Discovering ‘lead’ compounds with the potential to become usable drugs is a critical first step to ensuring a sustainable global pipeline for innovative products (see Figure 1). While the establishment of public-private partnerships (PPPs) has helped to stimulate product R&D for some neglected diseases, increased emphasis needs to be placed on the high-risk early discovery phase. TDR is helping to fill this gap through a coordinated initiative aimed at generating new lead compounds, which might result in more effective drugs for tropical diseases.

Essential to this innovative TDR effort is the establishment of multi-disciplinary networks and partnerships between researchers in industry and the public sector in both developed and developing countries.

A need for novel drugs
The need for new, effective and affordable drugs to treat parasitic diseases responsible for an enormous burden of disease in the developing world is one of the issues facing global health today. Available drugs to treat these diseases, such as malaria, African sleeping sickness, Chagas disease, leishmaniasis, filariasis, onchocerciasis and schistosomiasis, are limited by factors ranging from parasite resistance to safety, compliance and cost. Products representing entirely new innovations in medicinal chemistry are presently lacking. More effective diagnostics also are needed for these diseases – which often are misdiagnosed or diagnosed too late.

A new generation of PPPs have provided one kind of response to these challenges by supporting accelerated development and clinical testing for potential new products already in the pipeline. These partnerships include TDR-initiated ventures such as the Medicines for Malaria Venture (MMV), the Foundation for Innovative Diagnostics (FIND), as well as others such as the Drugs for Neglected Diseases Initiative (DNDi), the Global Alliance for TB Drug Development, and the Institute for OneWorld Health. Still, there remains a need for new chemical entities, or ‘lead’ structures, that have the potential to become innovative treatments. New approaches to ‘drug discovery’ for tropical diseases are required. “To develop a drug, you first have to discover it,” says Dr Solomon Nwaka, who came to TDR from MMV about 18 months ago. Drawing upon a broad range of experiences in academia, industry and PPPs, Nwaka hopes to position TDR at the forefront of drug discovery for neglected diseases.

“While working at MMV, I recognized the paucity of quality lead compounds feeding the development pipeline for malaria, and made the decision to help fill this gap, not only for malaria but for other neglected diseases,” says Nwaka, who trained as a molecular biologist. “Huge advances have been made in our understanding of the biology of many human pathogens and their vectors, especially with the sequencing of many genomes.”

(continued on page 14)
TDR generates broad media interest in 2006

The past six months have been a time of heightened interest in TDR for a number of reasons.

The development of a new 10-year strategy has drawn interest and involvement among an ever-widening circle of partners, collaborating scientists, and others who recognize the growing relevance of research to disease prevention and control.

One of the key elements in TDR’s new strategy is the enhancement of its stewardship and empowerment roles in research. Communications will be important to support this work, and plans are developing as to how best to complement TDR’s technical work with effective communications strategies. As part of our recent outreach efforts, we launched a readership survey on this newsletter. If you have not already responded to it, please go to our website at www.who.int/tdr and send us your thoughts.

The increased pace of recent TDR activity already has generated substantial interest in both general news and scientific media. In March and June, 2006, the governments of Nigeria and Ghana hosted high-level ministerial meetings in each of their countries, which TDR, the WHO Regional Office for Africa, and WHO country offices supported. Back-to-back with the second ministerial meeting, the vice president of Ghana addressed our 29th Joint Coordinating Board (JCB) meeting in Accra. All of these events attracted widespread media interest across Africa and high visibility for TDR, its partners and collaborators (as reported in the recent Special Issue from Africa).

This summer and autumn, BBC World broadcast two special documentaries on our work as part of the highly rated Kill or Cure series. The first programme, aired in August, followed the evaluation research of syphilis diagnostic tests in Haiti, led by TDR diagnostics manager Rosanna Peeling, in coordination with the WHO country office and Haitian health officials (pages 4-5). The second programme, broadcast in late November and early December, showcased a study on home management of malaria in Nigeria, where TDR has funded local researchers to assess whether local caregivers and drug distributors can provide new Artemisinin-based Combination Therapy (ACT) drugs safely and effectively (pages 12-13). If you would like to receive copies of either programme, please email us at: tdr@who.int.

At the end of October, TDR released a joint publication with the Foundation for Innovative New Diagnostics (FIND) that documented market opportunities for developing new tuberculosis diagnostic tools (pages 6-7). The WHO-organized press conference at UN headquarters in Geneva generated unique stories in major media of the United States, United Kingdom, China and Canada, as well as broad coverage through wire services across Europe, the Middle East, Africa, South America and the USA.

Our newsletter cover story, expansion of our discovery research networks that could help identify the next generation of new drugs for neglected diseases, also is attracting wider media attention. In November 2006, an article on innovative discovery research strategies for tropical diseases, co-authored by Dr Solomon Nwaka (the TDR manager of this initiative) and Alan Hudson, was published in Nature Reviews Drug Discovery. One of our pharmaceutical collaborators, Pfizer, described its contribution to this initiative in a worldwide press release in late October. And Dr Nwaka organized a session on the topic at the American Society of Tropical Medicine and Hygiene (ASTMH) November 14.

This year we will celebrate the 30th anniversary of our Joint Coordinating Board (JCB). We are collecting stories about TDR’s history and accomplishments, so if you have something that you would like to share, please send it by email, fax or phone. As always, we would love to hear from you about any TDR-related activities and upcoming events. Please email us at: tdr@who.int.

Warm greetings from all of us at TDR.
We at TDR are deeply involved in the development of our new, ten year strategy, with the help of input and feedback we have received from so many of you. My thanks to all for your support and assistance.

As you will read in this issue (pages 4-5), we held special meetings in October 2006 to review our proposal for a new strategy. That led to an endorsement to move forward with a business and operational plan, to be reviewed at the next Joint Coordinating Board meeting in June 2007.

The enhanced complexity of the research field, the interconnectedness of all our actions, and the commitment to building global research activity around the needs, capacity and aspirations of developing countries facing disease and associated poverty are all reflected in TDR’s core vision statement, namely: to foster an effective research effort on infectious diseases of poverty, in which disease-endemic countries play a pivotal role.

TDR will work with and through others to realize this vision, using a three-pronged strategy that: provides a collaborative framework and information service for research partners; empowers’ scientists from disease endemic countries as research leaders; and supports research on neglected priority needs. TDR will play an enhanced role in knowledge management, fully utilizing our convening power and links to national and international agencies and programmes, to underpin our actions and help provide a framework for the work of others. We term this ‘stewardship’.

TDR’s work in the context of this new strategy may take us into new diseases and fields of endeavor in the coming decade. Diseases do not stand still. Science does not stand still. TDR must move with the times while retaining its core values and competencies.

As TDR approaches its historic 30th anniversary as a UNICEF/UNDP/World Bank and WHO co-sponsored programme, I would like to mention some significant developments that impact on WHO, TDR, and global health research. WHO has a new director-general, Dr Margaret Chan. As former Assistant Director General of WHO’s Communicable Disease Cluster, Dr Chan also served as WHO’s Special Programme Coordinator for TDR, with special oversight responsibility for our activities. In that capacity, Dr Chan helped steer TDR through important milestones of the last year, including a high-level meeting of ministers of health and a JCB meeting in Accra, Ghana in June of 2006. We warmly congratulate Dr Chan on her election.

Upon the acceptance of her new post, Dr Chan highlighted the significance of science and research to WHO’s mission, stressing the need for health initiatives to work collectively and in harmony with each other. She also indicated that advances in health in Africa and women’s health will be priority indicators of WHO’s global performance.

In early December, WHO convened an Intergovernmental Working Group on Innovation, Intellectual Property and Public Health, following upon a recent report by a WHO Commission on the same topic. Research for neglected tropical diseases and research capacity strengthening in disease endemic countries will feature prominently on the agenda of this working group in the coming year.

While focusing on these high-level issues that are shaping global research agendas, it is important to remember the day-to-day activities and achievements of researchers worldwide, including those whom TDR supports directly. It is their work and efforts that generate progress in the field. This newsletter and our reports, combined with those of many other organizations, continue to demonstrate the remarkable innovation, progress and promise in tropical disease research. In the coming years we must maintain these advances by continuing our support both for institutions and for individual researchers whose activities represent the fruit of, and inspiration for, our broader goals and strategies.

It is an exciting time for tropical disease research, with many possibilities and strong interest and support. I look forward to working with you in the context of TDR’s new vision so that we can continue to support new scientific advances that improve health in communities globally, and particularly in ways that support alleviation of poverty.

Robert G. Ridley,
TDR Director
Over a period of four days in October 2006, representatives of some 35 governments and numerous other institutions from around the world attended two special meetings on TDR. The topic was the new ten year vision and strategy under development. The meetings, scheduled at the request of the Joint Coordinating Board (JCB) at its annual session in June 2006, in Ghana, offered an opportunity for focused review and discussion on the new strategy.

The new proposal
Following an analysis of the changed landscape of tropical disease research, which assessed where existing emphases are being placed globally and what requires further engagement, TDR identified areas where it can add value to the global research effort (see the following diagram).

Building on this analysis and TDR’s historical and current strengths, the following changes are being recommended:

**Develop stewardship for research** on infectious diseases of poor populations. This is a major new role for TDR as facilitator and information provider to support needs assessment, priority setting and progress analysis, and to provide a neutral platform for partners to discuss and harmonize their activities.

**Empower scientists and institutions** from disease endemic countries. This moves beyond traditional research training to build leadership at the individual, institutional and national levels so that disease endemic countries can better initiate research activities and develop a stronger presence in international health research.

**Conduct research on neglected priority needs** not adequately addressed by other partners, focusing on three strategic directions:
- Discovery and innovation for product development, emphasizing disease-endemic country engagement and leadership.
- Development and evaluation of interventions in real life settings.
- Research that increases access to interventions.

The proposed strategy also recommends the development of a disease portfolio that is flexible, but remains focused on a limited number of well-defined activities within this broader scope, and works more closely with regional leaders, organizations and countries.

**Discussion and recommendations**
Discussions for input and feedback on the draft strategy began with a special stakeholder session, followed by a meeting of TDR’s governing body, the Joint Coordinating Board.

The Stakeholder meeting was chaired by Professor Chitr Sitthi-amorn, dean of the College of Public Health, Chulalongkorn University, Bangkok, Thailand. The meeting brought together over 100 specialists from around the world, representing TDR’s sponsors, JCB members and observers from academic and research institutions, collaborating organizations, and governments.

This was followed by the JCB’s special thematic session under the guidance of the JCB Chair, Dr Bijan Sadrizadeh, senior advisor to the minister of health and medical education of the Islamic Republic of Iran. The new strategy and vision proposal was broadly
supported. Representatives of the WHO Regional Offices and TDR’s sponsoring agencies offered to help TDR build a stronger regional presence and enhanced impact. Properly positioned, TDR could become the infectious diseases research arm of WHO and its co-sponsoring agencies. TDR was also encouraged to maintain and extend its collaborations – with co-sponsoring agencies, WHO regions and control programmes.

The JCB emphasized that the new strategy will better utilize the strong leverage role that TDR has through its expanded range of partnerships. The JCB also encouraged TDR to work with research units and affiliates of country-level ministries of health, to provide evidence to policy makers, involve them at the outset of activities, help bridge the gap between health services and academia, and ensure political commitment and recognition of the need to invest in human resources for research.

**Next Steps**

A complete business plan with detailed business lines and budgets will be presented to JCB(30) at its June, 2007 meeting. In the meantime, there will be ongoing dialogue with major stakeholders to ensure continued broad support and commitment. The current portfolio will be phased into the new strategy, with existing commitments honoured. Current committees will continue until the new plan is finalized.

