On the making and writing of history

When the Communications Team set out to develop a history of TDR as part of the JCB 30th anniversary celebrations, the vision was of a coffee-table book that would tell the story in pictures, more than in words.

Then, as the new TDR editor of publications and author of this special book, I began to unravel a history so rich and extensive that I found it impossible to summarize merely in captions — however compelling the photo we unearthed!

It is not easy in the UN system to show results. I know that from experience, as a journalist working in the mainstream media for most of my career, observing and critiquing the performance of public institutions. It is not easy these days, either, for the global public sector to respond to critics who believe privatization of tasks is the answer to absolutely all of the world’s ills. What I found in TDR was a model of results-oriented public sector activities. Financed by a modest budget, getting the best heads together, and working from the “bottom up” with scientists worldwide, the list of accomplishments gathered for the TDR history book kept growing.

I now have a mental litany of TDR achievements that I can rattle off to colleagues when they ask me what I am doing with my life since I left news journalism. I tell them I am working for the programme that developed the multi-drug therapy that helped surmount leprosy; demonstrated the efficacy of insecticide-treated bednets for malaria prevention; and supported research on critical new malaria medications.

Then, I mention a few of the more “exotic” illnesses in which TDR has played a key role in finding innovations for disease control — onchocerciasis (river blindness), Chagas disease, leishmaniasis, and lymphatic filariasis. I always make the point that most of TDR’s R&D and capacity-building funding goes to experts and institutions in disease endemic regions, and those best positioned to do the research. That is empowerment.

Interviewing TDR directors and staff, JCB members and grantees, past and present, was an unforgettable experience. Dr Adetokunbo Lucas, TDR’s director from 1976–1986, spoke about his decade with the organization as if it had been yesterday, describing key moments like the Merck announcement to donate ivermectin as a treatment for river blindness with dramatic flourish. Dr Carlos Morel reviewed almost the entire book while globe trotting to meetings in Africa, Latin America and Europe. And Dr Robert Ridley, who would pass by my desk at 7 p.m. to look at the latest rewrite, offered careful commentary with enormous patience and modesty. He kept saying, “I don’t want to be history… yet. I want to make it!”

The many others who contributed essential elements, and combined critical review with moral encouragement, are noted in the book’s acknowledgements. A big thank-you to all from our entire team, including Communications Manager Jamie Guth, Designer Lisa Schwarb, and Administrative Support Laurie Ingels and Jocelyne Bruyère — who pulled out all stops to finish production on time.

The celebration is not over, and there is much work ahead as TDR implements its new Ten Year Strategy. As one facet of our strategy’s increased communications effort, TDRnews has been redesigned. Our new ‘look’ is based on feedback we received from you; more than 500 respondents to our TDRnews readership survey. You asked for more news on “scientific innovations” in the research areas and diseases that are TDR’s focus, and added “in-depth articles.” Enhanced coverage of the scientific and policy findings emerging from TDR-supported research also will incorporate expanded reference to added resources in print, multimedia and web. We will be profiling aspects of the new TDR business lines, and the work of individual scientists globally ‘making a difference.’

In future issues we also will add a section of “briefs,” as well as letters from you, the readers. A report on the survey as well as announcement of the winners of the prize book drawing for survey respondents will be included in the next TDRnews issue.

In this effort, we welcome all comments and suggestions. History is always in the making. Help us make it with you.

Elaine Ruth Fletcher
Editor, TDRnews
Now, the real work begins.

TDR has spent over two years reviewing and analysing all aspects of its operations, studying the research environment around us and examining options for adjustment and change.

In June, we celebrated the 30th session of the Joint Coordinating Board (JCB), an important milestone in TDR’s history, and received the JCB’s endorsement for TDR’s new ten year vision and strategy.

In recent issues of TDRnews we have attempted to keep you up to date on the development of this strategy. Our challenge now is to implement it.

This strategy includes the vision statement “to foster an effective research effort on infectious diseases of poverty in which disease-endemic countries play a pivotal role.” Supporting this vision is a three-pronged strategy for:

- **Stewardship** of research on infectious diseases of poor populations. This will involve TDR convening new groups of experts and broad groups of stakeholders to look at research gaps and opportunities, and new activities in advocacy and knowledge management, including the new TDR-sponsored knowledge base, TropIKA.net.

- **Empowerment** of researchers and public health professionals from disease endemic countries. This implies expanding research training to build leadership at individual, institutional and national levels.

- **Research** on neglected priority needs that are not adequately addressed by other partners, fostering innovation for product discovery and development; research on development and evaluation of interventions in real life settings; and research for improving access to interventions.

We are finalizing the details of the 11 new business lines, which target key gaps and opportunities within these larger aims and goals.

While we are still in a transitional phase, this issue of TDRnews highlights a number of the new activities already underway.

An article on the launch of a major research study to inform treatment policy for TB/HIV co-infection reflects an extension of our focus on diseases of poverty, going beyond the bounds of the traditional TDR parasitic diseases.

Other articles in this issue describe new developments in TDR-fostered discovery research networks, including publication of a new drug target data base and a helminth drug initiative. Also described here are stepped up efforts to facilitate clinical evaluation of candidate drugs for Chagas disease in coordination with the Pan American Health Organization/WHO Regional Office for the Americas.

This issue also covers various ‘empowerment’ initiatives, which involve not only the development of technical expertise, but the fostering of strategic and technical leadership. The initiatives featured include the SIDCER networks supporting sound ethical review of clinical trials and training networks in research project management. In both cases, institutions in disease endemic countries are now playing a leading role in further expanding those networks and training opportunities. Analysis of TDR-sponsored research published in the peer-reviewed press also shows how researchers from low and middle income countries are increasingly taking a lead role in publication efforts.

Implementation research is another key focus of the new strategy. The recent findings of the trials by Ghanaian investigators that artemisinin combination therapies (ACTs) can be utilized effectively for home management of malaria will contribute significantly to the case for expanding ACT use in community settings.

Finally, while we focus on the future, there will be ongoing celebration and coverage of TDR’s history through the coming year. This will include not only excerpts from the new TDR history book, but also “close-ups” with field researchers and partners who have made a particular contribution to TDR’s history, and whose efforts in farflung regions of the world have validated and justified TDR’s vision, mission and activities — then and now.

Dr Rob Ridley, TDR director
Introduction

Setting the scene, the three P’s — people, products and partnerships

Three decades of remarkable change — for our global village, for health, for scientific research and for TDR — give reason for reflection as TDR’s governing body, the Joint Coordinating Board (JCB), celebrates its 30th anniversary. TDR was formed in an era of growing awareness of our world’s interdependence. The Programme came of age as social and economic development to bridge the gap between rich and poor countries became a mainstream UN endeavour. It has matured at the turn of the millennium, in a period of heightened recognition of our continued vulnerability to infectious diseases of all kinds — from TB, malaria and HIV/AIDS to lesser known parasitic infections. Yet there is also growing awareness of the potential for scientific research — undertaken in innovative public and private partnerships — to generate new knowledge of how to reduce these threats, particularly in countries bearing the greatest disease burden.

It was in the early 1970s when the vision of a global, UN-sponsored research effort to tackle some of the world’s most neglected diseases was first formed. This was the end of the colonial era and a time when missions to the moon were giving rise to the concept of ‘Spaceship Earth’ — an awareness that we all lead interdependent lives. As researchers in biomedical science made giant leaps forward in genetics and molecular biology, and life expectancy improved dramatically in industrialized nations, attention turned to the plight of those in the less-developed world, where infectious diseases continued to cause enormous suffering, also slowing socioeconomic development.

As TDR celebrates the 30th anniversary of its Joint Coordinating Board (JCB), we share excerpts from a new TDR history of the ‘people, products and partnerships’ that made a difference to public health.

First in a four part series covering the key historic phases: ‘Heroic goals’ (1975-1986); ‘Innovations in field research’ (1987-1997); ‘The partnership decade’ (1998-2006); and ‘Research that makes a difference’ (2007-).
At a field survey to detect schistosomiasis, an infected child demonstrates that he has swallowed the medicine given to cure his infection. Children are weighed and the correct dosage of drugs (Praziquantel) is also prescribed by weight. (TANZANIA • 1988 • WHO/TDR/MORENA)
In the spring of 1974, the World Health Assembly called upon the Director-General of WHO to intensify activities in tropical disease research, while strengthening research and training activities in developing countries. In November, a meeting of experts on leprosy launched the activities of the new Special Programme for Research and Training in Tropical Diseases. This also spearheaded the development of scientific working groups for other TDR-targeted diseases, and convened scientists, public health experts and institutions that would play a role in TDR for years to come.

The gathering was supported by the Wellcome Trust as well as by the Government of Norway. The chair was renowned immunologist Professor Barry Bloom, now Dean of the Harvard School of Public Health. Bloom would later head TDR’s Scientific and Technical Advisory Committee (STAC), the top scientific oversight body. The Swedish physician Professor Sune Bergström, who would later win a Nobel Prize, also attended. He would be active in the Programme for many years, prior to his death in August 2004.

Creating the JCB; defining research priorities

By January 1975, TDR had come into being and over the next three years, its structure would be consolidated. In 1976, the United Nations Development Programme (UNDP) joined WHO as a co-sponsor, followed by the World Bank in 1977. In February 1978, a meeting of cooperating parties endorsed a Memorandum of Understanding on the Programme’s administrative and technical structures. These included the JCB, the Standing Committee and STAC. In November 1978, the first JCB session was held. The role of the JCB was — and still is — to review all TDR’s activities, evaluate its progress, decide on its budget, planning and execution, and approve arrangements for its financing.

The JCB’s composition was innovative because it opened decision-making processes to equal participation by both donors and recipients, effectively breaking down those distinctions and creating a new partnership paradigm, whereby representatives from disease-endemic countries had a major role in determining TDR’s strategic direction. TDR’s design thus reflected an emerging philosophy — that people in disease endemic countries, when properly ‘empowered’, could drive ‘bottom-up’ development, a vision that still guides the Programme today.

Fundamental to this approach was the research strategy and institutional framework that TDR adopted, which integrated diverse scientific viewpoints about TDR’s appropriate role in: basic biomedical research, research into new drugs and control tools, field research, and social science research. At the same time, capacity building to foster research in developing countries was viewed as a critical function. Welding these aims into a single vision and framework ultimately gave TDR the potential to respond flexibly to new research challenges. TDR also became a catalyst for some of the first high-level partnerships between the public and private sector, and a pioneer in community-based field research at the grassroots level.

Taking stock

Fast-forward 30 years, and the world has seen dramatic progress in the battle against many of the infectious diseases that TDR was first charged to address. Spectacular advances have been made towards elimination of leprosy as a global public health problem. Onchocerciasis is under control in most of Africa, and has been eliminated as a public health problem in savanna areas of 11 West African countries. Following elimination campaigns in the 1990s, transmission of Chagas disease has been interrupted in several countries of Latin America. In addition, a Global Programme for Elimination of Lymphatic Filariasis (GPELF) has been established by WHO, as has a framework in WHO’s South-East Asia Region for the elimination of visceral leishmaniasis, signalling new potential to address these diseases.

Integral to these achievements are new drugs and diagnostics; tools and strategies; and methods of vector control, developed and promoted through TDR-sponsored research. Of the 18 new drugs or new drug combinations that have been registered for TDR-targeted diseases since the 1970s, more than half have been a result of TDR collaborations (Trouiller et al., 2002). In terms of its field and applied research, TDR initiated the first large-scale trials of insecticide-treated bednets, which led to their introduction by WHO as a key malaria disease-control intervention. Similarly, TDR supported some of the early exploration of artemisinin-based drugs and combination drugs, the most effective anti-malarial therapy available today.

Yet no achievement could have been possible without collaborators, partners, donors and sponsors, notes Dr Howard Engers, former manager of TDR’s leprosy vaccine and malaria vaccine research programmes, and presently director of the Armauer Hansen Research Institute in Addis Ababa. “Far from trying to take all of the credit for TDR,” he says, “everything TDR has accomplished has been through partnerships.”
Early successes in drug development — leprosy, river blindness, malaria and HAT

Over the course of its first decade, TDR would develop new drugs, diagnostics and vector control tools for a wide range of diseases, notably onchocerciasis, malaria and human African trypanosomiasis (sleeping sickness). One striking achievement was TDRs lead role in developing a new leprosy treatment. Early on, TDR helped demonstrate that drug resistance to dapsona, the prevalent leprosy drug, was a significant problem, as was the lifelong course of treatment required.

TDRs experts and advisers also pointed out that several compounds had shown potential activity against M. leprae in laboratory tests, but had not yet been properly evaluated for use in humans. More generally, scientists were beginning to investigate how multi-drug therapy (MDT) acting against different chemical...
cattle harbouring a zoonotic strain of the filarial *Onchocerca* parasite was regarded by scientists as the best predictor of how a compound would act against human onchocerciasis (river blindness). Results showed the drug was ‘highly effective’ against the microfilariae, or infant larvae of the parasite, although it did not kill the adult worm.

This screening test was part of a broader TDR effort to search for a new onchocerciasis drug: “The two drugs we had for onchocerciasis at the time were notorious poisons,” recalls Lucas. “We were really desperately targets, might be more effective than monotherapy. TDR thus initiated clinical trials of drug combinations (dapsone, rifampicin, clofazimine and acedapsone) for leprosy treatment in Mali and India. Their success contributed to a landmark 1982 recommendation by a WHO Study Group that MDT be used for leprosy. Other partners would now carry forward a vigorous programme of control and elimination, led by the WHO Leprosy Unit and Programme for the Elimination of Leprosy, the Nippon Foundation through its sister organization, the Sasakawa Memorial Health Foundation; various non-governmental organizations and the pharmaceutical firm Ciba-Geigy (now Novartis).

