector management (IVM) including vector control and appropriate diagnosis and rapid treatment, are recognized as the most promising strategies. A landmark TDR-sponsored multi-country study on dengue vector breeding sites set the basic research groundwork for better environmental management of dengue (Focks, 2003; Focks & Alexander, 2006). Knowledge of how to identify and target breeding sites has helped drive more successful programmes of vector control in South-East Asia and elsewhere (Nam, 2003; Kay, 2005). Recently, TDR and the Canadian-based International Development Research Centre (IDRC) embarked on a multi-country initiative to examine a broad set of eco-bio-social factors affecting dengue transmission. The TDR/IDRC initiative includes six studies in high-endemic South and South-East Asian countries.
a pharmaceutical partner to final registration, now pending. And TDR continued to lead the development of gatifloxacin for TB, a drug that potentially shortens treatment from six to four months. Moxidectin, which is being investigated as a possible macrofilaricide for onchocerciasis, is now in Phase II trials in a collaboration with Wyeth Pharmaceuticals.

Genomics — towards a malaria-free mosquito

Genomics was another area where TDR would stimulate partnerships and collaborations, leading to major basic research advances. Already in 1991, TDR had convened a groundbreaking meeting in Tucson, Arizona, together with the MacArthur Foundation, to propose the genetic engineering of *A. gambiae*, rendering it incapable of harbouring or transmitting the *Plasmodium* parasite (Morel et al., 2002). However, at the time of that meeting, the idea of actually sequencing the entire genome of a mosquito was out of reach. Not so a few years later, when genome sequencing became possible not just for microorganisms, such as the Tritrys, but for more complex species.

In 1998, TDR organized a consortium to sequence the *A. gambiae* genome. The initial meeting was small and high-level. TDR contributed US$ 250 000 for the creation of the gene libraries and databases to house the sequence data, while other consortium members contributed a total of US$ 9 million to complete the project. In October 2001, TDR and the Pasteur Institute announced the formal launch of the initiative, while work was already underway. In 2002, just one year later, results were ready to be published. Although TDR’s monetary investment in the effort was relatively small, the initiative was an example of how strategic leadership and leverage at a critical moment can stimulate science advances.

Meanwhile, research to develop a transgenic mosquito had made enormous progress, aided by the new knowledge of the *A. gambiae* genome sequence. By 2001, TDR had supported more than 100 projects in 19 countries to identify parasite-inhibiting genes in mosquitoes, to genetically modify mosquitoes; and to drive selected genes into natural populations. As these advances paved the way for field trials, TDR initiated discussions on the ethical, legal and social implications of testing and evaluating transgenic mosquitoes (Macer, 2003). Meanwhile, in terms of capacity-strengthening, a South–South Initiative for Tropical Diseases Research (SSI) was launched in 2001 to bring together researchers in developing countries doing applied genomics research, and link them with partners and resources in developed countries.

Discovery research — facilitating global networks

The huge advances in the understanding of vector and pathogen biology would, in turn, shape and influence TDR discovery research strategies. The challenge is to harness that knowledge to the search for novel lead compounds that can form the basis for innovative disease treatments. TDR would cast its net into the sea of compounds that had so far not been explored, searching broadly but systematically for novel leads. Alongside traditional whole-parasite screening techniques, this effort would harness the new tools of genomics, combinatorial chemistry and robotics to full advantage.

Three decades earlier, the TDR network approach had proved itself with ivermectin. Now, the TDR compound-screening network was revitalized and expanded to include a broader range of academic and research institutes, and also industry partners. New research networks for medicinal chemistry, pharmacokinetics, drug target portfolios and helminth drug discovery were created to cover other stages of the drug discovery process.

Major industry collaborators have opened their vast medicinal chemistry libraries (for example, those at Pfizer, Merck-Serono and Chemtura) to the TDR research networks, also training developing country scientists in their laboratories, under TDR auspices. TDR’s discovery research programme has also supported the creation of a new global research portal, a Drug Target Database, to facilitate research on potential drug targets.

Diagnostics

Responding to the concerns of disease control partners, TDR took on yet another unmet need — research into diagnostics. With parasitic and bacterial drug-resistance on the rise, getting good diagnostics...
Research capacity strengthening (RCS) — networks for training

TDR’s third decade witnessed the development of major new research networks and regionally-based training centres, as well as short courses and training programmes in targeted areas of need. These new networks and training formats build clinical and research skills and awareness among diverse groups of health workers, including nurses and technicians, complementing ongoing grant programmes for institution-building and for academic degree work. All in all, over 1000 people have been trained in the new format of short courses between 2000 and 2005, along with the continued support for degree students.

In many cases, TDR catalyzed or supported new capacity-building partnerships that are now led by others. Key examples include SIDCER (Strategic Initiative for Developing Capacity in Ethical Review); FAME (Forum for African Medical Editors); and the South–South Initiative for Tropical Diseases Research.

In terms of institution-building per se, TDR turned its attention to long-term support in the least developed countries where research capacity is weakest. TDR training grants for academic studies at Masters and PhD levels, likewise, have evolved from the early days when they were merely another form of scholarship to enable students from developing countries to attend university abroad.

Today, 80% of holders of TDR-supported training grants pursue their research and training in local or regional institutions, and individual training grants are designed to contribute to institution development and sustainability.

The thousands of scientists trained, and the fact that some 70% of R&D partners engaged by TDR between 2000 and 2005 were from developing countries, may provide quantitative indicators of the cumulative impact of RCS. However, such measures still fail to capture the multi-dimensional impact of RCS activities over time, notes Dr Bernhard Liese, Chair of International Health Programs at Georgetown University and the World Bank’s former representative on the JCB.