**TDR’s new vision statement:**

*To foster an effective research effort on infectious diseases of poverty, in which disease endemic countries play a pivotal role.*
A large, untapped global market exists for improved TB diagnostic tests

A significant untapped global market exists for more effective and affordable tests to diagnose tuberculosis (TB) in low- and middle-income countries, where most cases occur. This is the major finding of a new report, Diagnostics for Tuberculosis: Global Demand and Market Potential, released in October 2006 by WHO/TDR and the Foundation for Innovative New Diagnostics (FIND). The TB diagnostics market review is a milestone in TDR’s expanding strategic effort to leverage cutting-edge research, innovation and capacity-building in development, use and evaluation of diagnostics for neglected tropical diseases. “Reliable diagnostics that provide rapid and accurate indicators of disease can be as important as drugs in saving lives and reducing morbidity,” notes Dr Rosanna Peeling, who heads up the TDR diagnostic team’s effort.

Yet in the case of many diseases that TDR addresses, both bacterial and parasitic, rapid and accurate diagnostic tools are largely inaccessible or unaffordable to populations most at risk. In other cases, new tools are rapidly being developed, such as for rapid malaria tests. However, clinicians and field managers require guidance to choose the best tests for their needs and geographic location. In seeking to leverage action on these issues, TDR’s role is multi-faceted, involving:

- coordination of systematic reviews of knowledge and expert evaluation of developments in the diagnostics field, e.g. through the Diagnostics Evaluation Expert Panel (DEEP);
- guidance in evaluation and choice of appropriate diagnostics through peer-reviewed publications such as the recent Nature Reviews Supplement Diagnostics series (see bottom of page 7);
- research and capacity-building in more effective use and delivery of diagnostics in clinical and field situations;
- collaborations with other public and private partners to spur development of new diagnostics or improve use of existing tools.

In the case of TB, the recent TDR co-sponsored report took an innovative look at diagnostic needs from the market perspective. The report calls for new public-private collaborations and investment in improved diagnostic tools for low- and middle-income countries. The report concludes that such tests could significantly bolster international TB control efforts and while responding to a clear market demand. Among other key findings and facts:

- 1.7 million people a year die from TB, many because diagnosis occurs too late or not at all.
- Most people who have TB, or who live in TB risk areas, do not have good access to rapid and accurate testing.
- One-third of the world’s population is infected with latent TB, at risk of developing the active disease. HIV is fuelling TB epidemics in many countries and multi-drug resistance is a growing threat.
- The global market for TB diagnostics is more than twice that of the market for drugs for treatment. Worldwide, about

**BBC Kill or Cure documentary on syphilis diagnostic tests**

BBC World’s highly rated Kill or Cure television series traveled to Haiti with TDR’s Diagnostics Coordinator Rosanna Peeling last summer to document how TDR-sponsored research into rapid diagnostic tests for congenital syphilis has helped prevent the disease from being passed on by pregnant women to their babies. The result was a half-hour documentary, aired by BBC in August 2006, following Peeling and the research team into remote areas where the test evaluations were being piloted. Globally, at least one-half million babies are born with congenital syphilis every year, while at least one-half million stillbirths and miscarriages also occur due to congenital syphilis. There are often no symptoms of syphilis among pregnant women, and the disease is thus unknowingly transmitted to the unborn child. Syphilis diagnostic tests traditionally required electricity and other laboratory infrastructure, so women in remote rural areas often did not get tested. There are, however, new rapid tests being marketed that do not need electricity, and TDR-supported positive evaluations of their efficacy thus have very broad relevance. The use of properly evaluated diagnostics already is saving lives now in Latin America, and holds the potential to save tens of thousands more lives if applied throughout Africa. After diagnostics evaluation has assessed the reliability of a new test, those with a positive evaluation can be put onto the WHO procurement list so governments can purchase the tests at discounted rates. The success of research and evaluation of new rapid diagnostics has led various governments to develop plans to eliminate congenital syphilis.

Copies of the DVD can be requested from tdr@who.int
US$ 1 billion is spent on TB tests and evaluations, while about US$ 300 million is spent on drugs for TB treatment.

“The TB and HIV threat continues to grow in many parts of the world, and governments need high-quality diagnostics to help manage these epidemics,” said Dr Robert Ridley, director of TDR, at the Geneva launch of the report last October. “We need simple diagnostics to help manage these epidemics,” said Dr Robert Ridley, director of TDR, at the Geneva launch of the report last October. “We need simple tests to accurately screen for active tuberculosis. New tests are needed to monitor treatment response, identify bacterial drug resistance, and detect latent infection in those at risk of progression to active TB.”

Of the estimated 9 million people who develop active TB every year, most still do not receive a laboratory-confirmed diagnosis. Only about 2.2 million TB cases annually are diagnosed and reported with sputum smear microscopy, the most widely available test. Other cases are diagnosed through an often inefficient and sometimes wasteful combination of chest X-rays, bacterial cultures and guesswork. These tests may fail to make critical distinctions between active and latent TB, particularly in HIV-positive patients, the report notes, and between drug-sensitive and drug-resistant forms of the disease. High-tech molecular and rapid culture diagnostics introduced in developed countries are too complex and costly for many settings where TB is most prevalent.

“The technology exists, and this report leaves no doubt that there is a large global market. There is a huge opportunity for diagnostics developers to expand their investments to meet this very real need,” said Dr Giorgio Roscigno, Chief Executive Officer of FIND, a non-profit organization dedicated to the development of improved diagnostics for poverty-related diseases of developing countries. Compared to vaccines and medicines, the cost of developing new diagnostics is relatively low, the report notes, at about US$ 1 to 10 million per technology platform. The report projects demand for seven hypothetical products that could feasibly be developed. Among those, a test that detects latent infection and predicts progression to active disease could have a potential available market of some 204 million patient evaluations a year. "Such a test, if widely implemented and accompanied by successful treatment, could revolutionize TB control,” the report concludes. Large markets also exist for less revolutionary ‘replacement’ technologies for smear, culture, and drug susceptibility testing. Jean-Francois de Lavison, President of the European Diagnostics Manufacturers Association, called the report "ground-breaking," adding, “it explains what kinds of improved diagnostic tools are needed and where they could have their greatest impact.”

TDR’s global TB specimen bank is another direct contribution to TB diagnostics research, present and future. Since its 1999 launch, the bank’s activities have gradually expanded to include approximately 40,000 serum, sputum and urine specimens from patients in a dozen countries worldwide. The use of bank specimens can greatly expedite the process of evaluating new TB diagnostic tests, avoiding the need for expensive field trials in the early stages of diagnostics development. This, in turn, helps lower their overall cost.

Specimens are collected with full consent both from patients infected with TB and from those who are not, as well as from those who are both HIV-positive and negative. A 2006 collection round has just been completed, which adds specimens from 1250 patients in diverse settings such as Viet Nam, Bangladesh, Kenya, South Africa, Colombia and Peru. These specimens are currently stored in central repositories in Europe and the USA, and efforts are being made to create regional repositories. For details on the bank see the TDR website: www.who.int/tdr/diseases/tb/specimen.htm

Diagnostics take centre stage in Nature Reviews Supplement series

Nature Reviews Microbiology, in collaboration with WHO/TDR, has launched a new supplement series Evaluating Diagnostics to offer guidance in testing and selection of appropriate diagnostics for major tropical diseases that are a focus of TDR’s work. Aimed at health policymakers, clinicians and field-workers, the guides represent a state-of-the-art synthesis of knowledge on diagnostic tools. First in the series was The Malaria Guide, published in September 2006, followed by the STI Guide on diagnostics for sexually transmitted diseases, published in December, 2006. Forthcoming supplements are scheduled to focus on diagnostics for dengue fever and for visceral leishmaniasis. The Nature Reviews Diagnostics Supplements series provide the results of expert review, consultation and synthesis through TDR’s Diagnostics Evaluation Expert Panel (DEEP). The panel examines innovations in diagnostic tests, bringing together best practice and evidence.

TO KNOW MORE...


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Mobilizing research to halt exponential growth of dengue

Three new TDR initiatives aim to respond to the alarming worldwide resurgence of dengue virus (DV) infection. The efforts seek to enhance knowledge about vector surveillance and control; better ecosystem management; and finally, appropriate disease classification and diagnostics that would support more effective treatment. The initiatives, all launched over the past two years, come at a time when the global impact of dengue is being compared to that of diseases like tuberculosis and malaria.

At the same time, new research findings on dengue prevention, treatment and vector control offer hope that new strategies emerging now can eventually bring the epidemic under control. This was the message emerging from an October, 2006 meeting of a global Scientific Working Group on Dengue, organized by WHO/TDR in Geneva and involving 60 experts on dengue research and control. A back-to-back WHO meeting to update global dengue prevention and control guidelines underlined the practical relevance of today’s research agenda to disease control.

The global dengue burden has increased more than four-fold in the last 30 years, making it now the most common mosquito-borne viral disease. South-East Asia and the Western Pacific are most seriously affected, but there also has been a rapid increase in the Americas; it is endemic in all these as well as in the Eastern Mediterranean and African regions. Along with this trend, there has been a rapid appearance of more virulent strains of the virus and a geographical extension of dengue vectors and disease across the tropical and sub-tropical regions of the world. This is thought to be due, at least in part, to major global demographic changes, especially uncontrolled population growth, mobility, and urbanisation. As a result, epidemic outbreaks are occurring with greater frequency and intensity, which can overwhelm unprepared healthcare systems. (See Fig. 1)

The challenges of dengue

Dengue disease poses a special research challenge insofar as there is no effective drug treatment for dengue infection. Proper clinical management is complicated by difficulties in proper diagnosis and variation in medical skills. The development of a vaccine, a promising approach to dengue control, has been hampered by the immunological complexity of the host response to the virus. Vector control, as well, is a special challenge. The Aedes mosquito which transmits the virus is well adapted to urban environments, where it breeds in the water accumulated in discarded debris, old tyres, and water storage containers. Some countries have instigated large programs of urban cleanup or spraying to eliminate such mosquito breeding grounds. However, these control measures are difficult to sustain over a long period of time. So while vector control, and particularly environmental management, may currently offer the best method of prevention of dengue virus infection, generalized

control campaigns often have been ineffective in reducing the relevant populations of *Aedes aegypti* mosquitoes below a threshold that could reduce dengue virus transmission.

**The TDR response**

While dengue has been part of the TDR portfolio since 1999, the recent initiatives offer particular promise in responding to the research gaps, and addressing the growing public health importance of this disease. The TDR projects on improving surveillance tools for vector control; examining the potential for ecosystem management of dengue in a multi-disciplinary fashion to support primary prevention; and testing diagnostic tools to improve clinical case management, are reviewed below and described in the figure on page 11.

**Improved vector control through pupal productivity surveys**

TDR is supporting multi-country studies that test the effectiveness of a new surveillance and control method that surveys and measures the “pupal productivity” of dengue breeding sites in various classes of water containers. This survey method identifies the most important breeding grounds for the vector in a given setting or community, and then targets vector control and cleanup to the most ‘productive’ containers or sites.

Preliminary results from an initial ten-country study in Latin America, Africa and Asia, found that the pupal demographic survey method identified epidemiologically important containers — e.g. containers that produce the most mosquitoes for disease transmission, as opposed to those that were unimportant to disease transmission. In each of the studies, moreover, the survey provided the information necessary to create targeted control strategies.

“By doing studies in 10 different countries we can identify common features and also provide recommendations that help health services to find their own solutions for their specific situation,” said Professor Axel Kroeger, TDR Disease Research Coordinator for Dengue. Ongoing research still is needed to determine if these interventions targeted at the most productive containers can also be more effective in reducing dengue virus transmission over time.

At the same time, more selective chemical and biologically-based vector control tools are being developed to control *Aedes* breeding sites. These include improved formulations of larvicides and insect growth inhibitors that are safe and acceptable for use in drinking water. Insecticide treated window curtains and water container covers have been found to reduce densities of dengue vectors and transmission in a recent WHO/TDR- co-sponsored cluster randomized-controlled trial conducted with several partners in Mexico and Venezuela.