“The argument was that before trying to develop an entirely new drug, we should look at known compounds that might be used better, in combination,” recalls Dr Adetokunbo Lucas, TDR director from 1976 to 1986. “Leprosy is an example of how we did not use the same strategy for every disease, but sat down and tried to find the most appropriate approach.”

**The development of ivermectin**

In July, 1978, scientists at the US-based laboratories of Merck, sent a compound that they had been researching for several years, called ivermectin, to a TDR-supported drug-screening facility at James Cook University of North Queensland, Australia. The screen in

Ivermectin comes free

“Merck and the WHO have collaborated extensively on the development of ivermectin for onchocerciasis. The special circumstances associated with this disease and the interest of several organizations and governments have caused Merck from the outset to consider ways of accommodating a variety of objectives... Merck is undertaking to make appropriate arrangements, if necessary, with other interested parties, to make needed quantities of the drug available to these governments and patients at no cost to them for the treatment of onchocerciasis.”

Excerpt of Telex from Robert D. Fluss, Merck, to TDR Director Adetokunbo Lucas, 20 June 1986.
looking for a new drug. When we visited the major drug companies, they were not interested. No one was screening. Perhaps there was a compound on the shelf that had not been discovered? The strategy put forward was to open a compound-screening network.”

Along with James Cook University, the network involved researchers at the University of Georgia (USA); the University of Giessen (Germany); the Wellcome Trust (UK); the London School of Hygiene and Tropical Medicine; and the University of Tokyo.

“We asked industry to give us compounds to test,” continues Lucas, “and we would give them the results, free of charge and confidentially. Since the smaller animal screens often yielded false positives, the most promising compounds were sent to the cattle screen. It was much more expensive, but also potentially more accurate. Among the first compounds to go through the cattle screen was ivermectin.”

Merck’s scientists were enthusiastic; TDR less so because the ultimate TDR goal was to identify a ‘macrofilaricide’, a drug that would sterilize or kill the adult parasite, and thus cure the disease altogether. Merck proceeded independently to Phase I clinical trials. But serious TDR-Merck collaboration resumed later on, as ivermectin’s efficacy as a control measure became evident. TDR also facilitated Merck’s links to collaborative networks in the Onchocerciasis Control Programme (OCP) of 11 West African countries (TDR, 1998).

In February 1986, as the drug was about to be registered, Lucas and Dr Brian Duke, head of WHO’s Filariasis Unit, held a decisive meeting with Merck’s then Chief Executive Officer, Dr Roy Vagelos, who had been negotiating with donor agencies over ivermectin’s sale. “Vagelos made us cups of coffee in his office,” recalls Lucas. “Then, he told us that he had not got any response from the donors. He said he wanted to see the drug widely used, so he had decided to donate it. But at the time, this remained confidential.”

In June 1986, as Lucas was concluding his ten-year TDR term, he contacted Merck once more. “I asked if I could make public Merck’s offer to donate ivermectin at the upcoming JCB meeting — the last one that I would attend as Director.” The result was a 20 June telex to TDR (see box). Vagelos was later awarded a medal by the Prince Mahidol Foundation for his “bold and unprecedented” decision. Lucas and his successor, Dr Tore Godal, received the same medal jointly for their contributions to TDR.

New malaria drugs — artemisinin

Malaria remained the biggest killer worldwide, and it was here that a new initiative, led by Chinese scientists and supported at an early stage by TDR, helped to pave the way for significant breakthroughs in malaria treatment. This was research into the anti-malarial properties of the indigenous Chinese plant known as qinghao (A. annua). The plant had been used in traditional Chinese medicine, and its active compound, artemisinin, appeared to be an anti-parasitic agent.

Interest in new anti-malarials was high as parasite resistance was developing against most other available drugs, some of which had substantial side effects. TDR, whose networks already included collaborations in China, would be among the first international institutions to dispatch scientists to China’s artemisinin research facilities, and transmit the value of the endeavour to colleagues elsewhere. Cooperation in an era when the Cold War was a dominant theme of international politics, involved delicate diplomacy. But researchers shared a common quest for a better treatment for one of the world’s deadliest diseases.

“The Chinese scientists who were working on artemisinin contacted the malaria section of WHO,” recalls Lucas. “They were very anxious to have the drug registered and widely distributed. We said it needed more workup, including pre-clinical laboratory testing of toxicity. Part of that was done through the TDR network.” Other public and private partners across Asia, Europe and North America would later lead development of main artemisinin derivatives (artemether, artesunate and arteether) and artemisinin combination therapies (ACTs). TDR’s role would evolve into supportive and focused endeavours, e.g. research into injectable artemisinin derivatives for severe malaria; field trials demonstrating the value of ACTs generally, and safety for young children. Still, TDR’s early appreciation of, and response to, Chinese research demonstrated critical leadership in the initial phases of discovery, bridging barriers of geography and politics to benefit public health. •

In the next issue of TDRnews: Making a difference, Phase II ‘Innovation in field research’ (1987-1997).

Full text available at: www.who.int/tdr/about/history_book/anniversary_book.htm
From LF control to elimination

How implementation research helped drive policy change

The Implementation Research (IR) carried out by Dr Kapa Ramaiah and his colleagues at the Vector Control Research Centre (VCRC) in Pondicherry, India, has demonstrated that Mass Drug Administration (MDA) for lymphatic filariasis (LF) is one of the most cost-beneficial public health interventions in the history of medicine. The research also has projected approximately how many rounds of MDA will be necessary to eliminate LF as a public health problem, as well as documenting how drugs can be delivered more effectively. Implementation research has thus generated critical evidence to support and guide the Global Programme to Eliminate Lymphatic Filariasis (GPELF). For more than a decade, funding support through TDR’s Research Strengthening Group and the Filariasis Steering Committee has been key to VCRC’s research efforts.

*First of two parts on the history of lymphatic filariasis: from control to elimination.*

**Interview with Dr Kapa Ramaiah**

Please explain what motivated you to become involved in LF research.

After joining VCRC, I realized that LF affects millions in India. Close interaction with affected communities as part of various studies and witnessing the suffering inflicted by the disease strengthened my resolve to work on LF. My Director at the time, Dr P.K. Rajagopalan, instilled discipline and encouragement. I read more and more... about the success story of LF elimination in Japan in the 1950s and 1960s under the leadership of Professor Manabu Sasa. The Japanese example gave me hope that one day India could also be freed from the disease. India is now, more than ever before, in a position to control/eliminate LF; thanks to the advent of annual single dose mass drug administration.

Implementation Research (IR) is not always very well understood. Please describe IR’s particular importance and relevance both to LF and more broadly to research, policy and disease control strategies.

Notable among the new tropical disease control tools developed over the last two decades are insecticide-treated bed nets for malaria control and annual mass drug administration for control/elimination of onchocerciasis and lymphatic filariasis. If implemented effectively, these can reduce disease burden significantly. However, inadequacies in logistics, community health policy, health systems, human resources and funds pose severe restraints. Unless these inadequacies are addressed systematically through research, we may not be able to move forward at the required pace and achieve the goals that are set. So implementation research is integral to disease control/elimination.

Implementation research has been an important aspect of TDR’s research programme. When did you first become involved in IR with TDR, and how did you, as a biologist, develop the capacity for undertaking such research?
The first TDR project I undertook in 1993 was on the socioeconomic impact of LF. This was a very big and important multi-site initiative undertaken at VCRC and two other institutes in India and three sites in Africa. It provided me with many opportunities to interact with sociologists and economists, and subsequently I received some training in sociological research techniques, while TDR funds allowed me to employ good economists and good sociologists. Issues such as drug delivery, the impact of MDA and its costs and benefits, are very relevant to the needs of the GPELF and to the Indian Lymphatic Filariasis Control Programme. Research on all of these issues has been aptly supported by TDR, as well as through the committed VCRC research team and administration, and the Global Programme objectives.

Knowledge translation is one of today’s buzzwords in scientific research, referring to the uptake of research results into policy and practice. Many of your results have very quickly been taken up into policy and practice. How?

We at VCRC maintain a close association with the Control Programmes at both the state and national levels, involving them in our studies so that they have a grasp of the problems and solutions offered by research. For example, when results from the field indicated that some communities might require as many as 10 rounds of MDA to eliminate LF, as compared to the 4-6 rounds previously deemed sufficient, we alerted control personnel to that finding — explaining that this also was partly due to the less-than-effective treatment coverage.

Our research teams also travel widely, interacting with primary health care officers and paramedical workers, as well as drug distributors, including those in remote villages.

How do you stimulate interaction between researchers and state or national control programme officers or decision-makers?

In some of the projects (Community-Directed Treatment [ComDT], advocacy), we involved the state (Tamil Nadu) level programme managers as co-investigators. They have taken part in the TDR workshops to develop project protocols, and were involved in project planning, supervisory field visits, and data analysis. They were also authors in publications. In the other projects, we share the results of research with programme staff, and incorporate their suggestions into further workplans. There is a good mechanism of information exchange between VCRC and the national programme. At the same time, we at VCRC still believe that the LF elimination programme should be a far bigger priority at various levels.

The introduction of Filaria Prevention Assistants (FPAs) is one of the success stories of research translated into policy within two to three years. Can you describe?

From our field studies supported by TDR and others, we saw that treatment coverage was a major problem and that with existing personnel, the goal of covering more than 80% of the eligible population with MDA would not be achievable. A significant proportion of people were receiving the tablets, but were reluctant to take them. These findings prompted decision-makers to introduce the Communication for Behavioural Impact (COMBI) strategy, which incorporated FPAs into the control effort in the year 2002 to stimulate behavioural changes. Afterwards, the national programme decided to incorporate COMBI in the MDA programme. FPAs have now become an integral part of control.

It’s interesting why so many people in India do not take the drug even though they receive it. Why is this?

The poorly perceived threat of filariasis, fear of side-effects, and many behavioural factors are responsible. Many of the people we spoke to during the COMBI research said “We didn’t know it was so terrible — now we want to take the drugs”.

There also are problems from the distribution perspective. Those include the time (morning vs. evening) of drug distribution, the credibility of drug distributors, and supervision.

Have you had any ‘eureka’ moments in your research, any moment that stands out as particularly exciting?

Perhaps the most exciting results were those we presented on the economic burden of LF and on the costs
Lymphatic Filariasis

LF is a cruel parasitic infection that leaves many people partially disabled and suffering for the rest of their lives. The more well known consequences of infection may include hydrocele in men, and the terrible swellings of limbs and organs called elephantiasis (an estimated 7.4 million cases in India alone). The condition is known since ancient times and thought to be depicted on 4000 year old artefacts from Egypt. Less well known is the life-long stigma many of the victims must endure. In addition to the overt abnormalities, internal damage to the kidneys and lymphatic system is a common and hidden problem. Today 500 million people in India alone live in areas endemic for this parasitic worm. Each year on National Filaria Day, the at-risk population receives up to 1.1 billion tablets of diethylcarbamazine (DEC). This year, DEC will be combined with albendazole, making it perhaps the largest one-time drug distribution effort ever conducted.

Can you please describe what is the greatest satisfaction you have received from your work in this area of IR/LF?

I cherish the work on impact of MDA at community level, estimation of economic burden of LF in India and cost-benefit analysis of LF elimination. I am able to undertake a lot of independent research work in close association with communities, contributing to the lymphatic filariasis elimination programme, and this has been made possible through the unflinching support of WHO/TDR and ICMR.

The Global Programme for the Elimination of Lymphatic Filariasis (GPELF) of WHO stands today as an evidenced-based monument to TDR’s field research, which directly contributed new and innovative tools towards the control and elimination of this disease of poverty.

PROFESSOR CP RAMACHANDRAN

Contact: Dr Kapa Ramaiah ramaiahk@yahoo.com

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and benefits of the MDA programme.¹ We showed that LF is responsible for a loss of nearly US$ 1 billion annually, and that MDA is one of the best and cheapest interventions in the annals of public health! These were exciting results from a very minor investment in a drug costing only US$ 0.35 per person for six treatments over six years — even allowing for the annual inflation rate.

Is there evidence that the infection will indeed die out? Has it happened anywhere yet?

There is evidence from China of the infection dying out, but there, the programme used a very intensive treatment (mass and selective treatment, plus administration of DEC medicated salt). Nevertheless, we need more information on disappearance/resurgence of infection in typical post-MDA situations.

How many years do you estimate until lymphatic filariasis is eliminated (as a public health problem) in India?

Before the advent of MDA, the national programme in India could cover only 10% of the population at risk! Now, with MDA, they can cover the entire population at risk. Still, while we will be able to achieve good control in many pockets, to achieve elimination as defined by WHO, my personal perception is that it will take 20-25 years. Still, this is not really a long time, considering the size of the problem and the time it has been with us.

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An international network of researchers has created an open access Drug Target Prioritization Database to facilitate the development of medicines to fight infectious diseases of the developing world.

“This is the first time that any group has assembled such a comprehensive set of information pertinent to drug target discovery, for such a diverse array of parasitic and bacterial diseases,” says Dr Wesley Van Voorhis from the University of Washington in Seattle, who coordinates the Drug Target Prioritization Network operating the new database. The Drug Target network, established by TDR in 2005, is a consortium including a global team of academic laboratories, research centres and industry scientists.

The network focuses on drug targets for malaria, tuberculosis, African sleeping sickness, leishmaniasis, Chagas disease and worm infections such as schistosomiasis and filariasis. Together, these diseases are responsible for billions of infections in the developing world, and more than six million deaths per year.