“Twenty-five years ago, if you went to Africa to do research, you would be running into a lot of expatriates,” Liese observes. “Today, if TDR organizes a meeting in Africa, it will be mostly African scientists attending, and sharing a common scientific culture and perspective about disease control problems that need to be addressed — and much of that is due to TDR’s influence. TDR, in effect, trained two generations of African scientists. You can count number of heads trained, but that still misses part of the story.”

to the field ensures that treatment is more effective and that drugs are used only when necessary. Sexually transmitted diseases provided the initial focus of TDR efforts. At least 500 000 stillbirths and miscarriages occur every year as a result of congenital syphilis, as many babies are born with the disease. Research at TDR sites in Haiti, China, Brazil and Tanzania in which rapid syphilis tests were tested has already stimulated several severely affected countries to increase prenatal screening for syphilis and foster initiatives for the elimination of congenital syphilis. Used widely in Africa, such diagnostics could help countries to reach the MDG goal of improving maternal health and reducing mortality of children under the age of five. Also, in 2003, TDR, together with the Bill & Melinda Gates Foundation, created Foundation for Innovative New Diagnostics (FIND), a public-private partnership (PPP) dedicated to the development of rapid, accurate and affordable diagnostic tests for developing countries. FIND and TDR have jointly launched projects to improve TB diagnostics. Most of the estimated 9 million people who develop active TB every year are not diagnosed with sensitive and reliable tools, if they are diagnosed at all.

Home management of malaria — diagnosis and treatment

Implementation research on home and community-based management of malaria became another key TDR focus in its third decade, continuing into the fourth. Home and community management involves the training of mothers, drug vendors, village volunteers and teachers in the first line of care for malaria when health clinics and health care providers are not accessible. The effectiveness of home management has been demonstrated by TDR over the past five years, reducing mortality by 40% or more in some studies. Further research is now underway to determine whether more complex artemisinin-based combination therapies (ACTs), as well as malaria rapid diagnostics, can also be administered at the home and community level.

Community-directed models for primary health care

At the turn of the millennium, community-directed treatment (ComDT) was well established in hundreds of thousands of African communities, with tens of millions of people receiving annual treatment. Recognizing this model’s potential, and at the request of the board of the African Programme for Onchocerciasis Control
(APOC), TDR in 2004 launched a multi-country study to examine to what extent a community-directed approach could be used for the integrated delivery of other underutilized drugs and tools.

Final results from multi-country study into ‘community-directed interventions’ (CDI) (see page 8) demonstrate how integrated delivery can dramatically increase access to certain underutilized interventions. In health districts using CDI, the percentage of people covered by insecticide-impregnated bednets and home-administered antimalarials was double or more the coverage of comparison districts, where delivery was by conventional means.

“The theory was that this same approach would be useful for other interventions, and we built upon it,” says TDR research coordinator Dr Hans Remme. “Presented with the evidence of the effectiveness of CDI, the board of APOC has now strongly recommended it should be used on a wider scale.”

Towards disease elimination

At the close of the programme’s third decade, four of the original eight TDR diseases — leprosy, Chagas disease, onchocerciasis and lymphatic filariasis — were advancing towards regional or global elimination as public health problems. Spurred by new drug innovations and other breakthroughs, WHO and partner countries India, Nepal and Bangladesh drafted a framework for the elimination of visceral leishmaniasis as a public health problem on the Indian subcontinent by 2015. Strategies are diverse and include mass administration of TDR-evaluated drugs, often offered at preferential prices by pharmaceutical companies; increased use of multidrug combinations rather than monotherapies; and finely tuned strategies for drug distribution that harness not only health systems but also the resources and interest of the communities themselves. Although elimination programmes are designed and carried out by WHO together with the countries themselves, and not TDR, they are underpinned by TDR-supported research.

“TDR research has helped us get to the stage of disease elimination,” says Ridley. “Continued TDR research is needed to make sure elimination happens and is sustained.”

In the next issue of TDRNews:
Making a difference, Phase IV

Full text available at:
www.who.int/tdr/about/history_book/anniversary_book.htm
Helping DEC authors publish

Welcome to AuthorAID@INASP

TDR has recently joined a new pilot venture by the International Network for the Availability of Scientific Publications (INASP), supporting developing countries authors to publish their research.

In the world of health research, publication in peer-reviewed journals is the primary tool for science communication – conveying new discoveries, findings and innovations to the global marketplace of knowledge. Yet researchers from disease endemic countries still remain seriously under-represented as authors of peer-reviewed publications, particularly in journals with global reach and reputation. This is despite the fact that these researchers are closest to the challenges that confront the developing world, and their findings and insights are critically relevant to addressing neglected diseases of poverty.

To address these barriers, TDR has recently joined a new pilot venture launched by the International Network for the Availability of Scientific Publications (INASP) that aims to support authors from developing countries in the preparation of research manuscripts, policy-relevant commentaries and editorials for publication.

The initiative, called AuthorAID@INASP, has designed a set of model activities to help authors move more easily through stages of research publication, from concept development, to writing/editing and placement. These activities are now being tested through TDR’s research networks and through a second pilot project partner, the Swedish-based International Foundation for Science (IFS).

The AuthorAID@INASP initiative aims to overcome many of the subtle barriers that exist for DEC researchers seeking to publish. For instance, authors frequently report uncertainty about suitable journals for their work. Unfamiliarity with editorial conventions and the persistent pressure to write in English also are concerns as are conflicts with collaborators about authorship and author order; unfamiliarity with statistical tools to analyse data; and, more generally, editors’ and publishers’ inattention to ‘development’ topics.

The editors of journals throughout the world present a complementary picture – many manuscripts have merit (including adequate research design and data collection) but may require too much additional analytic or editorial effort and are rejected early in the review process.

The new AuthorAID@INASP demonstration project includes three elements:

• matching and mentoring of developing country authors with experienced scientists and editors undertaken through a monitored and evaluated process;
• outreach for participants through workshops in the field;
• a web-based knowledge community focused on science communication promoting INASP and link the initiative with other similar endeavours, e.g. AuthorAID projects at the Council of Science Editors and the International Society for Environmental Epidemiology.