Acknowledging the importance of community participation in any control strategy, TDR also has contributed to the growing public health importance of this disease. The TDR projects on improving surveillance tools for vector control; examining the potential for ecosystem management of dengue in a multi-disciplinary fashion to support primary prevention; and testing diagnostic tools to improve clinical case management, are reviewed below and described in the figure on page 11.

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the development of a step-by-step guide on social mobilization and communication for dengue prevention and control.

Ecosystem management interventions
Effective dengue prevention increasingly is understood as a task requiring a multifaceted arsenal of vector control, environmental management, and community participation strategies. To examine more holistically the biological, ecological and social (“eco-bio-social”) factors affecting dengue transmission, TDR and the International Development Research Centre (IDRC) in Ottawa, Canada have now embarked on a major research initiative focusing on Asian high-endemic countries.8

The initiative will include six research studies on the eco-bio-social aspects of dengue, located in countries in South- and South-East Asia, including India, Indonesia, Myanmar, Philippines, Sri Lanka and Thailand. Interactions will be examined between ecosystem factors such as climate and the urban environment; biological factors such as vector density; social factors; the functioning of vector control measures and other public services. The most effective interventions for specific ecosettings will be identified.

“This means looking, for instance, at dengue virus transmission in light of the dynamics affecting people’s living conditions, their water storage behaviour, and urban services such as water supply and waste management,” explained Dr Johannes Sommerfeld, TDR’s project leader of the initiative. The initiative also will build a community of practice on dengue prevention. The partnership has great potential to more water storage in containers. Projects in this area than more affluent areas since the piped water supply in the poor community was irregular, leading to more water storage in containers. Projects in this new, and much broader, initiative will have both a research and an implementation evaluation stage.

Evaluating modified treatment strategies and diagnostic tools

Rapid diagnosis is essential for proper clinical management of patients. However, there has been no systematic validation of the many diagnostic tests available. A third new TDR-led initiative will evaluate field performance of existing and new diagnostics using a network of dengue labs in Latin America and Asia. The Pediatric Dengue Vaccine Initiative (PDVI), a programme based at the International Vaccine Institute (IVI) in Seoul, Korea, is the major partner in this initiative.9,10

Appropriate clinical classification of dengue cases also can facilitate case management and thus save many lives — since dengue can manifest itself as both a relatively mild or very severe illness. However, TDR research found that current dengue classification guidelines, developed over 30 years ago, are regarded by many clinicians as too complex.11 In response, TDR is now involved in a multicentre prospective clinical study in 7 countries to consolidate the current dengue case classification system and to better identify early warning signs of severe dengue across regions, age groups and nutritional levels. “We would like to see evidence for a simplified classification which will then be validated at different levels of the health system,” said Kroeger. This trial is funded by the International Cooperation with Developing Countries (INCO) programme of the European Commission and TDR.

In a related effort, Professor Jeremy Farrar from the Oxford University Clinical Research Unit based in Ho Chi Minh City, Vietnam, has been working closely with TDR in the integrated multicentre network in 7 countries in SE Asia and the Americas to conduct clinical research in dengue. He noted that “without TDR involvement, it would be impossible to bring clinical scientists from all these countries together in a collaborative way to address the real needs of dengue. Bringing dengue research under the umbrella of TDR has been a tremendously positive step which will enhance international collaboration on dengue research for years to come.”

Future directions: vaccine prevention

A dengue vaccine has been envisioned by many researchers as a more long term sustainable solution to the worldwide resurgence of dengue. Yet special challenges exist in vaccine development, as well, since any dengue vaccine must provide very high level protection against all four dengue strains to prevent pos-
sible vaccine-induced enhancement of disease. Responsibility for dengue vaccine development in WHO recently passed to the WHO Initiative for Vaccine Research, with whom TDR works closely. The most advanced strategy is production of live attenuated vaccines. TDR also supports research into the pathogenesis of dengue virus infection which could assist the design and implementation of vaccines. “A vaccine will be a very important tool for dengue control in the future,” said Kroeger, “but it will still take some time to develop.”

All in all, dengue research is seeing important advances. Research is contributing to: the design and validation of new intervention packages; accelerated development of diagnostics, vaccines and drugs; and improved dengue case management. New vector control tools and approaches for vector surveillance are being developed and modern information technology is being tested for its cost and usefulness in supporting district level decision-making, where vector control takes place.

Dengue research is beginning to attract not only increased funding from national and international sources, but also a diversity of young researchers – from molecular biologists to behavioural scientists. Admittedly the knowledge, tools and investment needed is still enormous. Yet the recent influx of talent and interest bodes well for the global effort to not only halt dengue’s epidemiological and geographic expansion, but reverse the current trend. ■

**FOOTNOTES** (continued):


6. Detailed reports of many of these studies have been recently published in a supplement to Annals of Tropical Medicine and Parasitology (Vol 100, Supplement 1, April 2006).


8. More information on the IDRC Ecohealth Initiative can be found at: www.idrc.ca/en/DO_TOPIC.html

9. www.pdv.i.org/


12. More information on DV vaccines can be found at the IVR website: www.who.int/vaccine_research/en/
Reducing infant deaths due to malaria

TDR implementation research to increase access to necessary drugs

An African baby dies from malaria every 30 seconds. At the end of each year, 1 million more babies are buried by their families – a scene that TDR is trying to prevent through its research into the innovative concept of home management of malaria intervention.

For many rural areas, there are no nearby healthcare workers or facilities, so families have to walk many miles and hours, and even then with no promise of care at the end of their trip. So people often do not even attempt to seek out care, and instead used local remedies or just "wait it out". TDR began supporting research in 1998 for a deceptively simple plan – train local mothers and other community members to recognize fevers, provide pre-packaged medications, and keep the medicines properly stored and recorded. The first results in Ethiopia using chloroquine showed a 40% reduction in under-five child mortality, and were published in the *Lancet*. Later, the work of Sodiomon Sirima and Franco Pagnoni showed that catching the malaria early with prompt treatment stopped it from progressing to a more severe and fatal form.

In 2002, the Ugandan government began teaching mothers how to recognize malaria symptoms, and to use a volunteer community medicine distributor for diagnosis and treatment. The treatment provided was HOMAPAK, a prepackaged combination of chloroquine and SP specially developed for home care. However, this medication no longer works in many areas, due to parasites developing resistance to it. WHO now recommends artemisinin-based combination therapy (ACT), such as Coartem.

“Early data suggests community members can be trained to administer these new medications properly and avoid drug resistance, and this should translate into a substantial reduction in child mortality."

Dr Franco Pagnoni, TDR research manager

Accurate and rapid diagnosis of malaria is important not only to guide treatment at the point of care but also to avoid unnecessary treatment that may foster drug resistance and waste precious health resources. However, given the many diagnostics on the market today, choosing the right kit can be a challenge, and the best diagnostic option may vary greatly from one setting to another. Two resources below that can be helpful include:

**Malaria Diagnosis: new guidance in diagnostics evaluation**

A September, 2006 supplement to the journal *Nature Reviews: Microbiology*, produced in cooperation with TDR, provides detailed guidance for clinicians and policymakers on how to evaluate diagnostic tests for malaria.

The supplement can be downloaded free of charge from either the TDR web site: [www.who.int/tdr](http://www.who.int/tdr) or from: [www.nature.com/nrmicro/supplements/index.html](http://www.nature.com/nrmicro/supplements/index.html)

Print copies can be requested by e-mailing: tdr@who.int

**The use of malaria rapid diagnostic tests (ISBN 92 9061 0883 3)**

This simple 2004 guide for field managers covers the basics of choosing and using rapid malaria diagnostics. It has recently been reprinted by WHO/TDR, and can be ordered, free of charge: tdr@who.int

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**Useful references and guides on malaria diagnostics**

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TDR WEBSITE
[www.who.int/tdr](http://www.who.int/tdr) in the malaria section
(artemether-lumefantrine), but this medication is slightly more complicated to deliver and more expensive, and there is no evidence that ACTs will work in the home setting. In a WHO Bulletin article on the topic, Professor Umberto D’Alessandro from the Prince Leopold Institute of Tropical Medicine in Antwerp, Belgium, said, “There are no data available on the effects of ACT when it is given by mothers to their children without proper diagnosis. It should reduce mortality, but we simply don’t know if it does.”

So TDR is supporting research using these newer medications. Studies using ACTs in home management settings are underway in Benin, Burkina Faso, Cameroon, Ethiopia, Malawi, Nigeria, Uganda and the United Republic of Tanzania. Franco Pagnoni, the TDR coordinator of this project, says final results will be published in 2007, but early data are promising. In an article published in Tropical Medicine and International Health (TMIH) in July 2006, the researchers showed that about 90% of caregivers in Ghana gave the correct artemether – lumefantrine dose. The research is gaining attention (see list of published articles and media attention), as could be expected for any intervention that could reduce the number of children’s deaths by 40%. “Early data suggests community members can be trained to administer these new medications properly and avoid drug resistance,” Pagnoni said, “and this should translate into a substantial reduction in child mortality.”

**RECENT REVIEWS ON HOME MANAGEMENT OF MALARIA (HMM)**


*RealHealthNews*, May 2006: [www.globalforumhealth.org/realhealthnews/news%20analysis/may06_home_based_mm.php](http://www.globalforumhealth.org/realhealthnews/news%20analysis/may06_home_based_mm.php)


BBC World *Kill or Cure* series, broadcast during November, 2006 (see below).

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**Malaria research on the BBC**

TDR-sponsored research into new home management and community directed models for malaria treatment was the recent focus of a BBC World documentary. The highly rated *Kill or Cure* television series programme aired five times in late November and early December, 2006. Filmed on location in Oyo State, Nigeria, the documentary profiles two TDR-sponsored research projects that are examining how to get new artemisinin-based combination therapy (ACTs) to African children in rural areas more efficiently. Coordination between the local researchers at the University of Ibadan, the WHO country office, and the Federal Ministry of Health was highlighted as key to the effort.
But, he adds, “the critical element now is to be able to translate the insight gained from basic research into lead compounds that can form the basis for innovative treatment. This is part of our lead discovery efforts.” Nwaka considers the fight against neglected disease a moral obligation; and sustaining the availability of much-needed health products for the poor despite all barriers is critical to the effort. Nwaka is from Nigeria and also has a Canadian citizenship. He did his early studies in Nigeria before moving to different countries in Europe, Asia and North America for further studies and training. “It is this truly international experience that drives my professional and personal passion for this work.” Nwaka has taken his passion to TDR, where its Genomics and Discovery Research Committees and team (GDR) are supporting several new networks for drug discovery involving developed and developing country researchers, institutions and industry. These networks are interactive and cover different aspects of the process (see Figure 2).

The networks include the following:

- **Compound Evaluation Network** – This network has been the engine of TDR’s drug discovery efforts for several years, but it has been strengthened recently with increased funding and access to compound supplies through new industry collaborations with TDR. The network currently has the capacity to screen over 20,000 compounds per year for antiparasitic activity. The network consists of five centres: the Swiss Tropical Institute (STI), Basel; the London School of Hygiene and Tropical Medicine (LSHTM); the Northwick Park Institute for Medical Research (NPIMR), London; the Theodor Bilharz Research Institute (TBRI), Cairo; and the Laboratory for Microbiology, Parasitology and Hygiene at the University of Antwerp (LMPH).

- **Medicinal Chemistry and Pharmacokinetics Networks** – TDR recently established these collaborative networks with the goal to further progress the ‘hits’ or ‘leads’ identified through the compound evaluation network. The medicinal chemistry effort currently involves one large pharmaceutical company, Pfizer, and two biopharmaceutical companies, Serono and Pharmacopeia. Academic institutions include: the University of Cape Town, South Africa; the University of Dundee, UK; and in the USA, the University of Nebraska, Ohio State University, and St. Jude Children’s Research Hospital, Memphis. The pharmacokinetics/metabolism network, which provides essential pharmacology data for medicinal chemists to help guide further synthetic work, includes Monash University, Australia, as well as Pfizer, Serono and Pharmacopeia.