The network database is unique in that it is freely accessible to any researcher, a particular boon to scientists in developing countries. Dr Fernan Aguero, a network member from Argentina, and responsible for much of the database architecture says, “I am very excited about the impact that this resource will have, opening new avenues for drug discovery.”

The database builds on a decade of intensive international investment that produced complete genome sequences for organisms responsible for five tropical diseases, with more anticipated for the parasitic worms known as helminths. At the other end of the spectrum, pharmaceutical firms have extensive libraries of chemicals that might act against disease pathogens. The new database adds an important additional resource that can help bridge such knowledge sets. For instance, users can search a particular protein of a pathogen’s structure for features that make it a more likely drug target. The entries rank potential targets on measures such as “druggability,” which indicates whether small molecules are likely to inhibit them. The database also links to genomic-scale datasets made publicly available by genome sequencing centres and other researchers around the world.

Dr David Roos of the University of Pennsylvania Genomics Institute, who has been primarily responsible for the database design, says, “This website allows researchers to prioritize drug targets by defining criteria tailored to the capabilities of their particular program. For example, a university laboratory that excels in studies on one class of drug targets can identify those enzymes that look most promising as drug targets, while a pharmaceutical company may select candidates tailored to their particular drug compound collections or expertise in assay development.”

Dr Solomon Nwaka, who leads TDR’s drug discovery activities, says the resource should expedite the time-consuming and high-risk early stages of drug development. “There is a growing awareness of the need for new therapeutic targets for these diseases. Pharmaceutical firms are increasingly interested in screening their chemical libraries against parasite targets, but a comprehensive list of validated drug targets for these organisms has not been readily available. The original intent of this project was to develop a ‘top 10 list’ of validated targets for each pathogen, but it quickly became apparent that enabling researchers to customize criteria for target selection in the database will provide added benefits, including the flexibility to continuously update the database.”

> Continued on page 29
One of largest studies ever on treatment for TB/HIV co-infection

TB-HAART study
One of the largest clinical studies ever undertaken on how to best treat TB/HIV co-infected patients began this year in four African countries suffering from a high burden of both diseases. The TDR-sponsored trial, also supported by the US Agency for International Development (USAID), will examine whether earlier use of both TB and anti-retroviral drug therapy in co-infected patients can reduce mortality and morbidity without a major increase in adverse drug-related events. The trial is part of a broader TDR strategic initiative to identify improved management strategies for TB and HIV co-infections, as part of the Programme’s new Ten Year Strategy.

Some 1800 patients are currently being recruited for the trial in South Africa, Tanzania, Uganda and Zambia. Two pharmaceutical firms, Merck and GlaxoSmithKline (GSK), have donated over US$ 3.2 million worth of anti-retroviral drugs to the initiative.

“What we are trying to do is to develop better evidence to guide policy recommendations for treatment of HIV-infected TB patients,” says Dr Philip Onyebuoh, leader of the TDR team coordinating the effort.

“At the moment, recommendations for treatment are based upon research conducted mostly in developed countries, and largely superimposed on developing country patients,” Onyebuoh adds. “We want to develop an optimized level of care specifically for the populations where a high burden of disease exists, alongside other conditions of poverty and illness.”

**Research goal: Improving patient treatment**

The TDR study thus has two primary goals:

1. To determine if combined simultaneous treatment for TB and HIV can reduce morbidity and mortality without adverse safety concerns.
2. To examine if anti-retroviral drug treatment (Highly Active Anti-Retroviral Therapy or HAART) at an earlier stage in the HIV/AIDS disease spectrum can reduce mortality and morbidity of HIV/AIDS patients, and prevent the later occurrence of TB and other opportunistic infections.

The TB-HAART study is one of six similar planned or ongoing trials in various parts of the developed and developing world.

However, along with being one of the largest trials in terms of the numbers of patients to be enrolled, the TDR-sponsored trial has two other unique features:

- It is one of the few trials in disease endemic countries (DECs) to explicitly consider whether HIV patients who receive HAART treatment at a much earlier phase of disease progression (220-500 CD4 T cells per microlitre of blood) than is commonly recommended, might have better outcomes.
- It is one of the few studies of its size to evaluate the effect of early and concomitant use of
4FDC trial launched

A second TB-related study addresses neglected questions about treatment formulations

TDR has initiated a clinical trial to determine if TB treatment combining all four recommended drugs into one ‘fixed-dose’ is as effective as the same drugs taken in separate, or ‘loose-dose’, formulations. The three year TDR study, being conducted in Ethiopia and Nigeria, involves 500 patients from each locale. The Nigerian arm of the trial began in January, while recruitment in Ethiopia commenced last spring. Along with being treated for TB by either the fixed-dose or loose-dose formulations, all patients taking part in the 4FDC clinical trial will be tested and treated for HIV/AIDS.

Fixed-dose combination drugs for TB have been used by the Directly Observed Treatment, Short-course (DOTS) in control programmes for several years — primarily in a form known as ‘4FDC therapy’ as it involves four combination pills a day — as compared to the 16 pills often required in loose-dose regimes. The 4FDC regime ensures that all four recommended TB drugs are, indeed, used, particularly in locales where drugs are difficult to obtain. Treatment by all four drugs in combination is presumed to reduce the risk of bacterial resistance to any one particular drug in patient populations.

By simplifying treatment, fixed-dose combination therapies also are presumed to improve overall compliance with TB treatment — which can take six to eight months to complete. Yet there has been virtually no systematic study of these assumptions, especially in TB and HIV high burden settings. The TDR study is thus the first to create an evidence base about benefits, as well as any possible drawbacks, of 4FDC therapies among TB patients who are both HIV seropositive and negative.

The single-blind randomized trial of the 4FDC regime was conceived in 2001, but delayed due to difficulties in obtaining a reliable source for loose-dose pills — as manufacturers had shifted rapidly to the fixed-dose TB treatment formulations.

In 2004, the Indian-based pharmaceutical firm, Lupin Pharmaceuticals, in a welcome philanthropic gesture, agreed to manufacture and donate a supply of both the loose and fixed drugs. It took another two years to organize the trial sites.

Boosting research capacity

Another aim of this project is to bolster the capacity of research and control efforts for both TB and HIV in the two countries where the studies are being conducted. “It’s a very good example of how we can introduce the culture of research into a national control programme,” says Dr Mahnaz Vahedi, project manager.

“One goal is to empower TB control programmes by embedding TB R&D and research capacity strengthening in national control programmes,” says TDR’s Dr Hashim Ghalib, who has led the capacity building effort. The Nigerian study site at Mile-4 Hospital in south-eastern Ebonyi State is one of the largest TB treatment centres in the region.

Due to the trial, the Mile-4 hospital laboratory also has become one of the few in Nigeria certified to diagnose TB through smear microscopy. The laboratory is being supported by Zankli Medical Centre in Abuja, Nigeria, for mycobacterial culture and drug sensitivity testing.

“We built a TB smear microscopy laboratory in Mile-4 Hospital and sent scientists to South Africa to get proficiency training in laboratory techniques,” explains Ghalib. “The new hospital capacity will give it potential to function as a centre for future clinical trials on new TB drugs or diagnostics.” Mile-4 also now boasts a CD4 cell counter — a test critical for assessing whether HIV seropositive patients should receive anti-retroviral drug therapy.

In both Nigeria and Ethiopia training has been offered in research proposal development; Good Clinical Practices and Good Laboratory Practices; data entry and management. Such training and improvements have a big impact on routine patient care and documentation, notes Dr Joseph Chukwu, principal investigator at the Mile-4 study site and medical coordinator for the German Leprosy Relief Association (GLRA) in Enugu, Nigeria, which also has a major involvement in TB control.

“In the past, we offered HIV testing only to confirmed TB patients. Now, we have been offering HIV tests to all TB suspects,” notes Chukwu. The overall improvement in the diagnostic facilities has led the Ebonyi State government to consider designating Mile-4 as a comprehensive HIV treatment centre. The project also has catalyzed new collaborations between Mile-4, which is a Catholic hospital, and other public health care and research institutions, including the University of Nigeria in Enugu and Ebonyi State Teaching Hospital.

“For us,” says Chukwu, “we see it as an opportunity to promote public-private partnerships, to get everyone together, the universities, the national programme managers, as well as WHO, and to build capacity for research. “And because the national programme is already part of the team, it will be easier to get the results of this research directly into policy and practice.”

[16]
HAART and TB treatment. TB treatment outcomes are confirmed by bacteriological culture methods, including long-term follow-up to investigate the incidence of TB relapse.

“Clearly this kind of TDR study has major policy implications globally, especially in TB and HIV high burden settings,” says Onyebujoh.

“There has been a desire to review policy guiding treatment. That is why there is an upsurge in these kinds of trials. However, due to the enormity of the undertaking, no single trial yet has generated sufficient evidence to really drive guidelines for recommended treatment approaches.”

**When to start anti-retroviral treatment**

The key biomarker determining when an HIV patient will receive anti-retroviral treatment is the blood level of CD4 T cells, a subclass of immune system T cells most affected by HIV/AIDS.

Currently, WHO guidelines recommend that HAART treatment begin when the CD4 cell count drops below the level of 200 cells per micro litre of blood — and that is the threshold observed in most developing countries where anti-retroviral drugs are available. However, the recommended entry point for treatment in developed countries is often much earlier. For instance, the US Centers for Disease Control (CDC) recommends that anti-retroviral drug therapy begin when the CD4 indicator drops below 350 cells per micro litre.

“There is no doubt that when properly used, ARV treatment is making an impact on mortality and morbidity,” notes Onyebujoh. “However, we need more systematic evidence to tell us how and at what entry points to use anti-retroviral drugs, especially among patients also suffering from TB.

“Our view is that waiting until patients become symptomatic may reduce the impact of the intervention. In addition, the immune systems of many people living in developing countries may have already been chronically challenged by other diseases, ranging from malaria to hepatitis and other viral infections, resulting in less than an optimal immune response to new infectious diseases. By the time someone gets to the recommended entry point for anti-retroviral treatment, there may have been irreversible immunological damage. The reduction in viral load may not be associated with the expected immune reconstitution. So if we initiate treatment for HIV/AIDS in a randomized control study among patients whose cell counts are above the 200 CD4 level, and examine the results, we may see the benefits on mortality and morbidity.”

Onyebujoh acknowledges that there are concerns among some researchers that the benefits of such an approach may be outweighed by major adverse events and poor compliance problems, potentially leading to drug resistance and reduced long term efficacy of anti-retroviral drugs. “While these concerns are valid, there is a need to systematically evaluate these possibilities in well-designed studies,” he notes.

The TDR-sponsored trial will thus involve groups of HIV patients with CD4 counts in the range of 220-500 cells per micro litre, as well as patients who are infected solely with either HIV or TB, so that further refinement of the analysis by individual disease is possible. This latter segment involves safety evaluation through well-designed pharmacokinetic studies.

TB drugs will be initiated immediately in all of the patients with bacteriologically confirmed TB cases. HAART treatment will be initiated right away in one-half of the HIV infected patients, while the control group will receive a placebo for the six-month duration of the TB treatment. Thereafter, all HIV co-infected patients enrolled will receive anti-retroviral therapy — and a commitment from governments participating in the study that all trial participants will receive those drugs for life.

**Measuring outcomes**

Primary outcome measures, at the end of six months, will be TB treatment outcomes. However, stratification of the analysis will also demonstrate if there is a value to earlier treatment of HIV/AIDS with anti-retroviral drugs.

“The main focus of the study is the means of improving treatment for patients with both HIV and TB,” notes Onyebujoh. “But the other spin-off is the relevance of...
the results to the improved management of HIV patients who may not have TB but are vulnerable to other opportunistic infections. If we can determine whether earlier HIV treatment results in a decline in incidence of other opportunistic infections, this will be another good result of this research."

Further laboratory analysis of blood samples and data will also aim to identify drug-drug interactions between the TB and anti-retroviral treatments that might reduce their efficacy. The most sophisticated laboratory analysis and interpretation of the data will be done under the auspices of the Medical Research Council of South Africa and the University of Cape Town.

National TB/HIV control programmes of all four participating countries are involved as well. In Tanzania, Uganda and Zambia, the start of the trials has been preceded by research and institutional capacity-strengthening.

“We purchased CD4 blood count machines and did a lot of training in research and laboratory practices, often in remote locations, to prepare for this study,” notes Dr Mahnaz Vahedi, TDR team member.

“For instance, one of the Tanzanian study sites is an eight hour drive from Dar es Salaam,” she observes. “But it is in this kind of rural setting, where the burden of disease is, where you find the patients. Building research capacity in such locations also can improve treatment access.”

**Need for more resources to sustain this ambitious study effort**

“Preparations for this massive and complex trial have been underway since 2003,” says Onyebujoh, who was the driving force in the conceptualization and initiation of the research that was based on his own extensive health policy experience in southern Africa.

As a first step, TDR negotiated the required HIV drug donations from Merck and GSK, while the TB drugs were purchased by TDR from the WHO-operated Global Drug Facility. TDR invested US$ 2.4 million of its resources in the study while USAID invested about US$ 1 million.

“However, to fully realize the study’s potential, we still aim to raise another US$ 1.5 million per year for the next four to five years,” says Onyebujoh, adding, “If we don’t act now, the risk is that by the time we come up with the evidence to support an evidence-based policy for TB/HIV treatment, policy makers will have found the process too slow — and will have already made decisions on their own.”