As a first step in the effort, TDR recently conducted through its e-network of scientists a survey of early career researchers who might benefit from AuthorAID support and a second survey of senior researchers interested in becoming mentors to less experienced colleagues. These results are now being processed.

Although the initial pilot with TDR will naturally relate to research on neglected diseases of poverty, the broader project will include all forms of science communication, and not be limited to a single discipline or set of problems. While it will also proffer assistance to publishers and editors who can help diminish the DEC publication gap, AuthorAID@INASP will be consciously “author-centric”, responding first and foremost to the needs of authors.

The three-year AuthorAID pilot project, supported by the Swedish International Development Corporation Agency (SIDA) and the UK Department for International Development (DFID), will be carefully monitored and evaluated to see what impact the activities have on the quality and quantity of publications by participants.

The project meanwhile has been well received by scientists and donors, says Steven Wayling who is coordinating the effort for TDR. He notes that while both developing countries and donors have supported enormous expansion of research capacity in developing countries as well as in information resources, e.g. libraries, there is increasing recognition of how closing the research publication gap can complement other capacity-building efforts – enhancing global access to DEC research results and knowledge.

More information:
http://www.authoraid.info/

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When is a disease neglected?

Most of the infectious diseases of poverty do not attract the level of research funding that they deserve, given their impact in terms of morbidity and mortality. Many infectious diseases are therefore categorized as ‘neglected’, but there is no universal agreement as to which infections are neglected and which are not. Typhoid fever is not usually considered to be neglected, as infection rates can be maintained at a very low level, providing supplies of clean water and good sanitation are available. There is also an effective vaccine. However, Professor Zulfiqar Ahmed Bhutta, of the Department of Paediatrics & Child Health, The Aga Khan University Karachi, Pakistan, has made a compelling case for typhoid to be given the ‘neglected label’. In an Editorial Opinion article on TropIKA.net, he says there is evidence that the infection is more common than generally recognised, particularly in children. There is insufficient use of the vaccine, reports of resistance to antibiotics are becoming common, and the most frequently used serodiagnostic test (the Widal test) is over a century old and lacks reliability. Nevertheless, Professor Bhutta writes, “… concerted action to address typhoid fever systematically within the research or development community is still sadly lacking.”

http://www.tropika.net/svc/editorial/bhutta

The world can well afford the malaria vaccine

A distinguished malaria researcher says that a shortage of funds should not stand in the way of developing an effective malaria vaccine. In an address to the Molecular Approaches to Malaria Conference, Lorne, Victoria, Australia – also published as an Editorial Opinion on TropIKA.net – Sir Gustav Nossal said that researchers have achieved things that 25 years ago would have been thought impossible. Research funding has also now reached a high level. He cautioned that it is not only money that is needed, “We need better and more benign governance structures in the developing countries and a great deal less corruption. We need to forge true partnerships with developing countries with their scientists and health officials putting major input into the programmes. We need better physical and human infrastructure in most of the developing countries.” Sir Gustav also warned of the dangers of overpromising; it is important to speak of control rather than eradication. Nevertheless, he concluded that “…if malaria researchers do their work well, then over the next decade or two we will have a malaria vaccine that works; we will have more and better drugs; we will have smarter vector control strategies; we will be combining these with bednets and diverse public health measures. The combination will gradually bring this wiliest of foes under control.”

http://www.tropika.net/svc/editorial/gn/Nossal20080331
In the old days, a ‘review’ in the context of the world of science journals was likely to refer to one recognized expert putting his own personal spin, and perhaps idiosyncratic view, on a known problem or issue. More recently, the term ‘review’ has become best associated with processes like that of the Cochrane Collaboration. Now, however, the new TDR-sponsored web portal, TropIKA.net, is pushing the definition of reviews one step further, creating a new review series geared to the infectious diseases of poverty. Dr Pecoul said that DNDi is on target for meeting the goal, set to be reached by the year 2014, of developing six new treatment drugs including two for malaria. However, he added that: “We know that before 2014 we won’t be able to develop the best treatment that is totally adapted to the situation. That is why in parallel we will have to go back to the discovery stage and build a pipeline.” Looking further ahead, he said, “We strongly believe DNDi is a model that should be transferred and made more sustainable. In the long term we consider these solutions should come from the countries affected by the disease.”

http://www.tropika.net/svc/interview/Anderson20080328

Focus on high-level genomic research comes under fire

In an interview for TropIKA.net’s ‘Stakeholders’ section, Professor David Molyneux, Director of the UK’s Lymphatic Filariasis Support Centre, said: “The world is starting to look differently at drugs for neglected diseases. I would never have believed the bandwagon would have started to run. People are beginning to take notice.” However, Professor Molyneux – formerly Director of the Liverpool School of Tropical Medicine and this year’s President of the UK’s Royal Society of Tropical Medicine and Hygiene – added that he disagrees with many of the current research priorities. He said the aim should be ‘maximum impact – minimal expenditure’ and argued against a focus on high-level genomic research: “There are cheap existing drugs that can treat the parasite effectively ... The money [spent on genomic research] would have been able to treat the majority of the population at risk in Asia.”

http://www.tropika.net/svc/interview/Anderson20080306

TropIKA.net reviews: Taking the review revolution one step further

In the old days, a ‘review’ in the context of the world of science journals was likely to refer to one recognized expert putting his own personal spin, and perhaps idiosyncratic view, on a known problem or issue. More recently, the term ‘review’ has become best associated with processes like that of the Cochrane Collaboration. Now, however, the new TDR-sponsored web portal, TropIKA.net, is pushing the definition of reviews one step further, creating a new review series geared to the needs of health decision-makers, researchers and donors.