- **Drug Target Portfolio Network** – This network is helping to create a globally accessible database containing a prioritized list of drug targets across the range of disease-causing parasites that are the focus of TDR research. This capitalizes on the investment made in research on parasite genome sequencing, and will help facilitate drug discovery based on molecular targets. The database is thus expected to become an important starting point in the search for new drugs for neglected diseases, according to Dr Wesley Van Voorhis of the University of Washington in Seattle, who leads the TDR target network group. The database also will be “freely accessible,” emphasizes Nwaka. The network includes groups at the University of Pennsylvania, USA; the Sanger Centre, Cambridge, UK; the Walter Eliza and Hall Institute for Medical Research (WEHI), Melbourne, Australia; and the Institute for Research in Biotechnology (UNSAM), Argentina.

- **Helminth Initiative for Drug Discovery** – This aims to support a network of academic and industry partners to develop new technologies in the search for new drugs against helminth infections such as schistosomiasis, onchocerciasis and lymphatic filariasis. This initiative is timely as it fills a gap created by a lack of a dedicated PPP for antihelmintic product R&D. An informal consultation convened...
The multiple tracks of drug discovery

How do we discover new drugs for tropical diseases? One of the fastest approaches is to examine how established drugs – for which there is already a body of clinical experience – might be used or adapted as treatments for parasitic diseases. This usually involves ‘whole organism’ screening of a known drug or compound against the parasite causing disease. TDR has had important successes with this strategy. For example, the drugs eflornithine and miltefosine have been developed for African trypanosomiasis and visceral leishmaniasis from drug compounds originally developed for cancer treatment.

Another approach is the ‘piggy-back’ strategy. This is most useful when a molecular target present in a parasite is also the focus of other commercial research, and thus provides a chemical ‘starting point’ for investigation.1 For example, the histone deacetylase inhibitor series developed for cancer treatment is now being explored in the context of anti-malarial drug research.

A more long-term strategy involves ‘de novo’ discovery of new chemical entities based on protein or enzyme targets. Methods such as ‘high throughput’ screening; virtual screening linked to cheminformatics; and x-ray crystallography may be part of this target-based, ‘rational’ approach. High-throughput screening exposes a parasite protein or enzyme to thousands of compounds in a highly automated process. Industry has played a leading role in developing this technology, which increasingly is being applied in academic environments. Rational drug discovery can be challenging – but it arguably has great potential for identifying drugs with novel modes of action.

Building capacity for drug discovery

Through the TDR-led initiatives, developing country scientists are now being trained in high-tech screening and medicinal chemistry techniques in industry settings. Collaborations so far include Pfizer, UK and Serono, a Swiss-based biotech company. Two research fellows from Brazil and Cameroon who trained in drug screening at Serono recently returned to their home countries to put their new skills into practice. At both individual and institutional levels, the TDR networks are strong instruments for capacity development and technology transfer to developing countries.

"Ultimately, it is the countries suffering from the diseases which need to play a leading role in searching for solutions," observes Nwaka. "Developing countries need to participate in discovering, developing and manufacturing their own drugs, and in establishing functional market mechanisms that suit their own needs."

Dr Kelly Chibale, a medicinal chemist from the University of Cape Town, South Africa, who is one of the researchers working with the TDR networks, underlines a similar theme. "It is vital for African scientists to enhance drug discovery capability in order to address the continent’s health needs,"...
he says. “The ability of TDR to rapidly deliver promising lead compounds through TDR-supported screening centres will enable medicinal chemists like myself to start at a higher level in a more focused manner.”

Cutting costs
The process of creating a new drug is “long, risky and expensive,” Nwaka notes. It begins with the discovery phase where drug targets, lead compounds and drug candidates are sought and identified through experiments in test tubes and animals, but continues into a development phase, in which drug candidates are tested for safety and efficacy in animals, and finally humans. The entire process can cost hundreds of millions of dollars and take well over a decade. Along the way, the attrition rate is severe: only about one of thousands of compounds screened make it into a useable product. So systematic coordination and collaborations between public and private sectors can go a long way towards reducing attrition and cutting costs.¹

Results so far
The TDR network and partnership model is already yielding results. A vibrant portfolio of drug discovery projects have been developed and are being managed with partners (see Fig. 3). Several new lead compounds have been identified through the compound evaluation network and are now being explored further through the medicinal chemistry and other networks. In addition, the Drug Target Portfolio has established an accessible database of potential drug targets. “This is perhaps the first time such an effort has been undertaken systematically across a range of parasite causing diseases,” Nwaka states. New collaborations with industry are helping facilitate drug discovery efforts, and supporting capacity-building in parallel. “This is an exciting time for drug discovery for tropical diseases. Our approach creates synergies with other organizations. As new drug leads are discovered, the technology is transferred elsewhere for further development.”

FOOTNOTES:
5. For more information on these PPPs, see the websites: MMV: www.mmv.org DNDI: www.dndi.org FIND: www.finddiagnostics.org Global Alliance for TB drug development: www.tballiance.org

Figure 3. TDR drug discovery portfolio

Dr Solomon Nwaka explains TDR’s network initiatives.
Integrated vector management in support of visceral leishmaniasis (VL) elimination on the Indian subcontinent

Along with promotion of more effective drug treatments, effective vector control strategies are among the pillars of the campaign to eliminate visceral leishmaniasis (VL) on the Indian subcontinent.

TDR, as a partner of the VL Eradication Initiative, is supporting research in Bangladesh, India and Nepal, designed to provide new evidence on what are the most effective and efficient vector interventions in an integrated vector management (IVM) framework.

A workshop and meeting in Kolkata in March 2006 involving 15 government control experts and researchers from all three countries drafted proposed terms of reference for the planned three-country study on cost-effective integrated vector management as a contribution to visceral leishmaniasis elimination on the Indian subcontinent. The participants were members of multidisciplinary research teams who will carry out the research, with results expected in the coming year.

In the case of Kala Azar, effective vector control may be based on indoor residual spraying (IRS); use of insecticide treated netting materials (ITNs); environmental management strategies; or may combine two or three of these interventions.

Areas of proposed focus for the research are to consider the following gaps in knowledge:
- vector ecology and efficacy of non-chemical interventions;
- efficacy of ITN curtains or bednets in reducing vector densities;
- cost, feasibility, acceptance and sustainability of strategies using insecticide based vector control tools (IRS versus ITNs) or using non-chemical ecological interventions;
- cost and quality of conventional vector control (IRS) and options for increased efficiency, safety and quality.

The Kolkata meeting included a brief review of the study designs developed by the five research teams in the three countries; development of overarching research questions along with questions specific to each study site; outline of research instruments and forms; and proposal submission formalities. The workshop also was attended by representatives of the WHO Regional Office for South-East Asia, as well as by WHO representatives from Nepal and India. WHO headquarters was represented by TDR and the Department for Neglected Tropical Diseases. A second back-to-back meeting also was held with a group doing research into VL treatment in Bihar.

Improved housing conditions can support visceral leishmaniasis (VL) elimination, by targeting vectors that live in the plaster of poorly constructed homes.
A TDR collaboration with the Joanna Briggs Institute

Res ipsa loquitur is a legal concept, essentially meaning, "the thing speaks for itself". For many researchers, the results of their work should speak for the overall endeavour, and findings should be implemented as a matter of course. In recent years, however, researchers have become more keenly aware that proof of principle is not always sufficient, and a caveat to this maxim has thus been suggested: Res ipsa loquitur, sed quid in infernos dicet? or "the thing speaks for itself, but what the hell does it say?"

Clearly the uptake of research into practice will only succeed if findings are grounded both in sound scientific methods and in conclusions that can be broadly understood. In the health and medical fields, evidence gathered through qualitative research methods is increasingly relevant to understanding the social, cultural and economic factors affecting disease transmission, health status and health care. Rigorous norms, standards and practices have, in fact, been developed for the conduct of qualitative health research, and for its systematic review. Yet these are less broadly familiar to health researchers – who still tend to view the quantitative health research, and its systematic review. These same social, economic and cultural factors, in turn, are particularly relevant in the translation of research into health care. Rigorous norms, standards and practices have been developed for the conduct of qualitative health research and its systematic review. Yet these are less broadly familiar to health researchers.

To address this gap in perception, knowledge and practice, TDR is now collaborating with the Joanna Briggs Institute (JBI), a global network promoting good practice in the design, dissemination and implementation of systematic reviews of studies involving qualitative research, economic research, and policy research.

Key to JBI’s mission and strategy is the fostering of international collaborations between collaborating centres, researchers and clinicians, and other health groups. There currently are 26 JBI Collaborating Centres – primarily located in Europe, North America and Australia – participating in the international outreach programme. The new TDR collaboration proposes to expand these networks and activities into developing countries with an initial focus on training and certification of research groups in Africa. "New disease control tools, as well as research findings, are more likely to be scaled up and incorporated into health systems if the endemic countries themselves participate in the evaluation of alternatives for prevention, control and treatment of neglected infectious diseases," notes Steven Wayling, manager of the initiative in TDR’s Research Capacity Strengthening team. "Expanding these kinds of networks to include researchers from developing countries can help that happen."

JBI was established a decade ago at Royal Adelaide Hospital and the University of Adelaide in South Australia. The Institute works closely with the Cochrane Collaboration, which sets good practice models and standards for the meta-analysis of results from randomized controlled trials; and with the Campbell Collaboration, which prepares, maintains and disseminates systematic reviews of studies of social interventions. In that array, JBI fills a complementary niche, promoting systematic review of research that utilizes more integrated or alternative approaches. JBI’s activities, likewise, provide synergies with the objectives of TDR’s implementation research and capacity building programmes.

JBI has developed methodologies and electronic systems to conduct meta-synthesis of both quantitative and qualitative evidence for health care. In addition, the Institute has well developed programs in evidence translation, evidence transfer and evidence utilisation.

Developing norms and promoting good practice standards for such research is critical to the acceptance of findings from studies that emphasize broader and more inclusive approaches to evidence. Such studies, in turn, may highlight critical associations between population health and social, cultural and economic factors that quantitative research, alone, cannot yet identify. These same social, economic and cultural factors, in turn, are particularly relevant in the translation of research into health care practices in developing countries, and for populations with diseases or conditions that are linked to poverty and health policy development.
Strengthening health economics capacity in Africa

"How much is this going to cost? How are we going to pay for it? Should we pay for it?"

When officials in a ministry of health anywhere in the world consider a proposed new policy or programme, the bottom line of costs and benefits, both financially and in terms of lives saved and illness averted, is a critical factor. The same questions are all the more relevant to developing countries, where basic health coverage and achievement of the health-related Millennium Development Goals depends upon the efficient and equitable use of scarce resources.

Yet trained health economists who can frame the issues properly, and then provide accurate answers, are in chronically short supply in these same settings – and particularly in Africa. According to one estimate, there are only about 100 health economists in all of Africa; talent is concentrated in just a few countries, and mostly in research and academic centres, rather than in ministries of health, where decisions are taken. One of the most fundamental reasons for the dearth of health economists in the African context has been the lack of training opportunities. There are no dedicated health economics PhD programmes in African universities, and opportunities to study health economics in the context of other PhD programmes, while expanding slowly, remain very limited.

For nearly a decade, TDR has been involved in the creation of master’s level programs in health economics in Africa to respond to this identified need. Now, building upon these past efforts, involving a wide range of partners, TDR is laying the groundwork for the development of a dedicated health economics programme at PhD level at an African university. One important milestone was an April 2006 meeting of interested parties, convened by TDR, together with the University of Cape Town, Health Economics Unit. Participants in the April 2006 meeting included former TDR PhD trainees in health economics; representatives of universities offering some form of health economics training; the Swedish International Development Agency, SIDA (the leading bilateral agency providing support for health economics capacity development in Africa); the African Regional office of WHO; and Brunel University, which has been assisting TDR in developing new African master’s level programmes in health social sciences. TDR is now following up on this initial meeting with a dialogue involving other potential partners in Africa and elsewhere, including the London School of Hygiene and Tropical Medicine and Sweden’s Karolinska Institute.