**Expert Consultation on TB immunotherapy held at TDR**

An expert consultation on TB immunotherapy held at TDR in late January considered how immune- booster treatments administered to TB patients alongside standard TB chemotherapy might optimize TB treatment regimens. Dr Philip Onyebujoh, who heads a TDR team exploring the issue, said that the treatment ‘adjunctive immunotherapy’ may have the potential for more effectively addressing drug resistant strains of TB, known as MDR and XDR-TB.

As a result of the expert consultation, TDR is now considering human clinical trials for adjunctive immunotherapy alongside TB treatment. “This is an attempt to optimize therapy for TB at a moment when there is still a shortage of new drugs in the pipeline,” Onyebujoh observes.

“By possibly enhancing the speed of bacillary clearance with adjunctive immunotherapy, you may improve the efficacy and efficiency of current TB drug regimens.” Onyebujoh added that the results of such a trial could feed into the broader TB-HAART study now getting underway in Africa by generating better guidelines for recommended treatment of TB and HIV co-infected patients.

Global Drug Facility. TDR invested US$ 2.4 million of its resources in the study while USAID invested about US$ 1 million.

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**Resources:**


**Contact:** Dr Philip Onyebujoh onyebujohp@who.int
Planning for success

Health research project management

Whether the study aims to analyse the genome sequence of a mosquito or examine the effectiveness of a new drug in a community, the planning and execution of a biomedical or social research project is a difficult task. This is even more true in today’s research world where studies may involve multi-disciplinary teams of specialists working in far-flung locales. To respond to this need, TDR has developed a systematic training programme in effective project management and evaluation for biomedical researchers and project managers. Dubbed “Planning for Success”, the TDR initiative is now coordinated from the Yale University/WHO Collaborative Centre for Health Promotion, Policy and Research. With the move to create reference training centres in various regions, the effort is taking on global dimensions.

Illustration: a comprehensive train-the-trainer programme has been developed to ensure the availability of local trainers

The beginning of an idea

The initial programme of study for the training was first developed in 2001 on behalf of the TDR/Multilateral Initiative on Malaria (MIM) collaboration. In this collaboration, researchers from both developing and developed countries were working in partnership on five-year projects. Given the number of collaborators, their geographical spread and duration of the projects, the need for strong organization, planning and management of projects became more evident.

The resulting course, entitled “Effective project planning and evaluation in biomedical research”, was pilot tested in Nigeria in June 2002 and in Tanzania in June 2003 by MIM/TDR grantees as participants. It was later expanded in collaboration with the South African Medical Research Council. A TDR-sponsored training manual and step-by-step guide were published in 2005.

Learning by doing: a four-day skill building course

The four-day training course takes participants through the basic steps of project planning and management. It begins with the establishment of a project statement and the development of goals, objectives and indicators, and continues through the development of a work breakdown structure, sequencing and timeline of activities, allocation of resources, implementation and reporting/evaluation.

“Participants ‘learn by doing’ by taking their own research project through the various steps of project management”, says Dr Beatrice Halpaap who is coordinating the initiative from Yale University. “Eighty percent of the course is spent on ‘hands-on’ activities.”

At the end of the course, clear strategic outputs and detailed implementation plans, including activities, timelines, milestones and resources, are developed. Participants understand the need for and are familiar with the process of constant monitoring, communication and evaluation during the project. A draft communications and teamwork strategy is also established. Participants acquire the skills and confidence to organize and conduct research projects effectively, to enhance teamwork, and be successful in their collaborations.

“The course is expected to have an impact not only at the individual level but also at the institutional level.”
Participants are better prepared to compete for research grants, to effectively conduct their research project and to properly report. This facilitates institutional programme management and leads to an increase in successful collaborations and in publications in peer-reviewed journals,” says Dr Romilla Maharaj, Executive Director of the Institutional Capacity Development Programme at the National Research Foundation in South Africa. Dr Maharaj is a member of the TDR Planning for Success Advisory Committee.

Responding to the need: training local trainers

The initial courses offered in Tanzania, Nigeria and then South Africa in 2002 and 2003, received an enthusiastic reception from participants, who emphasized the relevance this programme could have for colleagues in academic and research institutions in developing country regions. So, TDR began a collaboration with the South African Medical Research Council to develop a ‘train-the-trainer’ programme, aimed at equipping researchers in various locales to build capacity and skills in project management.

The train-the-trainer programme was pilot tested during 2005 and 2006 with the contribution of several institutions in Africa including the National Institute of Medical Research in Nigeria, Makerere University in Uganda, the University of Khartoum in Sudan, and the Trypanosomiasis Research Centre and Institute of Primate Research in Kenya. The WHO Regional Offices for Africa and the Eastern Mediterranean also joined forces to widely disseminate the course. The training material for trainers has now been published.

To date, more than 300 scientists from 15 institutions in 10 different countries have been trained in project management techniques, and 26 trainers are now operating in more than 10 countries. In 2006, five institutions started to integrate the course into their training curricula as the wave of interest grew.

Skills honed in Africa are being transferred to Latin America; the course was introduced in Brazil in 2006 at the University of Sao Paolo and at the Oswaldo Cruz Foundation (FIOCRUZ). A train-the-trainer course took place in May. The International Centre for Medical Research and Training (CIIDEIM) in Cali, Colombia, also recently organized its first training courses, and is working towards the integration of the course into the regular curricula, in collaboration with Yale University and the NIH/Fogarty Center.

“We are all very excited about appropriating the skills that will liberate us from the angst of project commitments and the wherewithal to meet them!” said Nancy Saravia, CIIDEIM Scientific Director. The centre will receive technical support from the Trypanosomiasis Research Centre in Nairobi, Kenya, to train local trainers and share lessons learnt.

Developing country institutions take a leadership role in the initiative

In 2007, the initiative is taking another major leap forward as three initial reference training centres prepare for, and lead, future dissemination of the training course in their regions.

“This is part of an effort to ensure that developing country institutions develop full ownership in this initiative and take the lead in building the research capacity they need,” said Halpaap.

These centres, selected from among academic and research institutions in developing countries, will integrate the research project management course into their
training programme and offer train-the-trainer courses to other institutions. The long-term goal is to establish a global network of training centres that can further develop capacity, collaborate and exchange experiences.

**Next steps: building partnerships to respond to the growing demand**

WHO and other funding agencies will play a time-limited and mainly catalytic role in facilitating the development of reference training centres, coordinating the initial dissemination of the course, and establishing an effective training network.

TDR and the Fogarty International Center have been joining efforts in supporting institutions to integrate the course in their training programme and are exploring a more systematic collaboration.

To address the growing demand and interest, academic and research institutions in developed countries can also play a significant role. They could, for example, support the development of additional reference training centres through twinning partnerships and provide assistance in effective coordination at the global level.

At Yale University, a team of MPH students help drive the project and work with research institutions in developing countries that are integrating the course into their training programme. Faculty members from the School of Public Health share their knowledge and experience and contribute to the efforts to explore innovative approaches for sustainable capacity development.

Transfer to local ownership, maintaining quality assurance and measuring impact are just a few of the many challenges to be addressed.

However, for people like Halpaap who have been involved from the early days, the real satisfaction is still seeing the way that such training can help improve the quality of research in the field.

“Participants have been very enthusiastic; they helped us realize that these skills can have impact not only on their daily work but also on their institutions.”

“They have been very active in ensuring that TDR supports a wide dissemination of the course. They continuously remind us of the necessity and are now ready to play a leading role.”

We tested TDR’s project management workshop in our own Unit last week. We came out with some specific improvements and achievements, and are very satisfied with this collaboration.”

LUIS GABRIEL CUERVO, Unit Chief, Research Promotion & Development, Health Systems Strengthening Area (HSS/RC), Pan American Health Organization

**Resources:**

- Effective project planning and evaluation in biomedical research.

- Effective project planning and evaluation in biomedical research.
  [www.who.int/tdr/publications/publications/effective_trainers.htm](http://www.who.int/tdr/publications/publications/effective_trainers.htm)

**Contact:**

Dr Beatrice Halpaap, Planning for Success initiative coordinator, School of Public Health, Yale University and WHO/TDR consultant
beatrice.halpaap@yale.edu, halpaapb@who.int

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**Learning by doing:** during the four day course participants work on their own research project by defining clear research outputs and developing a complete and realistic implementation plan. A communication strategy for effective team work must also be devised.
Regional networks help protect patients

Expanding clinical trials in developing countries

The dramatic growth in clinical trials for new drugs being staged in developing countries has generated demand for new national regulations and codes of ethical conduct of clinical research in settings where such frameworks did not previously exist. Under the umbrella of its Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), TDR has stimulated a series of initiatives worldwide in capacity-strengthening for ethical review practice. TDR also has fostered a series of national and regional networks active in the development of both binding regulations and voluntary codes of ethics. Several of these networks, such as the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP), now operate autonomously.

In less than ten years, the number of international trials has increased almost 20 fold (see graphic on next page). These trials need human participants — lots of them. Although initial Phase I and Phase II trials usually only involve a few hundred participants, Phase III trials can require several thousand volunteers or more to generate evidence of efficacy and safety sufficient for a drug to receive final regulatory approval.

At the same time, the number of qualified volunteers where most product R&D occurs (e.g. the USA), is limited. So pharmaceutical companies increasingly are conducting trials in developing countries to meet this huge demand.

The ethical conduct of clinical trials, and concerns about potential abuse, has been an issue in international and medical practice ever since the Nuremberg Trials following the end of World War II. In those trials, 23 physicians of the former Nazi German regime were found guilty of war crimes and crimes against humanity as a result of unethical medical experimentation on concentration camp prisoners and prisoners of war, including experiments with sterilization, poisons and infectious diseases like malaria, which killed many victims while maiming and disabling others.

The Nuremberg trials led to the creation of the Nuremberg Code in 1949, with successive international guidelines defining the parameters of human experimentation. Still, developing countries often do not have in place national regulations on ethical conduct, supervisory staff or systems to handle the consequences of the present-day boom in clinical trials.

In 2005, a *Fortune* magazine article found that nearly 40% of all clinical trials are now conducted in poorer countries, notably Russia and India. The article stated that Contract Research Organizations may exploit patients and research institutions in those locales because costs are lower and patients more vulnerable. In the same year, *Nature* published an article entitled: “Chinese clinical trials: Consenting adults? Not necessarily…” The *Nature* article also focused attention on the need for sound ethical review and regulatory oversight in order to provide public assurance of the validity and legitimacy of these trials.

A young Indian boy in a hospital bed taking a capsule of miltefosine, the first oral drug for treatment of visceral leishmaniasis.

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TDR identifies need and begins support systems

TDR has been involved in fostering capacity for good clinical research practices in developing countries since the early 1990s. By the end of that decade, as the need for more systematic ethical review of clinical trials also became apparent, the Programme recognized that there were few national systems in place to handle the ethical review component, and few ethical committees that were well trained and working efficiently.

Even for those in place, there was no one source for guidance and support. So in 2000, TDR helped to establish the first regional forum to foster and promote training in ethical review, as well as codes of conduct and regulatory frameworks. This was established in Asia, a popular site for many new clinical trials. It was called the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP).

At the same time, TDR supported the publication of: Operational Guidelines for Ethics Committees that Review Biomedical Research. These guidelines have been translated into more than 30 different languages through various initiatives. Two years later the complementary Surveying and Evaluating Ethical Review Practices Guidelines was published.

The level of commitment and country engagement increased rapidly. This led TDR to expand its effort worldwide, creating the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER). Out of this, other regional networks were created in Africa, Latin America, North America and Eastern Europe. These included: the Pan-African Bioethics Initiative (PABIN); the Forum for Ethics Committees in the Confederation of Independent States (FECCIS); the Forum for Ethics Committees in Latin America (FLACEIS); and the Forum for ERBs/IRBs in Canada and the United States (FOCUS).

The networks bring together governments, researchers and educational institutions to develop national guidelines and local standard operational procedures for ethical review of trials. The goal is to empower the national authorities to develop what fits their priorities and needs, gather together players, and to share what works across countries. It is a complex process that involves the research sponsors, investigators, national and international institutions, lawyers, public authorities, academics, journal editors, social scientists, community members, patient advocacy groups and scientific reviewers.

What it means?

TDR's early initiation provided unique support. Training was conducted within the context of actual research projects. TDR staff have worked with the constantly expanding networks to assist them in developing national guidelines, emerging out of real experiences and identified needs.

"Having an Institutional Review Board (IRB) process is not enough. Countries need to question the intent and content of a clinical trial," observes Thongchai Thavichachat, President of Thailand's Centre of Excellence for Life Sciences (TCELS), established in 2003 to promote medical and scientific research in Thailand.

The chart shows the dramatic growth of clinical trials all over the world.

<table>
<thead>
<tr>
<th>Year</th>
<th>All countries</th>
<th>Less developed countries</th>
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<tbody>
<tr>
<td>1991</td>
<td>400</td>
<td>10</td>
</tr>
<tr>
<td>2000</td>
<td>7500</td>
<td>70</td>
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Thailand’s Health Minister Dr Mongkol Na Songkhla opened the 6th annual FERCAP conference in Ayuthaya, citing the need for better understanding of ethical standards in order to develop quality health products.
Because there is so much clinical drug development in the United States, developing countries often look there to see what systems have been put in place, but analysis against a country’s own values and culture, and evaluation of other good practice models as well as systems in neighbouring countries is equally important.

The US Research Act of 1974 set up an Office for Protection from Research Risks, and in the year 2000 an Office for Human Research Protections (OHRP) also was established. China has required ethical review for drug clinical trials since 1987. India, with a population of over 1.1 billion people, is in the process of legislating ethical guidelines for biomedical research on human subjects. Dr Anbumani Ramados, Minister for Health and Family Welfare in India, says the government is concerned with issues related to non-compliance and wants strict monitoring so no one can be exploited.