Over the last two decades, and thanks in particular to the efforts of the Cochrane Collaboration, reviews conducted according to a rigorous methodology, addressing well-defined questions, and beginning with a data search, have become a cornerstone of an evidence-based approach to health care.

However, despite this ‘review’ revolution, Cochrane reviews are generally only concerned with the effectiveness of interventions, while researchers, as well as decision-makers and donors, often require reviews that consider a much broader range of study types. Donors, for instance, may find reviews of basic science needs and gaps to be important inputs to their funding decisions. Public health decision-makers, to give another example, need reviews of the evidence from epidemiological studies, which would not typically be included in a Cochrane review.

Beginning in autumn of 2008, TropIKA.net will introduce a series of specially-commissioned reviews, each of which will gather and assess all the available evidence on a clearly defined public health question that concerns an infectious disease of poverty. These rigorous and unbiased reviews will meet the needs of decision-makers, researchers, funding agencies and others involved in this area. They will highlight both implications and information gaps and will facilitate the translation of research findings into policy and practice.

TropIKA.net has established a review coordinating team (hosted at Hughes Hall, Cambridge University, UK) which will collate topics for review and find appropriate authors. The methodology for each review will be specified in advance and described in full in the published article. Authors will, as necessary for the topic at hand, consider all appropriate data; this may, for example, include data from studies in the fields of basic science, epidemiology, socioeconomics, product development, and implementation research, and range from lab data to intervention and modelling data.

TropIKA.net reviews will possess a number of other key distinctive features. For instance:

- In addition to the full review (typically about 5000 words in length), there will be five-page and two-page summaries for busy decision-makers, which highlight the implications of the research included in the review.

- After a review is published, TropIKA.net may also invite other experts to make comments that outline their own perspective on the topic; these comments will be published on the TropIKA.net website.

- As with all articles published on TropIKA.net, readers may submit their own comments. Subject to screening by the editorial team, these comments will also appear on the website. The comments posted will amount to what has been called ‘post-publication peer review’.

- Readers may also suggest topics that might be addressed in future reviews. They may also volunteer to act as authors or as referees in the rigorous pre-publication peer-review process which each article must undergo.

These features illustrate the interactive qualities that are a hallmark of the TropIKA.net initiative. This is not a top-down project but one in which all stakeholders concerned with the infectious diseases of poverty may contribute their experiences and opinions.
New EDAC chair speaks out:

Advancing the network approach

Dr Frank Douglas was global director of R&D and member of the Board of Management of Merrion Merrell Dow (MMD) and Aventis AG, and also founder of a Center for Biomedical Innovation at MIT, from which he resigned in June 2007, in protest over alleged discrimination against a minority colleague (see The.Scientist.com, 31 July 2007). Now, he has become the chair of the Expert Drug Discovery Advisory Committee (EDAC), in the context of TDR’s Lead Discovery for Drugs business line (BL 3).

What experiences did you have in industry with TDR priority diseases?

MMD was involved with WHO in the development of DFMO for human African trypanosomiasis (HAT), and when I became global head of R&D, I started to push for final registration, which had stalled. The main challenge we faced was not development and registration of DFMO, but finding a company to manufacture the drug once it was registered (as eflornithine®). So I helped negotiate an agreement with WHO whereby we produced it for three years and then turned it over to another firm. (DFMO is now produced by Sanoﬁ-Aventis). TB was another issue addressed by MMD; through our R&D centre in Geranzano, Italy we put the drug rifapentine on the market. In 2002-03, at Aventis, we funded South Africa’s Nelson Mandela Foundation in the training of lay people for home visits to TB/HIV co-infected patients, to improve compliance with drug therapies.

Why isn’t the private sector more active in research for neglected infectious diseases?

The need for new anti-infectives is a major global health issue, and yet most of pharma is not in a position, even in an opportunistic manner, to lead such research. It is not only that such drugs are not financially rewarding. Significant barriers also exist in bringing a drug to registration, having mostly to do with side effects. Like many large firms, MMD stepped out of anti-infectives around 1993; we sold our centre in Geranzano. Today, because of the increase in resistant bacterial strains, some companies are returning to this area. However, the likelihood that one will rapidly have compounds to work with are not that high. Companies must, and are, pursuing novel targets to treat these resistant strains.

There also is a personal side to your interest?

I was born in Guyana, and left in 1963 at the age of 20 to study in the United States on a Fulbright scholarship. But due to this background, I do have a natural interest. My mother suffered from filariasis when I was young, and there was a lot of TB in my hometown. So naturally, I grew up with a personal understanding of health issues in developing countries.

What prompted your involvement with TDR?

I have a longstanding interest in what I call the ‘network-centric’ organization. I began to develop this concept around 1999-2000, when I was with Aventis. I was convinced that the better way to do early drug discovery was through collaborations between academia and industry. When I was approached by TDR, and discovered that you had already been using this network approach, I was astounded as to how much had been achieved. So TDR’s work brings together my personal and professional interests in drug development and my interest in creating an environment that can make it happen.

How can TDR advance its networks?

When structures grow rapidly, it is important to find ways to support better communications, strengthened teams/partnerships, and operational excellence. TDR’s networks now have some potential lead compounds. So it becomes very important that you prioritize and define a compound progression process. Finally, TDR has a mandate to build capacity in countries where these diseases are most widespread. There is a natural tension between supporting well-equipped centres in the north and building capabilities in the south. I personally think TDR has to dedicate a portion of its drug discovery budget to capacity strengthening, in addition to twinning northern and southern centres. We need to recognize that this is an investment that will pay. Why? Disease endemic countries need the products, and necessity is the mother of invention.

What other advice would you offer?

TDR needs to lead the expansion and operational refinement of its networks while communicating its successes so far. And we have to have a sense of urgency. These diseases have been around for a long time. But in today’s globalized world, countries cannot thrive economically under such a burden. So if we are really concerned about long-term development, we have to deal with these health problems.