The proposal for a doctoral level programme builds upon a decade of TDR and partner involvement in building health economics capacity. In the mid 1990s, TDR and the WHO Strengthening Health Services programme were instrumental in the creation of a Master’s degree in Health Economics with the University of Cape Town. The only other Master’s programme in Health Economics is in Francophone Africa supported by CESAG (Centre Africain d’Etudes Supérieures en Gestion), Dakar, Senegal. In addition to dedicated degree programmes, a growing number of universities in Africa are now offering some other form of postgraduate health economics training, particularly as a module within another master’s programme (usually either a Master of Public Health or Master of Economics).

Increasingly, students in the generalist programmes, as well, are conducting their thesis research on health economics topics. Research institutions, such as the Kenyan Medical Research Institute (KEMRI) and Navrongo Research Centre, also make an important contribution by providing supervisory support to master’s level students undertaking health economics dissertation research in the field stations of these institutions. Beyond the walls of academia, several other regional networks and initiatives also are playing an important role in strengthening capacity among practitioners and researchers.

Among these are the Health Economics and Policy Network in Africa (www.HEPNet.org), which links ministries of health, research institutes and academic institutions involved in health sector development. Another recent initiative is the establishment of the African Health Economics Advisory Committee (AHEAC) by WHO-AFRO. The primary purpose of this committee is to advise the African regional director of WHO on issues relating to health economics. Through establishment of this committee, WHO and its regional offices, together with TDR, have demonstrated a commitment to placing health economics on the policy agenda in Africa.

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A recent issue of the African Health Monitor, portrayed here, featured health economics as the cover story, reflecting growing recognition of its importance to Africa’s health sector.

FOOTNOTES:
2. A similar programme was established with TDR support at Chulalongkorn University, Bangkok, Thailand.
Teaching research ethics to health sciences students in Brazil

Research ethics is a topic of growing interest in developing countries – due partly to the globalization of research, as well as to the increasing emphasis on product development for populations suffering from a high overall burden of disease and socio-economic vulnerability. In light of these trends, the importance of reinforcing principles of equity and respect for research participants is an ever more essential component in the training of research investigators.

The teaching of research ethics to research students has been the focus of a collaboration between TDR and Universidade de Brasilia, initiated in mid-2005. Following the recommendations of the initial workshop, a major meeting was held in Brasilia in May 2006.

The meeting was attended by research advisers and graduate students of 10 postgraduate programmes in Health Sciences and Tropical Medicine, as well as by research ethics committees of relevant public universities and university hospitals in central and western Brazil. It was held under the auspices of the Faculty of Health Sciences and Faculty of Medicine of the University of Brasilia, and FLACEIS – Latin American Forum of Research Ethics Committees, with the support of TDR, PAHO and the Brazilian Secretary of Science and Technology of the Ministry of Health http://www.unb.br/fs/eticaempesquisa/.

A new academic programme for the teaching of research ethics, as well as an educational package for the public at large, was launched at the workshop. The programme curriculum, available on CD-ROM, is being made available free-of-charge through the TDR web site (see Publications, page 31). The ongoing collaboration between TDR, the universities, and their research ethics committees is expected to support continued strengthening of good research ethics practices in the Americas, as well as improved recommendations on research ethics guidance and regulation for national authorities, academic institutions and ethics committees.

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Consultation on ethical review of qualitative health research

National and international guidance in ethical aspects of health-related research is typically developed within a biomedical paradigm. Such guidance, however, often fails to reflect principles and guidance drawn from social science research – which may be relevant and important to the ethical conduct of qualitative health science research.

This was the central message emerging from the recent meeting of a new initiative being undertaken by the Ethics Committee of the Sao Paulo Health Department in Brazil. The TDR-supported initiative aims to review and analyze ethical principles relevant to qualitative or interpretative research in health sciences – and eventually issue guidance relevant to such research.

An initial meeting of the initiative in Guarujá, Brazil, 28 August to 1 September, 2006, was attended by 30 national and international social science experts representing leading academic research groups. Discussion was guided by five TDR-commissioned working papers highlighting differences between the dominant ‘biomedical positivist’ paradigm for health research, and the ‘interparadigmatic paradigm’ in which social science and qualitative research is anchored.

Essential questions were posed and possible methodologies proposed as a framework for eventual guidelines. Key questions considered included:

- How to assess the risk-benefit relationship for the participants in research?
- What is the nature and process for obtaining a free-informed consent?
- Does the term “research” have the same meaning in different areas of knowledge?
Would it be possible to establish a single standard or guideline for the ethical review of research in different areas of knowledge?

As a next step, a learning document is being prepared by an editorial committee. This will be circulated for wider review and consultation among institutional ethics committees, prior to the proposal of guidelines on the subject.

Institutions and organizations represented at the meeting included: the Brazilian National Council of Ethics (CONEP); the Brazilian Society of Collective Health (ABRASCO); the Secretary of Science and Technology; Ministry of Health; the Brazilian Society for the Progress of Science; the French National Agency for Research on AIDS and Viral Hepatitis (ANRS); the American Society of Psychology; and the journals: Public Health Journal and Reports in Public Health; Brazilian Society of Bioethics; and the National Societies of Research and Postgraduate in Psychology, Social Science and Anthropology.

Building capacity in public health product research and development

Knowledge of pharmaceutical research and development is of increasing relevance to students of public health and health sciences. Particularly for students from developing countries, familiarity with commercial R&D processes can help train and empower young professionals in both the assessment and evaluation of product R&D initiatives, as well as in their management.

A month-long course offered by the University of Nagasaki Institute of Tropical Medicine in autumn 2006 has provided one initial model for teaching such a curriculum. The course was designed in collaboration with TDR, and along with experts from Japan, Colombia, Thailand, China and India. TDR also provided financial support for students from a wide range of countries in Asia, Africa and Latin America to attend. Along with supporting opportunities for students from developing countries to learn about the whole process of pharmaceutical R&D, from regulatory to post-registration issues, the course provides a platform for the development of professional networks and even new products. Involvement of faculty from the private sector can open up new opportunities to students to pursue research activities in collaboration with the pharmaceutical sector. One aim of TDR is to generate, from the Nagasaki course model, momentum for the creation of a full international diploma course at the MA level in Pharmaceutical Product R&D, tailored to meeting public health needs in developing countries.

A meeting held on 1-2 December 2006 at the University of Tokyo, and sponsored by Nagasaki University in collaboration with the University of Tokyo’s Graduate School of Pharmaceutical Sciences, TDR, and the Pharmaceutical Society of Japan, sought to provide a framework for an initiative that could yield such a diploma course, involving stakeholders from diverse cultures and geographical regions.

From left, Dr Janis Lazdins, TDR; Ms Mary Alpa T Cornelio, course lecturer; Dr Juntra Karbwang, TDR; Prof Kenji Hirayama, course director.

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In a related effort, The MIM/TDR Task Force on Malaria Research Capability Strengthening organized a workshop to improve the quality of proposals submitted in response to the call for MIM grants for 2007. The workshop was the third stage of a process designed to identify research projects with potential for significant contribution to reducing the malaria burden and capacity building.

Responding to a June 2006 TDR call, a total of 59 letters of intent were received from 14 African countries in the following areas:

- improving access and rational use of artemisinin-based combination therapy (9);
- preventive treatment in children and pregnant women (10);
- bacteria co-infection in malaria (5);
- role of parasitological diagnosis in management of malaria in areas of high transmission (4);
- improved prevention and management of severe malaria (1);
- effective delivery and use of available interventions (9);

The model is founded upon partnerships linking scientists from developed countries with their African counterparts. Examples presented at the symposium, attended by over 100 participants, drew upon the experiences in three MIM/TDR projects funded between 1998 and 2005, to demonstrate this in action. Drs Dicky Akanmori (University of Ghana, Legon), Abdoulaye Dijimde (University of Bamako, Mali), Anthony Holder (MRC London, UK) and Roseangela Nwuba (University of Ibadan, Nigeria) presented research findings on the role of host immunity in malarial anemia; response to chemotherapy; and propagation of the erythrocytic stages of P. falciparum. Along with a discussion of the implications of this research for vaccine development, management of malaria anemia, and drug resistant malaria in Africa, the scientists also highlighted how north-south, south-south and multidisciplinary partnerships contributed to the success of the projects. The symposium was co-chaired by Drs Lee Hall (NIH/NIAID) and Olumide Ogundahunsi (WHO/TDR).
• improved vector control strategies (13);
• other areas – including natural products (8).

Nineteen letters of intent were shortlisted for development into full proposals. Of these short-listed candidates, seventeen investigators participated in the workshop, including participants from: Burkina Faso, Cameroon, Congo, Democratic Republic of Congo, Ghana, Ivory Coast, Mali, Nigeria, Tanzania, and Uganda. Final proposals will be reviewed during the 10th meeting of the Task Force (26 - 30 March 2007) at the African Regional Office of the WHO in Brazzaville, Congo.

The 30th meeting of the Research Strengthening Group (RSG) took place in Nairobi in March 2006, under the chairmanship of Dr Ana Rabello of the FIOCRUZ Institute, Brazil. RSG is a multidisciplinary group of scientists that provides technical and strategic advice to TDR, supporting its unique mandate to engage developing countries in science and knowledge-based decision-making, as a pre-requisite for sustainable development of appropriate tools for disease control.

Dr Peter Eriki, WHO Representative, Kenya, opened the meeting, stressing the importance of promoting evidence-based health policy and supporting research relevant to public health goals. Dr Robert Ridley, director of TDR, presented a report on TDR’s progress, challenges and future activities. The directors of a number of international research organizations in Nairobi, including the International Livestock Research Institute (ILRI), International Centre of Insect Physiology and Ecology (ICIPE), Institute of Primate Research (IPR), and the Trypanosomiasis Research Centre (TRC) of the Kenya Agricultural Research Institute, gave overviews of their research lines. For the first time, the principal investigators of institutional program-based grants made presentations on their grant progress. The RSG reviewed 86 progress reports, and short-listed new applications for institutional-based programme grants as well as 34 applications for research training grants. RSG-recommended funding totaled about US$ 1.6 million.

A joint session of the RSG and the MIM/TDR Task Force, meeting the same week in Nairobi, also took place. Dr Fabio Zicker, TDR coordinator of Research Capability Strengthening, led discussions on: coordination of projects and activities; support for project planning and development; and good practice standards for non-regulatory clinical studies. RCS’s mentorship approach and its training of principal investigators in research project planning were acknowledged as positively impacting the quality of funded proposals. A list of approved projects is posted on TDR’s website.
Good Laboratory Practice (GLP) meeting in Rio de Janeiro

TDR’s new Good Laboratory Practice (GLP) Network – facing the challenge of R&D in the south

Along the pathway of developing effective drugs to control diseases endemic in poor countries, the pre-clinical stage of tests constitutes a major, but often unrecognized milestone – where a “GO” or “NO GO” decision must be made. Here, studies relating to the safety of the candidate drug are of critical importance. The importance of selecting the right candidate for exhaustive testing cannot be overstated. As a result, it is critical that research and development studies designed to demonstrate the safety of the drug candidate prior to launching clinical trials on human subjects be conducted in compliance with a set of principles called “Good Laboratory Practice” (GLP). Since regulatory safety studies are only acceptable internationally if they are performed in compliance with GLP, one means of building R&D capacity in disease-endemic countries is to facilitate training in Good Laboratory Practice.