International recognition for Thailand

Within FERCAP, Thailand has become a model. It has established its own national Forum for Ethical Review Committee in Thailand (FERCIT), and is assisting other countries in the region. Thailand’s ethical review system is being set up along the lines of that existing in the United States. Dr Vichai Chokvivat, FERCAP’s Chair, is also the first Director General for the Department of Alternative and Traditional Medicine Development in the Ministry of Public Health, a position created to improve medical training, research and development. Previously, he was Head of the Thai equivalent of the US Food and Drug Administration (FDA), and spent 10 years as the secretary of an ethics committee which was set up to review and streamline possible alternative medicines.

“At every meeting, I had many questions. Then I met her,” Dr Chokvivat said with a smile during a FERCAP meeting break, nodding toward TDR’s Dr Juntra Karbwang.

Karbwang is the driving force behind the development of FERCAP and then the broader SIDCER initiative. She does not believe that one model fits all, relying instead upon local initiative to develop the appropriate system for a particular country context. This approach has proven successful in stimulating growing involvement and expansion of the networks.

FERCAP’s last annual meeting held in November 2006, in Ayuthaya, Thailand, drew about 150 participants from 16 different countries. Meetings are held to review necessary processes and regulations, and sessions focus on specific topics such as children’s needs, informed consent or disease-specific issues like HIV/AIDS.

Thailand’s Minister of Public Health, the Honorable Dr Mongkol Na Songkhla, himself chair of an ethical review committee, says, “Ensuring people’s health and well-being has become a moral and shared responsibility. There is a need for transparency and accountability in the means that we use to achieve our goals.”

The Asia Pacific region has four major health burdens:
2. Increasing burden of lifestyle diseases like hypertension, cancer and drug addiction.
3. Localized incidence of neglected diseases for which there are no effective drugs.
4. Threats of emerging epidemics such as SARS and the avian flu.
As privatization became popular in the 1980s, the role of the government was reduced to its barest minimum, while at the same time, health research to address many of these issues began an upswing.

Thailand’s Deputy Prime Minister, Dr Suchai Charoenratanakul, says, “Research is such an important activity in the 21st century that governments cannot afford to play a passive role but instead they should assert their leadership to direct the thrust of research and promote justice, equity and beneficence in the research implementation process. In effect, the goal of government is to foster an enabling research environment that respects human dignity and promotes justice and beneficence towards the goal of ‘health for all’.”

Future directions

In 2005, TDR helped the regional groups develop a SIDCER Recognition Programme, a formal process that documents and recognizes the achievement and maintenance of minimum standards for ethical review committees. To date, 11 ethical review committees in four FERCAP countries have been recognized as having met SIDCER Ethics Committee standards by their peers.

The recognition programme is now being expanded to five countries in Africa: Ethiopia, Kenya, Nigeria, Tanzania and Uganda, and 10 countries in the Confederation of Independent States (CIS countries).

In Thailand and the Philippines, a pilot project is underway to help educate the general public about the issues involved in participating in clinical trials. Radio health promotion programmes include interviews and messages about things to think about before participating, with recommended questions and resources for additional information. A hotline is being established so people can call in with any questions or concerns during their participation in clinical research.

As more national governments get involved, the goal is to increase transparency of the process, and provide greater assistance to regions that are earlier in the development of regulations and guidelines. The success of SIDCER and the 5 regional networks is due to the approach taken from the very beginning — assisting local groups to identify their own problems and providing support to search for the solutions. The SIDCER network is now primarily run by people and resources within each country, with full ownership and participation.
In its 30 year history, TDR has supported individual career development and institutional strengthening projects involving over 400 research groups in 80 disease-endemic countries (see: www.who.int/tdr/grants/grants/default.htm), as well as research and development grants. Articles in scientific journals are regarded as one of the concrete outputs of that support.

For many years, TDR collected these articles when they were submitted by TDR grantees but unfortunately this has not always been a systematic process. Then, in 2002, TDR established strategic performance indicators. The number of peer reviewed journal articles originating from TDR supported research was regarded as one measure of the impact of TDR research funding and capacity strengthening in disease-endemic countries (DECs).

Two indicators were defined: the total number of TDR funded research articles indexed by Medline or Web of Science within a biennium and the number of those articles whose first author originates from a developing country.

Since the strategic performance indicator, by definition, refers to articles published in peer reviewed journals this analysis focused primarily on searches in the international bibliographic databases cited above. However, TDR is aware of the bias introduced by these databases due to the selection criteria applied by these databases to journals retained for indexation. Therefore, search engines such as Google Scholar also were used to retrieve articles published in peer reviewed journals from developing countries which, have a website, are available on gateways such as AjOL, African Journals On Line (www.ajol.info) or are indexed in regional databases.
Results of the analysis

From 2002 to 2006, 1250 articles acknowledging TDR support were published in peer reviewed biomedical journals, and were retrieved using PubMed, Web of Science and Google Scholar. In the case of 650 articles, the first author was affiliated to a university or a research institute in a developing country.

The journals in which these articles were most often published belong mainly to the tropical, parasitic and infectious disease journal group (Figure 1). The *American Journal of Tropical Medicine and Hygiene* is by far the most likely journal to publish TDR supported research, with 103 articles published there.

A sizable number of articles were also published in science journals such as *The Lancet*, *Nature* group journals and *Science*, regarded as having a “high impact factor”—as per the criteria of the Institute of Scientific Information (Web of Knowledge).

Interestingly, an increasing number of scientists are choosing to publish in open access journals of the Biomed Central (BMC) and PLoS groups. These journals are part of the Open Access movement which aims to make available free of charge, peer-reviewed scientific and scholarly literature on the internet. A publishing fee is borne by the authors of the article but in the case of developing country scientists, this fee is waived. Many public research funding bodies are now requesting their grant recipients to publish in open access journals or to deposit their published article in an open access repository such as PubMed Central.

### Table 2: TDR funded research articles published in open access journals

<table>
<thead>
<tr>
<th>Titles of open access journals</th>
<th>Nr articles 2002-2006</th>
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<tr>
<td>Malaria J (BioMed Central)</td>
<td>26</td>
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<tr>
<td>BMC Evol Biol; BMC Genet;</td>
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<tr>
<td>BMC Genomics; BMC Immunol.;</td>
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<tr>
<td>BMC Infect Dis; BMC Mol Biol;</td>
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<tr>
<td>BMC Public Health;</td>
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<td>BMC Genomics; BMC Infect Dis;</td>
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<tr>
<td>BMC Public Health (BioMed Central)</td>
<td>10</td>
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<tr>
<td>Filaria J (BioMed Central)</td>
<td>7</td>
</tr>
<tr>
<td>PLoS Med</td>
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</table>

Seventy-six articles were published in developing country journals, which represents 6% of the total number of articles published during the five years surveyed (see Table 3 on next page). Ten journals are published in Africa (Kenya (3), Nigeria (4), Ethiopia (2), South Africa (1)), six originate from Latin America (Brazil (3), Mexico (1)), ten are from Southeast Asia (China (7), Sri Lanka (1), India (1), Thailand (1)) and only 1 is published in the Middle East (Saudi Arabia (1)). This list represents only journals that are indexed in international databases (Medline, Web of Science) or can be retrieved on the web by Google Scholar.

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1 Since the definition of the TDR performance indicators implies that the authors acknowledge TDR support, the Acknowledgements section of an article can reflect that. However, this section is not indexed by international databases. A few journals, such as the *American Journal of Tropical Medicine and Hygiene*, make this section freely available along with the abstract and the authors’ affiliation. However, in most cases, successful retrieval is highly dependant on whether access to the full text is provided by institutional subscription (WHO Library in this study) or the open access policy of the journal.
On which diseases do TDR scientists publish the most?

Figure 2 indicates the disease topic breakdown of peer-reviewed publications from 2002 to 2006. Publications on tuberculosis and sexually transmitted diseases have increased in proportion to the earlier funding. The distribution of articles by disease concurs roughly with the percentage of funds that TDR spends on each disease, with a majority of papers on malaria; over the five years, 508 of 1250 articles have concerned malaria.

Figure 2: TDR funded research articles 2002-2006: breakdown by disease

Table 3: List of developing country journals which published TDR funded research 2002-2006

<table>
<thead>
<tr>
<th>Title of journal</th>
<th>Number of articles 2002-2006</th>
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<tr>
<td>Mem Inst Oswaldo Cruz (Brazil)</td>
<td>24</td>
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<tr>
<td>Southeast Asian J Trop Med Public Health (Thailand)</td>
<td>12</td>
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<tr>
<td>Afr J Med Med Sci (Nigeria)</td>
<td>4</td>
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<td>Saudi Med J (Saudi Arabia)</td>
<td>4</td>
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<tr>
<td>Indian J Med Res (India)</td>
<td>3</td>
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<tr>
<td>Afr J Biotechnol (Kenya)</td>
<td>2</td>
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<tr>
<td>Afr J Health Sci (Kenya)</td>
<td>2</td>
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<tr>
<td>East Afr Med J (Kenya)</td>
<td>2</td>
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<td>Ethiop J Health Dev (Ethiopia)</td>
<td>2</td>
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<td>S Afr Med J (South Africa)</td>
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<tr>
<td>Sheng Wu Hu Xue Yu Sheng Wu Wu Li Xue Bao (China)</td>
<td>2</td>
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<tr>
<td>Zhongguo Yi Sheng Chong Bing Za Zhi (China)</td>
<td>2</td>
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<tr>
<td>Afr J Reprod Health (Nigeria)</td>
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<tr>
<td>Afr J Trad.Compl Altern Med (Nigeria)</td>
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<td>Asian J Androl (China)</td>
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<td>Braz J Infect Dis (Brazil)</td>
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<tr>
<td>Ceylon Med J (Sri Lanka)</td>
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<td>Ethiop Med J (Ethiopia)</td>
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<td>Rev.Saude Publica (Brazil)</td>
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<td>Rev Soc Bras Med Trop (Brazil)</td>
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<td>Salud Publica Mex (Mexico)</td>
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<td>Wei Sheng Yan.Jiu (China)</td>
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<td>West Afr J Med (Nigeria)</td>
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<td>Yi Chuan Xue Bao (China)</td>
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<td>Zhonghua Kou Qiang Yi Xue Za Zhi (China)</td>
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<td>1</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>76</strong></td>
</tr>
</tbody>
</table>

Figure 3: Breakdown of DEC first authors by country of origin
The website provides genomic and bioinformatic data for each priority organism with automatically extracted and manually curated information from the research literature and other databases relevant to each putative drug target. The network has invested substantial effort in annotation to assist scientists in the identification of high-value drug targets.

The database encourages comments and inputs from experts in the field. User-defined weightings permit potential drug targets to be ranked according to their desirability, providing prioritized, customized lists. While developed to facilitate drug target identification, the network is likely to be useful in the identification of vaccine and diagnostic targets as well, and could spur research into areas such as target validation, assay development, biomarkers and drug resistance.

The network includes investigators from the Universidad Nacional de General San Martín (Argentina), the Sanger Institute (UK), the University of Melbourne (Australia), the University of Pennsylvania Genomics Institute (USA), and the University of Washington, Seattle (USA). In kind support and information relevant to target structure, essentiality, and druggability has been provided by Pfizer, Inpharmatica, the University of California, San Francisco and New England Biolabs.

The network “provides an outstanding example of how WHO can bring together multiple groups to develop joint solutions,” says Dr Robert Ridley, Director of TDR. “We convene individuals and develop expertise within the countries that need it, leveraging global research resources to develop new treatments.”

Brazil, India, Nigeria and Kenya are among those disease endemic countries who have most frequently had first authors noted (Figure 3). Each of these countries have active research institutions and TDR capacity building efforts have contributed to strengthen them for many years.

This analysis provides only a general overview of the publishing patterns and topics generated by TDR-funded research. As stated above, this study has been limited to the access that could be gained through the indexing of the source journal and the availability of that same journal through open access or institutional subscription. The TDR website (www.who.int/tdr) currently has a list of bibliographic references that are sorted by year, disease and research topic, and a database containing bibliographic information and abstracts will soon be available on the TDR website.
Artemisinin-combination therapies (ACTs) used effectively in Home Management of Malaria

Lucy Vulley, a 45-year-old mother of five and nursery school teacher, had an unusual lesson to teach. Appearing before a recent meeting in Accra, Ghana, of top health officials from WHO, UNICEF and the Ghana government, she explained how she and other community volunteers have been able to dramatically reduce malaria illness by administering life-saving drugs right in the community.

Lucy was a participant in one of several recent TDR-sponsored studies assessing new artemisinin-combination therapies (ACTs) through a system called ‘home management of malaria’ (HMM). In home management, drugs typically are dispensed outside health care facilities and managed by trained local volunteers, such as mothers and shopkeepers.

Two studies conducted over a two-year period showed that approximately 70% of feverish children received treatment through trained community workers, more than 85% of them within 24 hours of onset of symptoms and with the correct dose of ACTs (artesunate-amodiaquine). That figure is above the Abuja target set by African heads of state in 2000 — to ensure treatment for 60% of those with malaria symptoms within 24 hours.

A previous study in 2005 had shown that another ACT (artemether-lumefantrine, Coartem®) can be distributed by trained volunteers with a high degree of accuracy and that mothers administer the correct dose of ACTs (artesunate-lumefantrine, Coartem®) can be distributed by trained volunteers with a high degree of accuracy and that mothers administer the correct dose of ACTs to their children.

The studies were conducted by the Ghana Health Service and Kwame Nkrumah University of Science and Technology, supported by TDR and UNICEF Ghana. The results were detailed in the national meeting in June of research teams, community participants, and health service officials from around the country.