TDR Contact: Dr Solomon Nwaka, Leader BL 3 and EDAC Coordinator nwakas@who.int
BL3 - Drug discovery on fast track says expert advisors

The first meeting of the TDR Expert Drug Discovery Advisory Committee (EDAC) reviewed the broad spectrum of collaborations that have been undertaken by TDR under its new Lead Discovery for Drugs business line (BL 3). The meeting took place on 31 March to 3 April in Geneva.

EDAC commended TDR and BL 3 leader Dr Solomon Nwaka for the "social entrepreneurship" displayed in the development of the network concept and the catalytic role played in new initiatives, such as the Drug Target Database (http://TDRtargets.org). EDAC encouraged TDR to leverage additional partners for such promising initiatives.

EDAC noted that the TDR discovery network collaborations with industry, in particular, have yielded a significant number of ‘hits’ and potential ‘leads’ for new drugs worthy of future development, including compounds showing in vivo activity against protozoans and helminths.

The TDR team now needs to take the networks and collaborations to the next level of focused activities, including the implementation of a ‘team concept’ and closer interaction across networks. These include networks for screening, medicinal chemistry, drug metabolism and pharmacokinetics (DMPK), as well as the network for the Drug Target Database. The HEOs (Hit explorer operating system) database, recognized by EDAC as an important knowledge-sharing tool, should be exploited to its full potential, to improve communications among TDR-managed networks and also engage other users in the neglected diseases area.

Other key recommendations include:
1. TDR should maintain ongoing industry collaborations (e.g. Pfizer, Merck-Serono, Chemtura); recruit new collaborators with EDAC help as appropriate; and leverage collaboration with the International Federation of Pharmaceutical Manufacturer & Associations and other industry associations.
2. TDR should maintain support for the networks but should rationalize the use of screening centres and identify a strategy for optimizing use and improving on turn-around time of data from screening centres to support medicinal chemistry work.
3. TDR should continue to manage and develop the Drug Target Database while also identifying new partners for longer-term sustainability.
4. While TDR’s networks should remain focused on neglected parasitic diseases, TDR also may play a catalytic role in promoting strategic partnerships between other actors on other diseases when opportunities arise.
5. An EDAC-appointed subcommittee will evaluate the natural product plant extracts and compound screening centre in Africa to recommend next steps.
6. TDR should develop further the idea of a TDR Compound Bank and seek partners specializing in compound management and distribution.
7. TDR should explore the establishment of a TDR/EDAC Award for excellent achievements in network projects and training.

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TDR and the Global Fund develop framework for implementation and operations research

Implementation and operations research (IR/OR) holds great potential to provide health systems with evidence-based guidance on treatment and policy decisions that can then achieve a far greater impact. However, such research remains a new and cutting-edge activity in the broader health research arena.

Health and disease control officers therefore often require guidance in designing, planning, implementing, disseminating and using the results of IR/OR. In response to this need, TDR and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) recently convened a joint meeting to develop a framework for implementation and operations research in health and disease control programmes.

The meeting took place under the hospices of TDR’s Strategic Alliances unit. The fifty participants that attended the meeting, 3-5 April 2008, included representatives of multilateral, bilateral and technical agencies; donor institutions; field-based programme managers and implementers; policy makers and researchers; and also staff from WHO’s country, regional and headquarters’ offices. The framework developed was timed to be of immediate use to countries that are currently developing proposals for Round 8 of the Global Fund requests for research proposals.

During the two and a half day meeting, participants reviewed a draft framework that had been prepared by the Global Fund and TDR/WHO, with the help of a consultant. Along with providing guidance, participants stressed that capacity building in IR/OR must be an integral component of good operations research. Prior to the meeting, staff from TDR and WHO (Stop Tuberculosis, Global Malaria Programme) made site visits to five selected countries where operations or implementation research is currently ongoing, under the auspices of GFATM and other donors to observe best practice examples, as well as challenges in live field settings. The draft Framework for operations and implementations research is now available on the GFATM and TDR websites for comment and review (see links below). A final version of the framework will be published and made available shortly.

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http://www.who.int/tdr/topmenu/news/default.htm
BL2 - Empowerment BL launches strategy for developing DEC research leaders

TDR’s new ‘Empowerment’ business line will comprise four key functions that aim to build capacity for research management and leadership, networks, training and quality management. The functions were approved by the BL’s Strategic Advisory Committee (SAC), in its initial meeting convened in Geneva 5-6 February.

The SAC meeting was one of five advisory meetings convened by the BL over the past three months to move the new activity into full-fledged operations. The Empowerment BL (BL 2) builds upon TDR’s long record in capacity-strengthening, but it aims to go a step further – developing health research leadership in disease endemic countries with a special focus on quality aspects of training and capacity-strengthening.

The BL’s new emphasis on principles of Quality Management (QM) as a cross-cutting aspect of all Empowerment activities, and indeed of TDR’s broader functions, was welcomed by SAC. Disease endemic countries must be able to boost quality leadership, with good technical, ethical and conceptual skills, in order to assume a more effective role in global and regional research initiatives, SAC emphasized in its final report.

In line with TDR’s new ‘quality-focus’, the sheer numbers of researchers trained will receive less emphasis, and the quality of professional and leadership skills fostered will be given deeper emphasis. Quality management will become integral to the processes of selection and awards of research and training grants, monitoring and mentoring of young researchers.

Creation of a mentorship system for researchers, including the classification of researchers for capacity-strengthening purposes, is another central feature of the new BL, endorsed by the SAC at the meeting. Classifying researchers as ‘established’, ‘advanced’, ‘leading partnerships’, or ‘research leaders’ will help place researchers seeking TDR support within the context of appropriate activities, e.g. research projects, training or networking.