Train the Trainers to deploy more rapidly

Following the recommendations of a GLP Scientific Working Group in 2000, a TDR-sponsored training programme for GLP, together with a set of tutorial materials, was developed. Focused training was then undertaken in a number of R&D institutes in Africa, Asia and Latin America. The next stage was the development of the TDR-sponsored GLP “Train the Trainer” initiative.

"The concept of ‘Train the Trainers’ was adopted so we could have a real impact on large numbers of researchers," says Dr Deborah Kioy, TDR coordinator for pre-clinical activities, who has led the GLP training initiative. Now, the initiative has launched a third phase of activities – and that is a new GLP network. Such a network can further reinforce expansion of the training effort, and assist in the practical implementation of GLP principles.

The overriding aim is to bring laboratories in disease endemic countries up to international levels in the performance of safety studies and thus promote the international acceptance of these studies, their data and subsequently, the registration of new drugs. The first organizational and planning meeting of the new GLP network, involving 21 experienced GLP trainers, was held in Rio de Janeiro, June 2006. Alongside this event, a group of 60 Brazilian scientists attended one of the regular training workshops.

Train the trainer sessions throughout the world

How did it happen? A group of committed researchers selected from those already trained through initial TDR courses were identified and invited to be trained as future trainers. They are assisting TDR in the process of promoting the concepts and principles of GLP and improving the quality of pre-clinical studies. These trainers have since trained large numbers of researchers and GLP awareness is now becoming a more common feature of R&D in disease endemic countries.

GLP NETWORK FOCAL POINTS BY REGION

Latin America
Dr Myriam Arevalo
Herrera, Instituto de Immunologia del Valle, Calle 4B, 36-00, Cali, Colombia,
Tel.: 57 2 558 1931, Fax: 57 2 558 1061, myriama.2001@yahoo.com

Africa
Professor A. Walubo,
Department of Pharmacology, University of the Orange Free State, Post Box 339 (66), Bloemfontein 9300, South Africa,
Tel.: 27 51 401 3090 Fax: 27 51 444 1523 Waluboa@frm.uovs.ac.za and waluboa.MD@mail.uovs.ac.za

Asia
Dr Sudhir Srivastava,
Scientist-in-Charge, Division of Toxicology, Central Drug Research Institute, Post Box 173, Lucknow, 226 001 India,
Tel.: 91 522 21 411 418, Fax: 91 522 223 405, sudhir.srivastava@yahoo.co.uk

If you are a researcher in the field of non-clinical safety studies in a disease endemic country, consider adopting GLP in your institute. A TDR web forum on GLP is planned for the future. Those seeking information more immediately may contact:

Dr Deborah Kioy
TDR Pre-clinical Coordinator kioyd@who.int
What next?
So far, over 1000 people in 10 countries (India, Thailand, Kenya, Benin, Congo, South Africa, Ghana, Nigeria, Colombia, Brazil, Tanzania) have been trained in GLP practices through the TDR-led initiative. In the June meeting of the new GLP network, it was agreed that the network would have regional branches representing Asia, Africa and Latin America. TDR would retain an overall coordination function, while actual training operations would be outsourced as a non-profit activity in the regions involved.

The proposed activities of the network include:
- Continued training, organised regionally by the "outsourced" network groups. This will be accompanied by constant review and improvement of training materials already available.
- Support for GLP implementation in disease endemic country laboratories by providing a forum for advice and aid in the preparation of documentation.
- Encouraging national regulatory authorities to adopt GLP and set up monitoring bodies.
- Development of a web site for training and advice to institutes wishing to implement GLP.

WHO/TDR at ASTMH, 12-16 November 2006

The annual conference of the American Society of Tropical Medicine and Hygiene is one of the premier global events in the field of tropical disease research and control. A total of seven TDR-sponsored symposiums, presentations and posters were featured at the recent ASTMH meeting, which took place in Atlanta, Georgia, 12 -16 November, 2006.

Major presentations were organized by TDR on: Innovative drug discovery research for neglected diseases (see TDRnews cover story); Rapid diagnostics tests for malaria, where do we go from here? (see pages 6-7); and Immune responses in protection against malaria: seven years of MIM/TDR research (see page 22).

Presentations were also made on new research findings related to new Artemisinin-based Combination Therapies for malaria (ACTs) involving TDR researchers in collaborations with a range of research institutions from north and south. In all cases, what brings this diverse array of presentations together is the way TDR has used its leadership and stewardship roles to leverage initiatives bringing together research and training institutions in developed and developing countries and in the public and private sector to work for common goals. See the ASTMH website: www.astmh.org for links to abstracts and papers.

**Symposium 68**
Immune Responses in Protection Against Malaria: Seven Years of MIM/TDR Research
*Chair:* Lee HALL, National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA • Abdoulaya A. DJIMDE, University of Bamako, Mali • Anthony A. HOLDER, National Institute for Medical Research, MRC, London, UK • Roseangela Ifeyinwa NWUBA, University of Ibadan, Nigeria • Batholomew D. AKANMORI, Noguchi Memorial Institute for Medical Research, Legon, Accra, Ghana.

**Symposium 43**
Rapid Diagnostic Tests (RDTs) for malaria: where do we go from here?
*Chair:* John W BARNWELL, Center for Disease Control and Prevention, Atlanta, GA, USA • Peter L. CHIODINI, Hospital for Tropical Diseases, London, UK • John W. BARNWELL, CDC, Atlanta, GA, USA • Qin CHENG, Australian Army Malaria Institute, Brisbane, Australia • David BELL, WHO Regional Office for the Western Pacific, Manila, Philippines.

**Symposium 54**
Innovative Drug Discovery for Tropical Diseases
*Chair:* Dyann WIRTH, Harvard School of Public Health, Boston • Solomon NWAKA, Special Programme for Research & Training in Tropical Diseases (TDR), World Health Organization (WHO), Geneva, Switzerland • Michael WITTY, Pfizer Inc., Sandwich, Kent, UK • David ROOS, University of Pennsylvania, Philadelphia, PA, USA • Reto BRUN, Swiss Tropical Institute, Basel, Switzerland.

**Presentations at Scientific session 32**
Artesunate (AS) plus amodiaquine (AQ) for treating falciparum malaria – assessing its efficacy and tolerability during six years of field deployment in Southern Senegal
Philippe BRASSEUR, IRD, Dakar, Senegal • Patrice AGNAMEY, Laboratoire de parasitologie/mycologie, Université Paris V, Paris, France • Mustafa CISSE, Centre Hospitalier, Oussouye, Senegal • Philippe ELIDIN
Artesunate + Amodiaquine (AS+ AQ) for the treatment of uncomplicated falciparum malaria: an inventory and systematic review of safety and efficacy data.

Piero L. OLLIARO, Special Programme for Research & Training in Tropical Diseases (TDR), World Health Organization (WHO), Geneva, Switzerland.

**Poster Session A**

**Confirmation of emergence of mutations associated with Malarone® resistance in unexposed Plasmodium falciparum isolates from Nigeria.**

Christian T. HAPPI, College of Medicine, University of Ibadan, Nigeria • Grace O. GBOTOSHO, College of Medicine, University of Ibadan, Nigeria • Onikepe A. FOLARIN College of Medicine, University of Ibadan, Nigeria • Akintunde SOWUNMIM, College of Medicine, University of Ibadan, Nigeria • Dyann F. WIRTH, Harvard School of Public Health, Boston, MA, USA • Ayoade M. ODUOLA, Special Programme for Research & Training in Tropical Diseases (TDR), World Health Organization (WHO), Geneva, Switzerland.

**Poster Session B**

Spatial analysis of spill-over effects of insecticide-treated materials in a cluster-randomized trial against Aedes aegypti mosquitoes in Trujillo, Venezuela

Neal ALEXANDER, London School of Hygiene and Tropical Medicine, London, UK • Audrey LENHART, Liverpool School of Tropical Medicine, Liverpool, UK • Elci VILLEGAS, Universidad de los Andes, Trujillo, Venezuela • Michael LEVY, Emory University, Atlanta, GA, USA • Rana MOYEDD, University of Plymouth, Plymouth, UK • Axel KROEGER, Special Programme for Research & Training in Tropical Diseases (TDR), World Health Organization (WHO), Geneva, Switzerland; P. J. MCCALL, Liverpool School of Tropical Medicine, Liverpool, UK.

**Latest grants**

Research in molecular entomology

**New grants**

These grants will be funded for one year only.

A60266
Zakaria Bengaly • Centre International de Recherche Développement sur l’Elevage en Zone Sub-humide, Bobo-Bioulasso, Burkina Faso. Gene flow among populations of *G. palpalis* from the Comoé basin. **US$ 19 050**

A60311
Nancy M. DuTeau • Colorado State University, Fort Collins, Colorado, USA. Biology of disease vectors course – 2007. **US$ 50 000**

A60277
Patrick M. Guerin • Université de Neuchâtel, Neuchâtel, Switzerland. Understanding host seeking in tsetse fly vectors of African trypanosomiasis. **US$ 36 000**

A60312
Winston A. Hide • University of the Western Cape, South African National Bioinformatics Institute (SANBI), Bellville, South Africa. Mobilising tsetse genome information to address disease. **US$ 25 000**

A60345
Jaroslaw Krzywinski • University of Texas at Arlington, Arlington, Texas, USA. Identification of sex determination genes in mosquitoes. **US$ 28 653**

A60262
Maria Monastirioti • Institute of Molecular Biology and Biotechnology, Foundation for Research and Technology-Hellas (FORTH), Crete, Greece. Development of transgenic *Anopheles* strains carrying a dominant female sterilizing allele. **US$ 39 000**

A60347
Antonio Christophe Nkondjio • Organisation de Coordination pour la Lutte contre les Endémies en Afrique (OCEAC), Yaoundé, Cameroon. Bionomics and genetic structure of malaria vectors *An. moucheti* and *An. nili* in Sub Saharan Africa. **US$ 35 856**

A60169
David A. O’Brochta • University of Maryland Biotechnology Institute, College Park, Maryland, USA. Class II transposable element dynamics in *Anopheles gambiae*. **US$ 30 000**

A60278
Loyce Martha Alungat Okedi • NARO/Livestock Health Research Institute (LIRI), Tororo, Uganda. Human infective trypanosome transmission dynamics in the tsetse fly *G. fuscipes* from sleeping sickness foci in Uganda. **US$ 26 800**

A60258
Susan Marie Paskewitz • University of Wisconsin, Madison, Wisconsin, USA. Lysozyme and development of *Plasmodium falciparum* in *Anopheles gambiae*. **US$ 40 000**

A60235
Rosa Patricia Penilla • Centro de Investigacion de Paludismo, Instituto Nacional de Salud Publica, Tapachula Chiapas, Mexico. Molecular characterization of insecticide resistance in the malaria vector *Anopheles albimanus*. **US$ 27 068**

A60362
Om Prakash Singh • National Institute of Malaria Research ICMR, New Delhi, India. Molecular...
characterization of different q1 chromosomal forms of Anopheles fluviatilis. US$ 12 000

Renewed grants

A50363
Christopher Bosio • Colorado State University, Department of Microbiology, Immunology and Pathology, Fort Collins, Colorado, USA. Population genetics and vector competence for dengue-2 virus of Aedes aegypti in Senegal. US$ 27 200

A50241
George K. Christophides • Imperial College London, London, UK. Effects of the Anopheles gambiae immune system on the transmission of human malaria parasite Plasmodium falciparum. US$ 39 998

A50299
Gabriella Irene Gibson • University of Green-wich, Natural Resources Institute, Chatham Kent, UK. Field & laboratory investigation of swarming and mating activities in the Anopheles gambiae species complex. US$ 40 000

A30328
Elena A. Levashina • Institute of Molecular and Cellular Biology of CNRS, Strasbourg Cedex, France. Recognition and signaling during Plasmodium infection in the mosquito Anopheles gambiae. US$ 15 000

A50232
Yvonne-Marie Linton • The Natural History Museum, Department of Entomology, London, UK. Molecular systematics and vector incrimination of the Oswaldoi group (Anopheles nyssorhynchus) in Latin America. US$ 39 800

A30346
Thanasis Loukeris • Institute of Molecular Biology and Biotechnology, Foundation of the National Academy of Athens, Heraklion, Crete, Greece. A study of Anopheles and Plasmodium parasites focusing on oocyste/midge interactions. US$ 24 250

A50256
Jesus Martinez Barnetche • Instituto Nacional de Salud Publica, Cuernavaca, Morelos, Mexico. Functional genomics analysis of Anopheles albimanus immune response to infection with bacteria and Plasmodium. US$ 40 000

A50303
Maria Silva-Neto • Universidade Federal do Rio de Janeiro, Instituto de Biofisica, Rio de Janeiro, Brazil. Phosphoproteome of malaria-infected mosquito midgut. US$ 9 500

A50340
Kenneth D. Vernick • University of Minnesota, Center for Microbial and Plant Genomics, St. Paul, Minnesota, USA. Breeding and analysis of new malaria resistant lines of Anopheles gambi-ae. US$ 38 359

Research in pathogenesis and applied genomics

New grants

These grants will be funded for 1 year only.