“These results suggest that ACTs do work in the community setting in Ghana, and can be delivered by trained community members,” said WHO’s Representative in Ghana, Dr Joachim Saweka, adding that such approaches can help Africa meet its targets for reducing malaria mortality.

Every year nearly 25 000 children and 200 pregnant mothers die from malaria in Ghana. The parasitic strains endemic here have developed resistance to the cheapest and most widely used drugs — chloroquine and sulfadoxine — pyrimethamine (SP). WHO now recommends the newer artemisinin combination treatments. But since ACT administration is slightly more complex, it has been important to test their use in community settings. The Ghana studies were conducted in Ejisu-Juaben, Ho and Dangme West districts.

At the Accra meeting, both mothers and health care providers praised the program. Mothers can get to drug distributors close to you, it reduces expenses.” Professor John Gyapong, head of the Ghana Health Services Health Research Unit, and one of the principal study investigators, noted, “This has been successful because the community is in charge. Local drug distributors know the community. Through such channels, we can save many lives.”

The Director-General of Ghana Health Services, Dr EK Sory, is recommending that the country scale up home management strategies throughout the country. “Home management is surely the way forward,” Sory said.

“For a year now, no child has died and we have not sent any of them to the hospital.”

Contacts:
Mrs Sophia Twum-Barima, WHO Ghana
Tvum-Barimas@gh.afro.who.int

Ghana Health Service: Edith K. Wellington
Edith.Wellington@hru-ghs.org

Dr Franco Pagnoni, WHO/TDR
PagnoniF@who.int
MIM/TDR Task Force holds consultation and meeting on malaria research capacity strengthening in Africa

Strategies for building capacity for malaria research, and dialogue between research and control officers, was the focus of a Multilateral Initiative for Malaria (MIM)/TDR informal consultation with experts held recently in Brazzaville. The consultation at the WHO Regional Office for Africa (AFRO) dovetailed with the annual MIM/TDR Task Force meeting.

MIM/TDR aims to increase the contribution of African scientists to research that can reduce the malaria burden in Africa. The MIM/TDR Task Force oversees the research and capacity building grant-funding activities that facilitate core groups of African investigators and institutions to conduct high quality malaria research.

The MIM/TDR-sponsored informal consultation, which preceded the Task Force meeting, was attended by 70 researchers, control programme managers and partners from: Burkina Faso, Cameroon, Côte d’Ivoire, Gabon, Ghana, Italy, Kenya, Mali, Nigeria, Sierra Leone, South Africa, Sudan, Sweden, Uganda, United Kingdom of Great Britain and Northern Ireland, United Republic of Tanzania, Zambia and Zimbabwe.

The two-day consultation provided a forum for exchange between national malaria control programmes and malaria researchers on critical needs in malaria research in Africa. Key issues highlighted included:

**Basic and Strategic Research:** Addressing the brain drain from disease endemic countries by bolstering human resources and facilities; training younger scientists and building expertise in relevant research areas; and building skills and capacity in novel areas, e.g. immunogenetics (sequencing, SNP typing, genetic data management, analysis and interpretation).

**Applied/implementation research:** Training of social scientists, health economists, medical entomologists and system reviewers; training programmes for health-related social sciences in Francophone countries; creation or enhancement of reference laboratories; surveillance systems and monitoring mechanisms; and quality control of sentinel sites.

In addition, experts at the consultation observed that research agendas still need to better reflect health needs. To improve coordination, national malaria control programmes should work more closely with researchers to develop research agendas and identify resources available for research in their respective countries.

Members at the consultation urged immediate implementation of the commitment made last year by African health ministers to devote 2% of their ministry’s budgets to research. Representatives of national malaria control programmes affirmed their commitment to work closely with researchers at national and international levels to facilitate translation of research into practice, through evidence-based decision making and programming. They stressed, however, the need for guidance in doing that, and for technical assistance in developing research agendas. Periodic meetings with researchers within countries also are important to ensure effective linkage, as is the involvement of national malaria control programmes in the dissemination of research findings.

The MIM/TDR Task Force meeting, meanwhile, reviewed a total of 36 progress and interim reports and grant proposals. The task force recommended renewal of 15 grants (from investigators in Burkina Faso, Côte d’Ivoire, Kenya, Mali, Nigeria, South Africa, Sudan, Uganda and Zambia) and approval of two new funding proposals (from investigators in Kenya and Mali), for a total of US$ 1 215 496 in support.

Other recommended activities for 2007 include a symposium at the 56th meeting of the American Society of Tropical Medicine & Hygiene in November; publication of grants achievements; and workshops and a scientific meeting for investigators.

Support for those recommended activities, however, is highly dependent on the availability of funds to the programme in 2007, task members stressed, noting an urgent need to raise more funds. The announcement of a call for grants in 2008 will also be carefully focused on areas where previous support and grants have been limited.

**Contact:**
Dr Olumide Ogundahunsi
ogundahunsi@who.int
TDR and PAHO convene experts to review procedures for testing Chagas disease drug candidates

TDR and the Pan American Health Organization (PAHO) have stepped up efforts to evaluate new potential drug leads to be used against the chronic forms of Chagas disease, for which there is presently no adequate treatment.

The research initiative comes on the heels of a new WHO pledge made in July to eliminate Chagas disease as a public health problem by 2010. This parallels a broader WHO campaign against neglected diseases launched recently by Director-General Margaret Chan in collaboration with partners from public, private and non-governmental sectors.

Two drugs (nifurtimox and benznidazole) are in use for Chagas disease and can cure recent infections, but do little for long-term chronic forms. Use of the drugs has been limited because both have serious and frequent side-effects, require long treatment and are too expensive for many of the poor people affected by this disease.

To address this gap, TDR and its partners have been supporting the discovery and development of new drug leads through the creation of basic and clinical research networks and partnerships with the private sector. This work has yielded some positive results — a number of molecules were identified as potential new drug candidates against Chagas disease by Dr Julio Urbina of the Instituto Venezolano de Investigaciones Científicas, Caracas, Venezuela.

To move ahead in testing these leads, TDR and PAHO recently co-sponsored a meeting of experts in Argentina at the Medicine Academy of Buenos Aires to begin defining the technical framework on how to evaluate the clinical efficacy and safety of these molecules.

The meeting last April drew 35 participants from Argentina, Bolivia, Brazil, Canada, Chile, Colombia, Guatemala, Venezuela and the USA, and represented expertise in the areas of drug development and discovery (public-private partnerships, industry and academia); patient care (adult and children); national drug regulatory authorities (Argentina and Brazil); disease control programmes; and philanthropic organizations promoting access to drugs.

At the meeting, PAHO representatives and clinical and experto described the Chagas disease public health problem, the existing mechanisms for drug access and availability of treatments in the Americas, as well as the current diagnostic and treatment guidelines for infection and disease in children and adults. This information was then used to define the recommended profile for Chagas disease drugs, taking into account medical needs of diverse populations including children, pregnant women, and patients with other diseases; the diverse phases of the disease; key operational aspects such as dosage forms and pharmaceutical presentations; administration regimen; stability of the medication; drug costs and associated treatment costs. Representatives from the Argentinean and Brazilian drug regulatory agencies described their processes of evaluation and approval of innovative drugs.

The meeting also addressed methodological issues key to a clinical drug development programme for Chagas disease, including: study designs, strategies, safety, selection of patients, and endpoints for efficacy (parasitological, immunological, pathological and clinical). Regional clinical development capacities, as well as the gaps and needs, were reviewed. The Benznidazole Evaluation For Interrupting American Trypanosomiasis (BENEFIT) pilot trial project was presented as an example of a multi-country/multi-centre project that evaluates drug efficacy and safety that would serve as the basis for drug approval.

The discussions will also aim to promote standardization and validation of polymerase chain reaction (PCR) tests that can detect T. cruzi disease. Representatives from industry, PPPs and NGOs, such as the Schering Plough Research Institute, the Drugs for Neglected Diseases initiative (DNDI), the Institute for One World Health (IOWH) and Mundo Sano, highlighted how they can contribute to the drug development process.

Over the coming year, TDR will promote further discussions with key drug regulatory agencies in the Latin American region to agree upon a plan for harmonizing clinical study requirements for Chagas disease product development and define the major parameters that would serve as the basis for drug approval.

The discussions will also aim to promote standardization and validation of polymerase chain reaction (PCR) tests that can detect T. cruzi infection in humans and will be used to define drug efficacy in clinical trials.

Contact: Dr Janis Lazdins
LazdinsJ@who.int

Chagas-related publications and meeting reports: www.who.int/tdr/diseases/chagas/default.htm
Helminth Drug Initiative moves into action

A small task force of experts is hammering out an operational plan for the nascent Helminth Drug Initiative following a major meeting in Tokyo with leaders from government, academia, industry and the donor community.

The Helminth Drug Initiative is part of the larger panorama of drug discovery networks being promoted now by TDR. The initiative was first conceived in 2005 to address diseases caused by parasitic worms. These are among the most neglected by conventional private sector R&D activities, and there is also no public-private partnership dedicated specifically to helminth product development.

TDR’s helminth initiative was launched at an Informal Consultation of Experts held in Japan in March 2006. A follow-up meeting was held in January 2007, in Tokyo, to review progress and define a strategic direction. The scientific working group was co-hosted by the Japanese Parasitology Society. TDR-coordinated task forces are now being set up to expedite progression of molecules with promising bioactivity against helminthic diseases through various networks and partnerships. Diseases initially targeted include schistosomiasis, onchocerciasis and lymphatic filariasis.

A series of scientific articles defining the initiative, its objectives, and relevance to research on neglected diseases is being prepared in advance of another expert meeting planned in late 2007. The ever-present threat of increased parasite resistance to drugs now used against helminthic diseases underlines the urgency of the search for new compounds, notes Dr Solomon Nwaka, the TDR expert coordinating the helminth effort. This is particularly a concern when disease control is dependent on a single drug, such as ivermectin for onchocerciasis and praziquantel for schistosomiasis.

The initiative follows several new TDR collaborations with industry and other partners to accelerate the pace of drug discovery for infectious tropical diseases more generally. Among those is a new TDR-Pfizer collaboration in drug discovery research, announced in October 2006, which opens Pfizer’s medicinal chemistry library to TDR’s global research networks, and trains developing country researchers in Pfizer’s UK laboratories, specializing both in human and animal health product research.

The deeper involvement of agrochemical and animal health firms in the TDR-led effort can generate new synergies, Nwaka observes. A number of products now used for human tropical diseases were first developed for veterinary use.

Growing resistance of livestock nematodes to available veterinary drugs has heightened the interest of the commercial animal market in drug discovery collaborations. That was evident in the Tokyo meeting, where agrochemical companies such as Chemtura, a TDR collaborator, described how the company is proactively screening compound libraries for new lead compounds.

On another front, the Helminth Drug Initiative also is collaborating with academic institutions and industries involved in screening natural organisms for bioactive compounds.

Virtual collaborations between public sector institutions and industry raise special kinds of challenges, particularly with regards to programme coordination, resources, and intellectual property rights (IPR). However, experience has shown that these problems are not, and should not be, a barrier to finding new products to fight neglected diseases, said Nwaka.

Nwaka outlined some of the key issues that need to be addressed by the new helminth initiative, including needs for:

- new molecular targets for high-throughput screening (HTS)
- appropriate assay development
- access to quality compounds
- new or expanded screening centres
- technology transfer to support research in disease endemic countries
- dramatically increased resource investment, both financial and human
- additional, innovative and entrepreneurial partnerships
- development of human capacity and attracting more researchers

Control agencies have an important role to play, Nwaka emphasized. The collaborative support of WHO’s Neglected Tropical Diseases (NTD) department, as well as the U.S.-based Global Network for Neglected Tropical Disease Control (GNNTDC), has been welcomed by TDR.

The new initiative’s most immediate goal is to finalize an integrated programme of work to deliver two early drug development candidates by 2010. A second objective is to attract attention, investment and new partner firms, agencies and individuals into the initiative, and to help build capacity in countries and regions where that is lacking.

“We are confident that these objectives can be met,” said Nwaka. The Helminth Drug Initiative is presently hosted in TDR, but may be developed as an independent entity depending on progress and resource availability.

References:

Contact: Dr Solomon Nwaka
nwakas@who.int
TDR’s new strategy for ‘empowerment’ is a focus of discussions at RSG meeting

TDR’s Research Strengthening Group (RSG) held discussions on transitioning the current capacity strengthening activities to TDR’s new strategic ‘empowerment’ function at its 32nd meeting in Geneva.

The RSG is a multidisciplinary group of scientists that provides technical and strategic advice to TDR on capacity strengthening of researchers, research institutions and networks in disease-endemic countries.

For TDR, the focus on ‘empowerment’ means placing even greater emphasis on the engagement of developing countries and the development of scientific leadership at individual, institutional and national levels. This, in turn, should help countries to better define research priorities, initiate and lead research, develop a stronger presence in international health research, and use research more effectively to inform policy and practice.

The meeting, which took place at TDR, was chaired by Dr Ana Rabello of the Oswaldo Cruz Foundation (FIOCRUZ), Brazil.

While the RSG was briefed on the preliminary concept of the new TDR strategy in 2006, this year’s meeting provided an opportunity for considering the final strategy text and implementation plans, subsequently endorsed by TDR’s Joint Coordinating Board in its June session. TDR’s overall strategic vision and business line managerial concept was presented by Dr Fabio Zicker, RCS Coordinator. Dr Juntra Karbwang further developed the strategic concept and plan of activities for ‘empowerment’.