Following the SAC, a new Empowerment Training Steering Committee convened 7-8 February to revise TDR training grant procedures and priorities. Training grants are offered by TDR for Masters and PhD level studies. The revisions aim to provide more focus on training research leaders and integration of institutional strengthening goals into individual training programmes.

“We want the individual trainee to be following a career development plan that builds him or her individually, as well as the institutional environment in which he or she is operating. We want the institution to be part of the discussion about the individual’s career path, research plan, etc.” explained Dr Juntra Karbwang-Laothavorn, BL 2 manager. Following the meeting, a new and revised call for training grant applications was posted 19 March on the TDR website. Final TDR training grantees will be announced in November 2008.

In other related events:

• A new TDR Network Advisory Committee (NAC) met 15-16 April to plan strategies for expanding TDR-sponsored networks of researchers. A new Capacity Strengthening Stakeholders Forum, involving donors funding capacity strengthening projects around the world, is among the new networks planned.

• TDR’s Research Strengthening Committee (RSG) also met 31 March to 2 April to review proposals for research grants, approving nine applications and renewing another 21 ongoing projects. In addition, a meeting to plan the definition of ‘quality standards’ for short courses was scheduled for 21-23 May.

• The MIM/TDR Task Force, 10-14 March, approved 16 projects (12 renewals and four new applications) for funding for US$ 749 184. Areas of research covered include: social sciences and community based studies; immunology and pathogenesis; molecular entomology and insecticide resistance; and malaria treatment and prevention (see box).

MIM/TDR Task Force discusses quality management

The concept of ‘quality management’ in research was a key theme at the Multilateral Initiative for Malaria (MIM)/TDR Task force meeting in Addis Ababa, Ethiopia, 10-14 March. The meeting brought together over 40 principal investigators involved in MIM/TDR projects, along with task force members and other MIM partners.

Quality management strategies are being promoted through TDR’s new ‘Empowerment’ business line, in which MIM/TDR is a partner activity. Quality management principles such as ‘team-building, commitment and zero-defect attitudes’ were introduced and discussed in the context of how they could be applied to scientific research being carried out under MIM/TDR auspices.

TDR’s new Ten Year Strategy also was introduced and discussed more broadly, particularly as it relates to capacity-building and empowerment of MIM/TDR investigators. In addition to obtaining feedback on the new strategy, TDR staff attending the meeting were able to engage investigators, and get a better sense of issues that they face in implementing their grants, said Dr Olumide Ogundahunsi, the TDR coordinator of MIM/TDR activities.

A post-discussion survey of attendees revealed that investigators welcomed the introduction of quality management principles into TDR’s Empowerment business line, and viewed the concept as valuable to successful execution of research projects, he added.

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BL5 - New research for innovative vector control

Seven planned projects testing new methods of innovative vector control in Africa, Asia and Latin America were introduced and discussed at a 31 March-1st April meeting between principal investigators, WHO staff and TDR’s Strategic Advisory Committee (SAC) for Innovative Vector Control (BL 5).

The meeting in Geneva examined recently-approved grants for research into improved control methods for the vectors of human African trypanosomiasis (HAT), malaria, dengue and Chagas disease. The grants are to run for a minimum of three years and involve outlays of US$ 150 000 to US$ 250 000 annually.

The meeting also represented a first-time effort to improve execution of such research grants by providing field project leaders with in-depth review and guidance at the very outset of their research projects, as well as an ‘orientation’ into TDR research grants technical and financial management procedures.

“This has been our first experience in bringing principal investigators (PIs) to Geneva to introduce them to the TDR grant management system, and discuss project management from the very start. And the feedback we received was that this has proven to be very helpful to them,” said Dr Yeya Touré, leader of the BL 5 activity.

The two-day gathering involving the PIs was followed by a three-day strategic and planning meeting of the business line’s Scientific Advisory Committee (SAC). The SAC reviewed new research proposals, final reports from outstanding projects, and recommended new initiatives and strategic directions.

The vector control research projects just recently approved and now being launched under the new business line activities include the following:

**HAT:** A research collaboration in eight African countries with varying eco-climatic and epidemiological conditions will examine how to improve the trap system for HAT vectors (tsetse flies). A second collaboration in five African countries will examine how to strengthen decision-support mechanisms to improve choices about vector control, in light of evidence obtained regarding local epidemiological and ecological conditions.

**Dengue:** Two research projects are to be implemented to assess the efficacy of integrated vector management (IVM) of dengue vectors in eight countries of South-East Asia and five countries in Latin America, including Mexico, Guatemala, Cuba, Venezuela and Brazil.

**Genetically modified malaria and dengue vectors:** One research project in collaboration between Brazil, Kenya, India and Mexico will address the best-practice guidance for deployment of genetic control methods against mosquito vectors in disease endemic countries.

**Chagas:** One project will examine the factors driving vector reinestation in four countries of Latin America: Argentina, Bolivia, Brazil and Paraguay.

Contact: Dr Yeya Touré tourey@who.int

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BL7 - SAC: assess impact of improved access to diagnostics

The impact of improved access to diagnostics needs to be measured and documented to support advocacy and awareness of the benefits of TDR diagnostics research and evaluation activities.

This was one of the main recommendations emerging out of the meeting of the Scientific Advisory Committee (SAC) on Accessible, Quality-assured Diagnostics, 27-28 March in Geneva. The SAC recommended that the upcoming November meeting of TDR’s Diagnostic Evaluation Expert Panel (DEEP) be devoted to defining indicators and methods for impact assessment. Estimates of the adverse impact and wasted resources attributable to poor quality diagnostics would also be valuable, stated the SAC committee in its final report.