A60193
Christine Clayton • Universitat Heidelberg, Germany. Proteomics and phase display for sleeping sickness diagnosis. US$ 35 000

A50314
Malcolm Jones • Queensland Institute of Medical Research, Australia. A hidden antigen approach to schistosomiasis vaccination. US$ 26 500

A60186
Krisster Kristensson • Karolinska Institute, Sweden. Genetic profiling in African trypanosomiiasis to determine the stage of neuroinvasion of the parasite. US$ 35 000

A60246
Mariano Jorge Levin • Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, Argentina. Molecular immunology of protozoan infections. US$ 5 000

A60281
Marcela de Freitas Lopes • Federal University of Rio de Janeiro, Brazil. Immunomodulation in Chagas disease and leishmaniasis: crosstalk between cell death signalling and cytokine responses. US$ 25 400

A60291
Paulo Pimenta • Centro de pesquisas Rene Rachou - FIOCRUZ, Brazil. Vector saliva effect on the development of cutaneous leishmaniasis considering wild-caught and colonized sandflies. US$ 28 600

A60194
Michal Shapira • Ben-Gurion University of the Negev, Israel. The cap-binding complex of leishmaniasis as a novel drug target. US$ 30 000

A60214
Chairat Uthaipibull • National Center for Genetic Engineering and Biotechnology, Thailand. Identification of antifolate resistant mutations on Plasmodium falciparum DHFR using Plasmodium surrogate model. US$ 24 000

A60244
Cristiana Valle • Institute of Cell Biology, Italy. The calcium channel hypothesis for the mechanism of action of Praziquantel. US$ 33 250

New south-south collaboration grants

These multicenter grants will be funded for one year only.

A60265
Marcus Oliveira • Federal University of Rio de Janeiro, Brazil. Hemozoin formation as a potential taget for chemotherapy of schistosomiasis. Pending finalization.

A60251
Guilherme Correira de Oliveira • Centro de pesquisas Rene Rachou - FIOCRUZ, Brazil. Population genetics of schistosoma species in endemic areas of Brazil and Nigeria. US$ 40 000

Renewed grants

AS0312
Walderez Dutra • Universidade Federal de Minas Gerais, Brazil. Mechanistic analysis of the role of CD28+ and CD28-cells in human Chagas disease: towards the understanding of pathology. US$ 27 000

A40204
Zahra Hasan • Aga Khan University, Pakistan. Chemokines as immunopathological markers in tuberculosis infections - pulmonary and extra-pulmonary. US$ 30 000

A40278
Maria Susana Leguizamon • Universidad Nacional de General San Martin, Argentina. Differential expression of virulence factors and human infection by the main parasite lineales of Trypanosoma cruzi. US$ 20 000

A50354
Daniel Masiga • Kenya University, Department of Biochemistry, Kenya. The development and improved production of a diagnostic for Human African Trypanosomiasis. Pending report on site visit.

A50230
Anuja Mathew • University of Massachusetts Medical School, USA. Humanized SCID mice for dengue infection and immunity. US$ 35 000

A50304
Leila Mendonca-Lima • Fundacao Oswaldo Cruz Bioquimica e Biologia Molecular, Brazil. Mycobacterium bovis BCG moreau RJ: functional genomic studies applied to the improvement of vaccine production. US$ 25 000

A50252
Laura Ines Rutitzky • Tufts University, Department of Pathology, USA. Glycan residues on the Sm-p40 schistosome egg antigen: characterization and role in T cell response. US$ 34 500

A50098
Sumalee Kamchongwongpaisan • National Center for Genetic Engineering and Biotechnology, Bangkok, Thailand. Applications of transfection technology for drug screening and immunological studies in tropical parasitic diseases. US$ 19 150

Renewed grants in south-south collaboration

AS0337
Christian Happi • University of Ibadan, College of Medicine, Ibadan, Nigeria. Molecular determinants of drug response and resistance in P. falciparum from Africa and South-Africa. US$ 50 000

A50271
Mariano Jorge Levin • Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, Argentina. Specific molecular mechanisms as targets of novel anti-parasitic drugs - pending report on site visit to partner lab in Kenya.
Research Capability Strengthening

Programme grants

New grants

A50881 Yewhalaw Delenesaw | Jimma University, Ethiopia. Malaria incidence and transmission among children near hydroelectric dam: baseline study to malaria control program. US$ 51 850

A51001 Sambo Guengo | Centre de Support en Santé Internationale de l’Institut Tropical Suisse au Tchad. La tuberculose chez les chameliers nomades au Chari-Baguirmi/Tchad: prévalence et facteurs de risque. US$ 44 380

A50845 Stafford Nikulamba Kibona | National Institute for Medical Research, Tabora Research Centre, Tanzania. Drug sensitivity of T. rhodesiense isolates and the role of domestic animals in epidemiology of HAT in Tanzania. US$ 35 000

Renewed grants

A20785 Laura Arcos | Pontificia Universidad Católica del Ecuador, Ecuador. Institutional capability strengthening in tropical disease research and training at Catholic University, Quito, Ecuador. US$ 46 200

A20766 Vinod Joshi | Desert Medicine Research Centre, India. Studies on dengue and dengue haemorrhagic fever in Rajasthan, India. US$ 17 100

A41486 Grace Adira Murilla | Trypanosomiasis Research Centre, Kenya Agricultural Research Institute, Kenya. Capacity strengthening for trypanosomiasis research and control. US$ 50 000


A41490 Omran Fadl Osman | University of Khartoum, Faculty of Science, Sudan. Transmission of visceral leishmaniasis in eastern Sudan: studies on reservoir hosts and vectors. US$ 43 000

A41430 Jean-Bosco Ouedraogo | Institut de Recherche en Sciences de la Santé, Burkina Faso. Improvements of indirect haemagglutination assay as sustainable tools for schistosomiasis diagnosis and control. US$ 56 070

A30931 Sadri A. Said | Institute of Marine Sciences, Tanzania. Discovery of new antimalarial drugs from marine invertebrates. US$ 46 000

Re-entry grants

New grants

A50904 Collins Stephen Ahorlu | Noguchi Memorial Institute for Medical Research, Ghana. Community intervention to reduce malaria-related morbidity and mortality in the Shime sub-district in Ghana. US$ 16 700

A50839 Luciana de Oliveira Andrade | Universidad Federal de Minas Gerais, Instituto de Ciencias Biológicas, Brazil. Study of the mechanism of T. cruzi entry and development in non-phagocytic cells. US$ 26 500

A50993 Daniella Bartholomeu | Universidad Federal de Minas Gerais, Instituto de Ciencias Biológicas, Brazil. MASP gene family of Trypanosoma cruz: from in silico to wet-bench characterization. US$ 12 974

A50967 Alia Benkahla | Institut Pasteur de Tunis, Tunisie. Global analysis of leishmania genes expression using SAGE libraries. US$ 8 000

A50984 Mawuli Dzodziyemo | University of Ghana School of Public Health, Ghana. Inducible nitric oxide synthase 2 promoter polymorphism and malaria disease severity in children in Southern Ghana. US$ 14 000

A50990 Ana Lineht Garcia Orellana | Universidad Mayor de San Simon Facultad de Medicina, Bolivia. Peridomestic cutaneous leishmaniasis transmission in Cochabamba, Bolivia: evidence & implications for disease prevention/control. US$ 21 100

A50892 Jonathan Kayondo | Uganda Virus Research Institute, Uganda. Genetic structure, host seeking & feeding preferences in the main Anopheles gambiae malaria vectors across Uganda. US$ 21 225

A50987 Guillermo R. Labadie | Instituto de Quimica Organica de Sintesis, Argentina. Ergosterol biosynthesis as target of antiparasitic agents. US$ 13 500

A50879 Thembra Mzilahowa | Malawi-Liverpool-Wellcome Trust Clinical Research Programme Malaria vector breeding sites and assessing their impact on local malaria risk. US$ 16 410

A51005 Ana Acacia Pinheiro | Universidad Federal do Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Brazil. Molecular mechanisms triggered by P. falciparum derived GP1s in cells of innate immune system: involvement of TLRs. US$ 19 000

A50982 Hakim Sendagire | Makerere University Department of Biochemistry, Uganda. Efficacy of artemether-lumefantrine therapy & assessment of possible molecular markers of resistance in Uganda. US$ 18 350

A50880 Rodrigo Pedro P. Soares | Centro de Pesquisas Rene Rachou, Fundação Oswaldo Cruz—FIOCRUZ, Brazil. Role of L. chagasi & L. braziliensis LPGs & GPIs in the innate immune response in murine neutrophils & macrophages. US$ 18 500

Renewed grants

A41481 Josiane Desiree Etang | Organisation de Coordination pour la Lutte contre les Endémies en Afrique, Cameroon. Kdr-based insecticide resistance in Anopheles gambiae s.s. from Cameroon: origin, spread and levels of resistance. US$ 16 350

A41413 Wamadoso Moussa Guelbego | Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso. Genetic and vectorial component of leishmaniasis in Eastern Sudan. US$ 20 200

A30849 Moses Lutaakome Joloba | Makerere University, Department of Medical Microbiology, Uganda. Evaluation of various methods for rapid detection of multi-drug resistant tuberculosis. US$ 13 300

A41418 Marcelo Tavora Mira | Pontificia Universidad Católica del Ecuador, Ecuador. A study of host genetic risk factors for leprosy susceptibility. US$ 16 560

A41329 Neelima Mondal | Jawaharlal Nehru University, India. Functional characterization of gyrase enzyme from Plasmodium falciparum. US$ 17 450


A30848 Clara Beatriz Ocampo Duran | Centro Internacional de Entrenamiento e Investigaciones Médicas, Colombia. Differential gene expression in dengue-2 infected & non-infected midguts of susceptible & refractory strains of A. aegypti. US$ 13 000

A41403 Lyda Elena Osorio | Centro Internacional de Entrenamiento e Investigaciones Médicas, Colombia. Population genetics of drug resistant P. falciparum in Colombia. US$ 18 000

A30891 Edith Sanogo | Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso. Résistance des vecteurs du paludisme aux insecticides au Burkina Faso: mécanismes impliqués et facteurs favorisants. US$ 13 050
Research training grants

A60114 James Akazili • Ghana • M • PhD
Health sector reforms and its implications on equity, efficiency and quality of care (malaria).

A60157 Hampate Ba • Mauritania • M • PhD
Contribution a l’étude d’An. gambiae s.l. et de la dynamique de transmission du paludisme, en bordure du Sahara Mauritanien.

A60158 Nana KwadwoBritwum • Ghana • M • PhD
The epidemiology and control of Lymphatic filariasis in four districts in Ghana.

A60156 Chhordaphrea Chhea • Cambodia • F • PhD
Behaviour change, communication and community participation in Tuberculosis control in Cambodia.