Along with empowerment, the strategy emphasizes a cross-cutting role for TDR in ‘stewardship’ for research on infectious diseases of poor populations. In this role, the Programme aims to engage broad groups of stakeholders, and provide a neutral platform for diverse partners to discuss and harmonize their activities. The stewardship activities also will emphasize enhanced knowledge management, including a web-based knowledge platform, to support improved needs assessment, priority setting, progress analysis and advocacy.

The RSG welcomed TDR’s new strategy and its renewed commitment to foster the role of disease endemic countries in global research efforts on infectious diseases of poverty. The need to expand support to neglected areas of work and to drive empowerment within a public health framework were highlighted, reinforcing research capacity strengthening field as a unique niche for TDR.

RSG members highlighted issues for further consideration including: the role of gender and social sciences research in the new strategy; the apparent expansion of disease scope; and the public health impact of TDR-funded projects. The group also discussed issues of internal staffing and management to meet the new strategy’s operational needs; possible mechanisms to move RSG activities closer to country level; and implications of the new strategy on current grant mechanisms. While not all the questions had clear-cut answers, the overall view was that TDR will build on its past accomplishments while expanding its activities with new partners, where appropriate, based on decisions made with the best available knowledge.

The RSG concluded that the ultimate purpose of TDR is to make an impact on public health problems, and this should guide the focus of the work on empowerment. Issues of appropriateness, affordability, health system capacity and access, and translation of evidence into policy are intrinsic to TDR’s research efforts. To that end RSG highlighted the importance of balancing support between academic institutions and other stakeholders through collaborations with WHO control departments, country representatives, regional offices, ministries of health, and local initiatives and networks.

A step-wise transition process will be implemented to ensure the continuity of ongoing activities during the implementation of the new strategy in the 2008-2009 financial biennium.

For more information on the strategy: www.who.int/tdr/about/strategy/strategy_06_summary.htm

Contact: Dr Fabio Zicker zickerf@who.int
South-East Asia advisory committee meets

The need for increasing and coordinating health research among the three levels of WHO was one of the topics of discussion at the 30th session of WHO’s South-East Asia Advisory Committee on Health Research (ACHR). Meeting in Jakarta in March, Indonesia’s Minister of Health, Dr Siti Fadilah Supari, inaugurated the opening.

There are two levels of advisory committees on health research — global at the Geneva headquarters and 4 regional committees. Dr Samlee Plianbangchang, the Director of WHO’s Regional Office for South-East Asia (SEARO), welcomed the 21 members of this committee, which was chaired by Professor N.K. Ganguly, of India and co-chaired by Dr Somsak Chunharas of Thailand.

Dr Samlee reminded the committee of its focus on emerging infectious diseases research during the last meeting, underscoring the need to discuss avian influenza, particularly with its spread throughout Indonesia. He also encouraged the committee to conduct a brief review of WHO research in the WHO South-East Asia Region (SEAR) during the past 2 biennial periods, to deliberate on the issues and challenges and use them to identify priority activities for the future. He was particularly interested in how to build national research capacity, listing three specific areas:

- Strengthening human resources for health research;
- Improving health research management;
- Promoting the utilization of health research results;

The regional director also stressed the need to promote research that can enhance country capacity in technology development and innovation.

Dr Tikki Pang, WHO Director of Research Policy and Cooperation, discussed activities related to WHO’s global health research policy and strategy. Dr Ayoade MJ Oduola, TDR Coordinator, Strategic and Discovery Research, presented TDR’s new Ten Year Vision and Strategy. Draft comments on TDR’s strategy included the following suggestions:

- Disease endemic countries should have a say in priority-setting for research activities to be funded by donor countries.
- TDR should consider reducing the gap between the institution/university conducting research and users, such as ministers of health.
- TDR should continue and increase the resource allocation for small scale research grants to SEAR countries.
- TDR should consider the investment pattern for research funding in the context of the impact to be achieved by conducting the research.

In closing, Dr Samlee called for research efforts to be relevant to the needs of today’s health development. “Our efforts must be in response to the countries’ needs in their development endeavours, in both short and long term.”

Contact:
Dr Ayoade MJ Oduola
oduolaa@who.int
Vision for the future

TDR screens ‘A Vision for the Future’, a film on TDR’s new strategy, before thousands of participants at the Global Health Council annual meeting in Washington, DC and hosts a panel discussion on research and capacity building partnerships.


TDR hosts a panel discussion at the Global Health Council meeting on lessons learned from sustained partnerships in research and capacity-building.

From far left to right: Jane Kengeya Kayondo, a TDR coordinator, Robert Ridley, TDR Director, and Uche Amazigo of the African Programme for Onchocerciasis Control (APOC). Above: Roger Glass of Fogarty International Center and Jimmy Whitworth of The Wellcome Trust.
Publications

**Making a Difference**
30 Years of Research and Capacity Building in Tropical Diseases

[TDR History Book]

For over three decades, TDR has been making a difference to scientific research on diseases of poverty and to health in disease endemic countries. In celebration of the 30 year anniversary of the founding of TDR’s Joint Coordinating Board (JCB), its key governance body, TDR has published a historical review of achievements and challenges still to come. The history is organized into four chapters covering the key phases in institutional focus and organization: Phase I ‘Heroic goals’ (1975-1986); Phase II ‘Innovations in field research’ (1987-1997); Phase III ‘The partnership decade’ (1998-2006) and Phase IV ‘Research that makes a difference’ (2007-).

**Lessons learned in Home Management of Malaria**

84 pp., 2007 (ISBN 978 92 4 159518 6)

Since the majority of children who die from malaria do so within 48 hours of onset of illness, the early use of effective antimalaria medicines close to the home can help to reduce the burden of the disease. As a result, HMM has become a cornerstone of malaria case-management and, more generally, of malaria control in sub-Saharan Africa. Many countries are now moving to large-scale implementation of HMM. This guide focuses in particular on four countries — Burkina Faso, Ghana, Nigeria and Uganda — where country teams have completed community-based studies on HMM, assessing its operational feasibility, acceptability and (in Burkina Faso) impact on severe disease.

**Scientific Working Group on Schistosomiasis**

124 pp., 2006 (TDR/SWG/07)

The Scientific Working Group (SWG) on Schistosomiasis (Geneva, 14-16 November, 2005), reviewed the current situation in relation to research needs. Improved documentation of the full range of morbidities among the more than 600 million people at risk of schistosomiasis is one key issue discussed. The SWG recommended that investigators regularly collect data on, for example, anaemia in endemic populations, and develop standardized measures for more intricate outcomes of infection such as on work capacity and cognition. The SWG also encouraged TDR to expand research networks, including partnerships with industry. The SWG encouraged coordination and, when possible, integration, between control activities targeting different diseases in the same geographical area. Acknowledging the link between schistosomiasis and poverty, the SWG pointed to the acute need for research on the social determinants of schistosomiasis.

All TDR publications can be downloaded from the TDR website: [www.who.int/tdr/publications](http://www.who.int/tdr/publications) or are available free of charge upon request.
Tuberculosis is a major global health problem, responsible for more than 4500 deaths each day. However, unprecedented efforts to address deficiencies in TB control — including new drugs, diagnostics, vaccines, and strategies to implement proven interventions — bring hope of tangible progress. Led by the Stop TB Partnership, the global community of TB public health officials, clinicians and researchers is poised to achieve within ten years the Millennium Development Goal (MDG) target for tuberculosis, which aims to halt the growth and then begin reducing incidence of TB by 2015. This report reflects the consensus of the TDR Scientific Working Group on Tuberculosis, convened in Geneva in October 2005. The proposed research agenda accommodates the public health concerns expressed in the Stop TB Partnership’s Second Global Plan to Stop TB (2006-2015).

The Lymphatic Filariasis Scientific Working Group (SWG) was convened by WHO/TDR to review the current state of knowledge regarding the Global Programme to Eliminate Lymphatic Filariasis (GPELF) and to recommend research priorities that could best address the questions facing this global programme. More than 30 experts from around the world participated in the discussions, 10-12 May 2005, in Geneva. Issues discussed included: the effectiveness of mass drug administration (MDA) in different epidemiologic settings, the status of the disability prevention programme, and state of art of diagnostic and modeling tools to support the global programme.

Dengue is the most rapidly spreading vector borne disease. An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries. The 2002 World Health Assembly Resolution WHA55.17 urged greater commitment to dengue control among Member States and WHO. The goal of the Scientific Working Group was to outline a research agenda by identifying bottlenecks and making detailed and specific research recommendations. The SWG sought to identify areas of research that could lead to tangible benefits for people in disease endemic countries within the coming years as well as outline a strategic vision for applied and basic research from which benefits would be felt in the medium to long term.

The review presents the market and policy context of nets, insecticide treatment and antimalarial drugs, and summarizes the evidence regarding access and equity issues. The bulk of the evidence presented comes from sub-Saharan Africa. Country experiences are used to illustrate issues and strategic options. The review emphasizes that interventions must consider health care utilization patterns of poor people and the limited capacity of governments to provide quality services, enforce regulatory control and protect consumers’ rights. Provision of antimalarial treatment is dominated by the informal and formal private sector, and suffers problems such as inefficiency, issues of profit motivation, low quality commodities and counterfeit drugs. The document discusses key strategic options for private sector engagement in order to scale up malaria prevention and treatment.

This review considers ethical challenges to research design and informed consent in biomedical and behavioural studies conducted in resource-poor settings. A review of the literature explores relevant social, cultural, and ethical issues in the conduct of biomedical and social health research in developing countries. Ten case vignettes
illustrate ethical challenges that arise in international research with culturally diverse populations.

Neglected diseases: A human rights analysis
Social, Economic and Behavioural Research - SPECIAL TOPICS No. 6
64 pp., 2007 (TDR/SDR/SEB/ST/07.2)
(ISBN 978 92 4 156342 0)

The failure to respect certain human rights, such as the rights to water, adequate housing and education increases the vulnerability of individuals and communities to neglected diseases. Also, people afflicted by neglected diseases are vulnerable to violations of their human rights, including the rights to health, life, non-discrimination, privacy, work, education, and to enjoy the benefits of scientific progress. This report aims to introduce and explore some of these connections. It is the result of collaboration between the Special Programme for Research and Training in Tropical Diseases (TDR), several WHO departments, the Office of the United Nations High Commissioner for Human Rights (OHCHR) and the United Nations (UN) Special Rapporteur on the right of everyone to the highest attainable standard of health.

Higher degree research training for implementation research on tropical diseases
Applied Social Sciences for Public Health (ASSPH)
56 pp., 2007 (TDR/RCS/07.1)
(ISBN 978 92 4 159558 2)

Building and retaining of research capacity in applied social sciences for public health (ASSPH) in resource-poor countries has been a challenge. There is a serious shortage of ASSPH researchers and thus a dearth of related, high quality research on social, economic and behavioural aspects of tropical disease control. The initiative reviewed here draws on existing capacity in sub-Saharan Africa with support from Southern and Northern partners to develop high quality, internationally recognized, higher degree interdisciplinary and multidisciplinary research training that is grounded in theoretical and applied social science and public health disciplines, and relevant to local contexts.

CD-ROMs available for order through TDR

PlasmoCD - The Plasmodium Genomes
Produced by PlasmoDB and the Institute for Genomic Research (TIGR), with financial support from other parties. V. 4.1-12/05

PlasmoCD presents the genome sequence data for three Plasmodium species: the human malaria parasites Plasmodium falciparum and Plasmodium vivax, and the rodent malaria parasite Plasmodium yoelii, a useful model system for studying malaria parasite biology. PlasmoCD has been generated in response to the completion of the P. vivax genome sequence, and includes recent updates to the P. falciparum genome sequence.

Malaria: Genomics and functional genomics research tools
Version 1.2 Disc 2; WHO/TDR 2007

The Malaria Research Tools CD (version 1.2) was developed as part of the activities of TDR to enhance the capacity of scientists in disease-endemic countries and to promote the utility of bioinformatics and currently developed tools such as transfection and DNA microarrays technologies in malaria research.

All TDR publications can be downloaded from the TDR website:
www.who.int/tdr/publications or are available free of charge upon request.
• e-mail: tdr@who.int
• fax or mail the publication order form accompanying this issue.
In collaboration with others/available from elsewhere

Nature outlook, Neglected diseases Supplement to Nature Publishing Group
Reprinted from Vol. 449, No. 7159, 13 September, 2007

This special issue includes a range of forward-looking articles about the world of research into neglected diseases, including a contribution on TDR-supported collaborations in drug discovery research networks for parasitic diseases, (Nwaka et al). The entire issue is available for a limited time (six months) for free download from the NATURE site.

To order: www.nature.com/nature/outlook/neglecteddiseases/index.html

Innovative lead discovery strategies for tropical diseases
Nature Reviews, Drug discovery, Volume 5, November 2006

Lead discovery is currently a key bottleneck in the pipeline for much-needed novel drugs for tropical diseases such as malaria, tuberculosis, African sleeping sickness, leishmaniasis and Chagas disease. Here, we discuss the different approaches to lead discovery for tropical diseases and emphasize a coordination strategy that involves highly integrated partnerships and networks between scientists in academic institutions and industry in both wealthy industrialized countries and disease-endemic countries.

This strategy offers the promise of reducing the inherently high attrition rate of the early stages of discovery research, thereby increasing the chances of success and enhancing cost-effectiveness.