During the two-day meeting, the committee also approved budget allocations and grants totalling over US$ 2 million for new and ongoing activities related to diagnostics research. Those included projects for the evaluation of new or improved diagnostics for HAT, TB, malaria, schistosomiasis, and dengue. Projects in diagnostic target discovery, conducted in collaboration with TDR’s drug discovery business line (BL3) and in Good Clinical Laboratory Practice (GCLP), also were approved. TDR activities related to diagnostics for sexually transmitted infections will be supported exclusively by a recent US$ 9.2 million three-year grant from the Bill and Melinda Gates Foundation, as per the grant requirements.

The committee noted that TDR’s diagnostic activities had leveraged impressive results in light of the modest investments made. It identified, however, two key cross-cutting issues that should be addressed in the coming two years.

Those include:

- Regulatory issues: There is a need for more effective regulation of diagnostics at the country level in order to prevent flooding into the markets of cheap and unreliable products that discourage quality manufacturers. The committee recommended that the Diagnostics BL should explore with key countries options for providing quality standards and improving the regulation of diagnostics tests.

- Raising the diagnostics BL profile: The committee recommended that communications (e.g. web portal, advocacy brochures) be enhanced in order to improve awareness of the activity and its impact.
BL1 - Priority setting in health research: a look at methods

Disease endemic countries, and indeed the global community, must constantly cope with health and disease threats on multiple fronts. And yet resources for research to find new solutions and approaches will inevitably remain limited.

As a result, methods for explicit and rational setting of priorities for investment in research need to be promoted among national-level decision-makers, while training and good practice experiences with these methods should be shared more widely in the global community.

These were among the recommendations emerging from a two-day meeting on Priority Setting Methodologies in Health Research, 10-11 April, at WHO headquarters in Geneva.

The meeting, convened by TDR and WHO’s Department for Research Policy and Cooperation (RPC), brought together experts in the field to examine how user-friendly methods for priority setting could be promoted more widely. The workshop was held to reflect on ongoing discussions in the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG-PHI) on the need to assist member states with good priority setting practices for health research.

The meeting took note of the priority setting methodologies that have been devised by various institutions, such as the Global Forum for Health Research (GFHR), the Council on Health Research and Development (COHRED), the Child Health Nutrition Research Initiative (CHNRI) and TDR. However, participants concluded that in many countries research priorities still are not examined or defined systematically, and much still needs to be done to accelerate priority setting methods at the national level.

The participants recommended that activities to advance the concept of systematic priority sharing should focus around capacity-building/training and communications/advocacy. It was recommended that a web portal and community of best practice be established around capacity-building/training and communications/advocacy. It was recommended that a web portal and community of best practice be established.

In terms of the methods reviewed, the group identified key principles for good priority setting. Those include:

1. Legitimacy and fairness as fundamental principles underlying effective processes.
2. Priority setting processes that include ‘leadership’ and ‘buy-in’ from leading stakeholders, including communications strategies that identify target audiences, frame and portray the initiative, and offer a platform for debate.
3. Selection of appropriate tools and methods to guide the process, reflecting principles such as objectivity, transparency, validity and replicability.
4. Measurement of outcomes from the research agenda, but in such a way as to allow room for change and adaptation based on emerging issues, while also protecting the research agenda from political, economic and environmental shocks.

More information: A detailed report on the meeting resources is forthcoming on: www.tropIKA.net or www.who.int/tdr

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Integrated functional genomics on the road to leishmaniasis control

The increased ability of scientists to genetically manipulate the leishmaniasis parasite and to undertake detailed genetic analysis of its vectors and mammalian hosts, promises to revolutionize the next decade of research on the disease. However, translating outputs from this ‘scientific utopia’ into meaningful measures for disease control remains a great challenge for the research community. This was the observation of Dr Paul Kaye, co-organizer of a recent conference to review the state of leishmaniasis research. The conference, held in Worcestershire, United Kingdom in September of 2007. The meeting co-sponsored by six public and private sector institutions, including TDR, brought together key scientists involved in leishmaniasis research to critically evaluate the current state of research and develop priorities for the coming years. A special focus was placed on research with high potential for translation into new avenues for leishmaniasis control.

Dolby House II: Integrated Functional Genomics on the Road to Leishmaniasis Control, met in Worcestershire, United Kingdom in September of 2007. The meeting co-sponsored by six public and private sector institutions, including TDR, brought together key scientists involved in leishmaniasis research to critically evaluate the current state of research and develop priorities for the coming years. A special focus was placed on research with high potential for translation into new avenues for leishmaniasis control.

TDR participated actively in the meeting, providing full funding for six endemic country participants to attend. Dr Hashim Ghalib, Leishmaniasis Disease Research Coordinator, present there on behalf of TDR, described the gathering as a “forward-looking event which set the tone for leishmaniasis research and control for the next ten years.”

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Innovative vector control interventions

NEW GRANTS

The Scientific Advisory Committee on Innovative Vector Control Interventions of the TDR business line met in Geneva, Switzerland, 17-19 December 2007, to deliberate and recommend projects for funding by the Programme. The projects listed below were selected from among a number of applications received from investigators worldwide.

A70594
Patrick Guerin
University of Neuchatel, Institute of Biology, Switzerland.
Development of trapping and target devices for controlling vectors of human African trypanosomiasis. US$ 240 000

A70596
Ricardo Gurtler
Universidad de Buenos Aires, Facultad de Ciencias Exactas, Argentina.
Sources of reinfection by major vectors of Chagas disease after residual insecticide spraying. US$ 243 600

Pattamaporn Kittayapong
Mahidol University, Faculty of Science, Thailand.
Innovative dengue vector control intervention and network based on novel tools and eco-bio-social strategies. US$ 150 000

Pablo Manrique-Saide
Universidad Autonoma de Yucatan, Mexico.
Expanding targeted dengue vector control in Latin America: maximizing the potential of insecticide-treated materials. US$ 150 000

John David Mumford
Imperial College London, United Kingdom.
Best-practice guidance for deployment of genetic control methods against mosquito vectors in disease-endemic countries. US$ 186 880