Download from TDR: www.who.int/tdr/topics/discovery_research/files/discovery_strat.pdf
Download and reprints from Nature Reviews/Drug Discovery: www.nature.com/nrd/index.html

Research with children living in situations of armed conflict: concepts, ethics and methods
Jason Hart & Bex Tyrer,

This was a paper for the symposium on “infectious diseases among children in conflict situations: risk, resilience and response” in Manila, 9-12 January, 2006. It was organized by the School of Public Health and Community Medicine at the University of New South Wales, Sydney, in partnership with De La Salle University. It was sponsored by WHO/TDR as part of the work plan of TDR’s Steering Committee for Social, Economic and Behavioural Research to promote research on conflict and infectious diseases.

To download from TDR: www.who.int/tdr/topics/social-research/files/armed_conflict.pdf
To order:
Social Development Research Center,
De La Salle University
3/F William Hall, 2401 Taft Avenue
1004 Manila, Philippines
E-mail: sdrd@dlsu.edu.ph

The regional strategic plan for malaria in the Americas, 2006-2010

In the five years since the region officially adopted the objectives of the Roll Back Malaria Initiative and commenced its intensified battle against the disease, PAHO has made considerable progress. The strategies planned and implemented by PAHO, individual country plans, and successful collaborations and partnerships on topic of malaria control, malaria research, and prevention of DDT use for malaria vector control, are detailed here.

To order: dissemination@paho.org
To download in html: www.paho.org/Project.asp?SEL=PR&LNG=ENG&CD=document

Integrating poverty and gender into health programmes: a sourcebook for health professionals

This module is designed to improve awareness, knowledge and skills of health providers regarding poverty and gender in malaria prevention and control. Examples of good practice are presented to illustrate interventions. The booklet also includes notes for facilitators and a collection of tools, resources and references.

To order: bookorders@who.int
In memoriam

Sir Ian McGregor

Sir Ian McGregor, one of the world’s leading malarialogists and a past member of numerous TDR expert committees, died suddenly of a heart attack on 1 February at his family home in Great Britain. Beginning in 1949, McGregor undertook groundbreaking research in The Gambia on malaria immunity, malaria in pregnancy and its consequences for the infant. He was co-editor of the 1988 "Malaria: principles and practice of malarialogy" dubbed the "malaria bible" and still regarded as an essential reference on the topic.

McGregor was a member, and occasional chairman, of a wide range of TDR malaria-related expert committees and scientific working groups including: Vaccines for Malaria (IMMAL) Steering Committee (1977-1988) and the Applied Field Research in Malaria (FIELDMAL) Steering Committee (1984-1990). Born in 1922 in the UK, and educated in Glasgow, McGregor began his career in Africa in 1949 with the scientific staff of the newly established British Medical Research Council (MRC) facility in The Gambia. He subsequently became director of MRC Laboratories, a position he retained until 1980, when he returned to the UK as a professorial fellow with the Liverpool School of Tropical Medicine. From his base in The Gambia, McGregor carried out fundamental research into the human immune response to malaria. His work on acquired malaria immunity, and subsequently malaria in pregnancy and its consequences for the infant, set the stage for recommendations on effective malaria-control strategies during pregnancy. He helped establish the scientific reputation of MRC as a premier institution, leading rigorous epidemiological and clinical studies in remote field locations. McGregor was supportive of research by young scientists and provided an encouraging environment for research in The Gambia from which many careers were launched. He is survived by his wife Joan, a son and a daughter.

Dr David Walliker

Professor David Walliker, who undertook seminal work on malaria genetics, a field in which he was a longtime TDR collaborator, died in May 2007 at the age of 58. Professor Walliker, a Professor at the Institute of Immunology and Infection Research of the University of Edinburgh, was born on 5 April 1940 in the UK, and was educated at the London School of Hygiene and Tropical Medicine. His research included studies on the genetics of resistance to antimalarial drugs and field studies on the genetic structure of parasite populations in African countries; 10 of his research projects received funding from TDR between 1983-1998. He was well known for his global collaborations, which significantly contributed to determining the cause of chloroquine resistance in certain strains of malaria parasites. His laboratory also served as a repository for malaria strains for TDR for many years. He is survived by his wife Patricia and two daughters.

Prof Sornchai

Professor Sornchai Loareesuwan, Head of the Division of Critical Care in the Tropical Diseases Research Unit, and former Dean of Faculty, in the Faculty of Tropical Medicine, Mahidol University, Thailand, died Sunday, 22 July 2007 at the age of 58. Professor Sornchai, as he was known to colleagues and students, served as the Government of Thailand’s representative to TDR’s Joint Coordinating Board in 1997, 1998 and 1999, also serving as JCB vice-chairman of the Board in 1998. In the 2001 and 2003 JCB sessions, he served as the Government of Thailand’s observer. Over the years he also served as a periodic consultant and advisor to the World Health Organization, and was involved in numerous WHO-AND TDR-related research endeavors. He was born in 1949 in northeastern Thailand and attended the Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand, undergoing additional training at the Faculty of Tropical Medicine, Mahidol University. As a young researcher, he gained an international reputation for his work in malaria chemotherapy, including original work on atovaquone and artemisinin derivatives. His colossal productivity in research publications earned him many national awards, including a 2001 award for The Most Cited Author from the Thailand Research Fund. Professor Sornchai served on numerous international boards and advisory groups, including the Expert Scientific Advisory Committee of the Medicines for Malaria Venture (MMV), and the International Federation for Tropical Medicine, where he held the post of President between 2000-2005. He also was a founding member of the Wellcome Mahidol University-Oxford Tropical Medicine Research Programme, initiated in 1978-9. His administrative talents were recognized in his appointments as Mahidol University’s Dean of the Faculty of Tropical Medicine (1996-2004), and as Secretary-General of the SEAMEO-TROPMED Network (1998-2007).

His close friend and colleague, Professor David A. Warrell, described him as ‘a delightful, energetic, enthusiastic and resourceful physician, clinical investigator and teacher with a unique, lovable and irresistible personality.’ Professor Sornchai is survived by his wife, Dr Vaeawta Loareesuwan MD, and a son and daughter.
Latest grants

Implementation Research

NEW GRANTS IN IMPLEMENTATION RESEARCH

These grants will be funded for 12 months in the first instance, and for an additional 1 year if sufficient progress has been made in the first 12 months toward reaching the scientific objectives, and if sufficient funds are available.

A60461
Shireen Akther
National Institute of Preventive and Social Medicine NIPSOM, Dhaka, Bangladesh.
Cost-effectiveness of residual spraying, treated bednets and environmental management for sandfly control in Bangladesh. US$ 21 600

A60482
Dinesh Mondal
ICDOR, Centre for Health and Population Research, Parasitology Laboratory, Dhaka, Bangladesh.
Management of pre-existing programme, assessment need and community perception for vector control in Bangladesh. US$ 20 000

A60155
Richard Ndyomugenyi
Vector Control Division, Ministry of Health, Uganda.
Integrated community-directed treatment with ivermectin and SP IPT to pregnant women in rural communities of Uganda. US$ 25 500

A60490
Abraham Rexford Oduro
Navrongo Health Research Centre, Navrongo, Ghana.
Home management of acute febrile illness in northern Ghana using ACT: the role of rapid malaria diagnostic testing. US$ 49 890

A60487
James Kanaruma Tibenderana
Malaria Research Centre, c/o Malaria Consortium, Kampala, Uganda.
Assessment of use of rapid diagnostic testing in the context of home management of malaria with ACTs, Uganda. US$ 51 687

A60486
Alfred B. Tiono
Centre National de Recherche et de Formation sur le Paludisme, ex-CNLP, Ouagadougou, Burkina Faso.
Role of rapid diagnostic testing in context of home management of childhood malaria with Coartem*: an open randomized controlled trial. US$ 48 500

A60547
Anand Joshi
Institute of Medicine, Tribhuvan University, Kathmandu, Nepal.
Cost-effective integrated vector management as a contribution to the visceral leishmaniasis VL elimination initiative in the Indian sub-continent. US$ 20 450

RENEWED GRANTS

A41054
Ikyoluwope Oyeneye Ajayi
University College Hospital, Malaria Research Laboratories, Institute of Medical Research and Training, Ibadan, Nigeria.
Improving home management of malaria using artesunate-amodiaquine combination in rural communities in Southwest Nigeria. US$ 21 250

A41076
Fred Bateganya
Makerere University, Department of Sociology, Kampala, Uganda.
Feasibility, acceptability and safety of ACTs in home based management of fever/malaria among U5s in rural Uganda. US$ 39 924

A00638
Daniel Adjei Boakye
Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana.
Impact of albendazole on bancroftian filariasis in communities of Uganda. US$ 72 926

A41075
Benta Na Ayae Garshong
Ministry of Health, Accra, Ghana.
The feasibility/acceptability of using artesunate-amodiaquine pre-packeted tablets for home management of malaria in children. US$ 42 500

A50518
Mohan Digambaram Gupte
Indian Council of Medical Research, National Institute of Epidemiology, Chennai, India.
WHO study ‘uniform-MDT regimen for all leprosy patients’. US$ 50 000

A20133
Margaret Gyapong
Ministry of Health, Accra, Ghana.
Impact of large scale rectal artesunate deployment in the initial management of non per OS ill under five children. US$ 36 576

A50249
Roch A. Houngnihin
Programme National de la Lutte contre le Paludisme, Cotonou, Benin.
Evaluation de la faisabilité de l’utilisation des CTA pour le traitement à domicile du paludisme au Bénin. US$ 20 804

A00257
R. Rajendran
Centre for Research in Medical Entomology, Madurai, Tamil Nadu, India.
Control of bancroftian filariasis in villages of Tamil Nadu by integration of vector control with chemotherapy. US$ 29 650

A41072
Sodionmien Bienvenu Sirima
Centre National de Recherche et de Formation sur le Paludisme, ex-CNLP, Ouagadougou, Burkina Faso.
A randomized controlled trial to evaluate impact of home/community management of malaria on children under five mortality. US$ 77 236

A00583
Sekou Fantamady Traore
Malaria Research and Training Centre, Department of Parasitic Diseases, Bamako, Mali.
Impact of albendazole-ivermectin combination treatment on Wuchereria bancrofti infection and transmission in Mali. US$ 52 600

A20679
Marian Warsame
National Institute for Medical Research NIMR, Dar es Salaam, Tanzania.
Real life deployment of rectal artesunate as an initial treatment in management of malaria non per OS children in a rural community, Tanzania. US$ 100 000
Malaria research capability Strengthening in Africa

NEW GRANTS

A61026
Mamadou B. Coulibaly
Université du Mali, Malaria Research and Training Center, Bamako, Mali.
Gene expression profile associated with blood meal and *P. falciparum* infection in the malaria vector *Anopheles funestus*. US$ 61 400

A61018
Josephat Inyama Shililu
International Centre of Insect Physiology and Ecology ICIPE, Nairobi, Kenya.
Ecological and physiological adaptations of malaria vector species in semi-arid zones in Kenya as a basis for improved implementation. US$ 82 116

RENEWED GRANTS

A40066
Oladele Benjamin Akogun
Common Heritage Foundation, Yola, Nigeria.
Can community directed intervention strategy be applied for home-management of childhood malaria among Noradic Fulani populations. US$ 62 400

A60039
Taiwo Samson
Nigerian Institute of Medical Research, Yaba Lagos, Nigeria.
Field and laboratory investigation of pyrethroid resistance in the malaria vector *Anopheles arabiensis*. US$ 60 500

A30046
Simon Kamau Kariuki
Kenya Medical Research Institute, Kisumu, Kenya.
Effect of insecticide-treated bed nets on the genetic diversity of *P. falciparum* parasites in Western Kenya. US$ 60 500

A40036
Lizette Leonie Koekemoer
National Health Laboratory Services, National Institute for Communicable Diseases, Johannesburg, South Africa.
Insecticide resistance in the major malaria vector *An. arabiensis* from southern Africa.
US$ 49 850

A30044
Christine Manyando
Tropical Diseases Research Centre, Ndola, Zambia.
A study of cost-effectiveness and role of rapid diagnostic tests for malaria in reducing unnecessary administration of costly anti-malaria drugs. US$ 13 000

A30030
Robinah Najjemba
Makerere University, Institute of Public Health, Kampala, Uganda.
Comparing performance of two different channels of drug distribution in home based management of fever strategy in Uganda.
US$ 54 852

A50090
N’Fale Dabire
Université du Mali, Malaria Research and Training Center, Bamako, Mali.
Mechanism of the decreased infectivity of post S-P *Plasmodium falciparum* gametocytes to anopheline mosquitoes.
US$ 78 050

A40044
Christine Manyando
Tropical Diseases Research Centre, Ndola, Zambia.
A study of cost-effectiveness and role of rapid diagnostic tests for malaria in reducing unnecessary administration of costly anti-malaria drugs. US$ 13 000

A50075
Hastings Ozwara
University of Khartoum, Institute of Endemic Diseases, Khartoum, Sudan.
Epidemiological studies of malaria in two areas characterized by seasonal malaria transmission in Sudan and Ethiopia.
US$ 96 750

A40076
Benjamin S. Chudi Uzochukwu
University of Nigeria Enugu Campus, Dept of Community Medicine, Enugu, Enugu State, Nigeria.
Characterisation of placental malaria in baboons infected with wild type and transfected *Plasmodium knowlesi*.
US$ 90 758

Correction

TDRnews No.77, page 12, erroneously stated that an “African baby dies from malaria every 3 seconds.” In fact, an African child under age 5 dies from malaria roughly every 30 seconds – for about 1 million deaths every year. Still far too much, by anyone’s calculation!
TropIKA.net, a new service from TDR, will be launched 30 October at the Global Forum for Health Research meeting in Beijing. Part of TDR’s new strategy of stewardship, the website is a joint effort with other partners to provide a global knowledge management portal to share essential information and help identify priority needs and research gaps among infectious diseases of poverty.