Stephen Torr
Natural Resources Institute, The University of Greenwich at Medway, United Kingdom.
A user-friendly decision support system to improve vector control operations against human African trypanosomiasis. US$ 199 784

BL9 - Global Registry planned to monitor health effects of artemisinin use in early pregnancy

Little evidence exists as to the risks of artemisinin treatment in early pregnancy. And yet the high therapeutic value of artemisinins overall, as well as their increased use worldwide, makes it inevitable that some women are receiving artemisinin treatment in early stages of pregnancy, when their lives are at risk for malaria and they may be unaware of the pregnancy. To address this issue, TDR and departments of the World Health Organization, including the Global Malaria Programme and Making Pregnancy Safer, met in December 2007 and April 2008 to finalize the protocol for a planned new Global Antimalarial Pregnancy Register, which would allow monitoring of birth outcomes following ‘inadvertent’ exposure to artemisinin compounds in the first trimester of pregnancy.

Creation of such a registry will greatly contribute to a better understanding of the health impacts of medicine exposures in early pregnancy, including of artemisinin-based antimalarial medicines. The measurement of the frequency of congenital malformations in the exposed group as compared to non-exposed (or background frequency in the general population) will provide the basis for developing evidence-based treatment policy recommendations.

Meanwhile, a recent TDR-GMP analysis published in the online open access journal BMC Infectious Diseases reported that the use of rectal artemisinins in emergency malaria treatment, especially for children, can help ‘buy time’ for malaria patients who face a delay in accessing effective, injectable antimalarials. The analysis of individual patient data of over 1000 patients from 15 clinical trials, including TDR-supported sponsored studies, compared the efficacy of rectal artemisinins – artemisinin, artesunate and artemether – with each other and with conventional injectable antimalarials such as quinine.


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Eliminating River Blindness
Highlights from TDR’s - Making a Difference 30 Years of Research and Capacity Building in Tropical Diseases

Onchocerciasis control is one of the outstanding public health achievements of this century. Over 55 million Africans annually receive treatment – and elimination of onchocerciasis as a public health problem is well advanced. For three decades, TDR has been a driving force behind a special research/control partnership for onchocerciasis control, initially in collaboration with the Onchocerciasis Control Programme (OCP) in West Africa and now with the African Programme for Onchocerciasis Control (APOC). Featured here are highlights of this history from TDR’s recent publication Making a Difference, 30 Years of Research and Capacity Building in Tropical Diseases.

Community-directed interventions for major health problems in Africa
A multi-country study • Final report
125 pp., 2008 (ISBN 978 92 4 159660 2)

Many infectious diseases continue to pose a very heavy health burden in developing countries largely because of the lack of efficient delivery of inexpensive interventions. To address this issue, community-directed strategies developed by TDR and its partners have been tested in the delivery of a broader range of primary health care measures. This report is the conclusion of a three-year study of community-directed interventions (CDI), conducted in collaboration with the African Programme for Onchocerciasis Control (APOC). The study demonstrated that the approach successfully delivered multiple interventions, doubling the use of bednets and more than doubling treatment with artemisinin-based combination therapies (ACTs) for malaria.

Strengthening health-economics capability in Africa
47 pp., 2007 (ISBN 978 92 4 259522 2)

This report provides an overview of initiatives in sub-Saharan Africa and outlines a strategy for promoting further health-economics capacity in the region. It is the result of a process initiated by TDR’s Research Capacity Strengthening (RCS) area of work, including a Consultative Workshop in 2006, and completed with support from the Swedish International Development Cooperation Agency (SIDA).

Malaria: Genomics and Functional Genomics Research Tools (version 1.2)

This DVD provides scientists in disease-endemic countries with information and training on transfection technologies in malaria research. It is a compilation of selected presentations from a number of TDR-sponsored international training courses.

For more information about the DVD contact: Dr Ayoade Oduola, oduola@who.int

Available through TDR

Defining and Defeating the Intolerable Burden of Malaria III. Progress and Perspectives
American Journal of Tropical Medicine and Hygiene Vol. 77, No. 6, Supplement (pages i-327) 2007

The third supplement volume of scientific articles in the Intolerable Burden of Malaria series. The 42 articles feature contributions from epidemiologists, entomologists, microbiologists, economists and social scientists globally detailing the latest developments in research and control of malaria.
TDR launches a new website!

Programme’s operational focus. Each theme will be briefly introduced by a topic page, leading the user to multiple layers of more in-depth resources. Other new features include a search mechanism on every page by disease, research area, and region. A new grants section for both past and current calls for applications as well as training will make it easier for users to look for funding opportunities. There also will be constantly rotating news features on key TDR activities. In terms of publications, the newly revamped ‘e-version’ of TDR News will also be available on the site for easy download, as well as all other new and archived publications. And, there will be easy links to the TDR co-sponsored site, TropIKA.net, which provides resources on the world of tropical disease research.

TDR staff and consultants are spending considerable time transferring the thousands of pages of existing information and archives into the new site organization – a process that will continue some months after the official launch.

Brazil’s Minister of Health welcomes JCB 31 to Rio de Janeiro

“As one of the countries that signed the original Memorandum of Understanding creating TDR, Brazil is very proud to host the 31st Session of the Joint Coordinating Board. TDR is one of Brazil’s major partners in neglected diseases research, development and innovation, areas that constitute a top priority for our country. I would like to welcome TDR’s Joint Coordinating Board members, as well as all the participants of this 31st Session, for a productive and also pleasant stay in Rio de Janeiro.”

José Gomes Temporão, Minister of Health, Brazil

TO OUR READERS:
We want to hear from you. Please send us your feedback, as well as letters and ideas on possible stories for TDR News and on TDR-related tropical disease research issues, events, institutions, publications and personalities. Thank you!

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