A60118 Jean RousseauDjouaka • Benin • M • PhD
Analysis of developmental & molecular changes induced by petroleum products in Anopheles species with focus on changes.

A60168 Sabelo VusiDiamini • Swaziland • M • PhD
In vitro or in vivo activities of effects of artemether-lumefantrine combination treatment on parasite survival & transmission of Pf.

A60120 Noelia MustafaKhalid • Sudan • F • PhD
A study on the Taxonomy and molecular diversity of the subgenus phlebotomus phlebotomus sandfly species in Sudan.

A60122 Pharah Lim • Cambodia • F • PhD
Multi-drug resistance genes in Plasmodium falciparum in Cambodia.

A60170 Abdelrafe Makhawi • Sudan • M • PhD
Vectorial capacity and molecular characterization of malaria vectors in Eastern Sudan.

A60124 Joao Soares Martins • Timor-Leste • M • PhD
To assess effectiveness of redeveloping malaria control program in Timor Leste.

A60125 NicholasMidzi • Zimbabwe • M • PhD
Distribution of mixed infection from Pf, schisto & soil transmitted helminths in primary schools aged children.

A60133 Clarisse YaliNjua • Cameroon • F • PhD
The impact of intermittent preventive treatment in pregnancy on maternal naturally acquired & transplacental immunity.

A60137 Diana Iris S. Quelhas • Mozambique • F • PhD
Intermittent preventive treatment in infants.

A60159 Jane JemeliRutto • Kenya • F • PhD
Assessment of the impact of land use & land cover on the epidemiology of sleeping sickness.

A60148 Salazar AnitaVillacis • Ecuador • F • PhD
Phenotypic variation of Rhodinus ecuadoriensis populations from Loja & Manabi provinces using antennal sensilla patterns.

Social, Economic and Behavioural Research (SEB)

New grants

A60307 Dr Peter Agyei-Baffour • Kwame Nkrumah University of Science & Technology, Kumasi, Ghana. Efficiency morphology of institutional arrangements and their implications for improving contracts structuring in Malaria. US$ 34 820

A60450 Dr Duane Blaauw • Centre for Health Policy, School of Public Health, Witwatersrand University, Johannesburg, South Africa. The efficiency of institutional arrangements for tuberculosis control in South Africa. US$ 41 000

A60192 Dr Andrea Gazzinelli • Universidade Federal de Minas Gerais, Belo Horizonte, Brazil. Access to and utilization of schistosomiasis chemotherapy and information in a rural and urban area in Brazil. US$ 40 000

A60334 Dr Jessica Jitta • Child Health and Development Center, Makerere University, Kampala, Uganda. Major factors affecting children’s decision-making in response to infectious diseases in conflict areas in Uganda. US$ 10 000

A60449 Dr Hamilton Moura Ferreira Junior • Instituto de Saude Coletiva, Universidade Federal da Bahia, Salvador, Brazil. Institutional arrangements and efficiency of the tuberculosis control program in the decentralization context in Brazil. US$ 37 700


A60346 Dr Loveday Anna Penn-Kekana • Centre for Health Policy, University of the Witwatersrand, Braamfontein, South Africa. Exploring the interactions between foreign-trained doctors and malaria control and treatment programmes in South Africa. US$ 39 300

A60152 Dr Qiang Zhenhua • School of Humanities and Law, University of Science and Technology, Beijing, China. Access barriers for temporary construction workers to TB care in China. US$ 26 200


Renewed grants

A40299 Dr Paul Wako M. Bukuluki • Makerere University, Kampala, Uganda. Health seeking patterns of families with under-five children for malaria treatment in conflict areas: a case of Gulu district. US$ 16 090

A40300 Dr Pablo Kreimer • Facultad Latinoamericana de Ciencias Sociales, Buenos Aires, Argentina. Global dynamics, periphery & social actors: the limits to development and access to diagnosis and treatment of Chagas Disease. US$ 16 400

A40153 Dr Mariana Romero • Centro de Estudios de Estado y Sociedad (CEDES), Buenos Aires, Argentina. Decentralization policies and health system reform in Argentina: its impact on Chagas vector prevention and control. US$ 14 312

A50384 Dr Susilowati Tana • Center for Health Policy and Social Studies, Yogyakarta, Indonesia. Understanding factors contributing to the resiliency of Aceh health workforce. US$ 64 458

A40099 Dr Shaokang Zhan • Fudan University, Shanghai, China. Globalization and TB in migrant populations in China. US$ 19 750

A30298 Dr Xiao-Nong Zhou • National Institute of Parasitic Diseases, Shanghai, China. Biosocial & environmental risks related to disease burden of schistosomiasis in the Yangtze River Basin, China. US$ 32 200

A reader notes

The picture on page 12 of TDRnews No. 76 was mistakenly identified as the photo of Professor Awa Marie Coll Seck. In fact, it is the photo of Dr Dorothy Djeuma, rector of the University of Yaounde I, Cameroon. TDRnews apologizes for any error.
Publications

Now available from TDR

- Diagnostics for tuberculosis: global demand and market potential

  A significant untapped global market exists for more effective and affordable tests to diagnose tuberculosis in countries where the disease is most prevalent. This report by WHO/TDR and the Foundation for Innovative New Diagnostics (FIND) is the first time an international network of researchers and policy experts has made a comprehensive review of the TB diagnostics market; it calls for greater industry investment in diagnostics targeted to low and middle income countries.

- Laboratory-based evaluation of rapid syphilis diagnostics
  Results from 8 SDI Sites, 40 pp., 2003 (TDR/SDI/DE/03.1) reprint

  This is the first in a series of laboratory-based evaluations assessing rapid syphilis tests and identifying candidates for further evaluations in field settings. Six rapid treponemal tests were evaluated in eight SDI laboratory sites. All showed reasonable reliability and were considered easy to use. Four tests have been selected for further evaluations of test performance and utility in field settings.

- Gender and tuberculosis: cross-site analysis and implications of a multi-country study in Bangladesh, India, Malawi and Colombia
  97 pp., 2006 (TDR/SDI/DE/09.1)

  More than half a million women annually die from TB, and gender-related barriers to TB-related control and treatment persist. The findings of this multi-country study suggest specific strategies for improving TB control through gender-sensitive and locally appropriate community action, clinic operations, programme monitoring and action-oriented research for TB control.

- Multicountry study of Aedes aegypti pupal productivity survey methodology - findings and recommendations
  55 pp., 2006 (TDR/IRM/DEN/06.1)

  Dengue fever is a fast-growing public health problem worldwide. Reducing vector populations in domestic and peri-domestic water containers is the main strategy used to reduce transmission. TDR financed a multicountry study involving nine Latin American, Asian, and African countries to evaluate a new pupal demographic survey method, and determine whether it can consistently identify and classify categories of containers where the dengue vector, Aedes aegypti (L.), breed most productively, providing a reference base and guidance for targeted control strategies.

- The use of rapid syphilis tests
  28 pp., 2006 (TDR/SDI/06.1)

  Syphilis is a curable infection caused by a bacterium, Treponema pallidum. Yet syphilis infection often is not diagnosed and treated, and along with being transmitted sexually, it can be passed from mother to fetus in pregnancy, leading to stillbirth, prematurity, and neonatal death. As a cause of genital ulcers, syphilis also has been associated with an increased risk of HIV transmission and acquisition. This booklet describes the use of rapid syphilis tests important to early detection and treatment. In press but available on: www.who.int/tdr/publications/publications/rapid_syphilis.htm

- Recherche concernant les maladies tropicales: progrès de la recherche 2003-2004
  98 pp., 2005 (TDR/GEN/05.1)

Quality information in field research: training manual on practical communication skills for field researchers and project personnel
134 pp., 2005 (TDR/IRM/PCT/05.1)

This manual is the outcome of a training process developed at the Kenyan Medical Research Institute (KEMRI)-Wellcome Trust Collaborative Research Programme in Kilifi, Kenya, a centre for multidisciplinary research focusing on prevention and treatment of severe childhood malaria. The aim of the training was to build upon the communication skills of the field workers collecting the data, and thus improve the quality of the information they gathered.

TDR summary report 2004-2005
16 pp., 2006 (TDR/GEN/06.4)

Available in English, Arabic, French, Spanish and Portuguese. The report covers achievements of the 2004-2005 biennium and aims for 2006-07. Key activities covered include: visceral leishmaniasis elimination, halting congenital syphilis; treatment safety for river blindness; and ethical guidelines for clinical research. There is also a brief review of: new knowledge generation; new and improved tools and strategies; and capacity building. Also addressed are TDR’s structures of governance, partnerships, financial contributions, key publications and strategic performance indicators.

Evaluating diagnostics: the malaria guide
Nature Reviews Supplement: Microbiology
Vol. 4, No. 9, September, 2006

Effective, quality-assured diagnostics are important for patient management and disease control. This supplement, produced in a collaboration between TDR, the WHO Regional Office for the Western Pacific region (WPRO) and Nature Publishing Group, is the first in a series of user-friendly operation guides explaining how to design and conduct evaluations of diagnostic tests for infectious diseases that are of public health importance to developing countries. Available free on the TDR website and at: www.nature.com/nrmicro/supplements/index.html

Evaluating diagnostics: the STI guide
Nature Reviews Supplement: Microbiology
Vol 4, No. 12, December, 2006

This second supplement in the new Nature Reviews supplement series on diagnostics evaluation focuses on diagnostics for the bacterial sexually transmitted infections: syphilis, chlamydia and gonorrhoea. Taken together, these are responsible for an enormous burden of morbidity and mortality, particularly in women in developing countries. Available free on the TDR website and at: www.nature.com/nrmicro/supplements/index.html

CD-ROM – Bioethics and research ethics: academic and extension programmes.
2006. In Spanish and Portuguese

This tutorial CD-ROM is the product of a pioneering initiative developed by the University of Brasilia, in partnership with Anis – Institute of Bioethics, Human Rights and Gender and the Latin American Forum of Research Ethics Committees in Health – FLACEIS. The initiative is supported by WHO/TDR, the Ministry of Health of Brazil and UNESCO. The CD-ROM provides academic programmes on research ethics for undergraduate and graduate students and the public-at-large, including lecture plans, cases studies, discussion questions; reference and regulatory background; slides; and bibliography. Available free at: www.nature.com/nrmicro/supplements/index.html For CD-ROM copies contact: Prof Dirce Guilhem, Universidad de Brasilia, at guilhem@unb.br

In collaboration with others

Control of human parasitic diseases
Advances in Parasitology, Volume 61, 2006 (ISBN: 0-12-031761-3)

A state-of-the-art source on parasitic disease control, this volume covers latest developments in methods for control of eleven parasitic infections, including all the parasitic diseases that TDR addresses. The impact of recent research findings on control strategy, and the health policy implications of these findings, are emphasized, as are control strategies of extremely low cost and high efficacy – many of which currently fail to reach the poorest populations most afflicted by these parasites. Price: US$ 169.95. To order see: http://www.books.elsevier.com

Publications available from elsewhere
## Call for courses/applications

<table>
<thead>
<tr>
<th>Course Details</th>
<th>Deadline</th>
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</thead>
<tbody>
<tr>
<td>Implementation research on drug delivery strategies for lymphatic filariasis elimination in urban areas in Africa</td>
<td>28 February 2007</td>
</tr>
<tr>
<td>Implementation research on validation of improved dengue clinical guidelines</td>
<td>28 February 2007</td>
</tr>
<tr>
<td>Cours de spécialisation en immunologie, vaccinologie et biotechnologie appliquées aux maladies infectieuses</td>
<td>23 Mars 2007</td>
</tr>
<tr>
<td>Advanced course on immunology, vaccinology and biotechnology applied to infectious diseases</td>
<td>27 April 2007</td>
</tr>
<tr>
<td>10th International Dengue course: 20 years strengthening capacities</td>
<td>May 2007</td>
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In addition, grant applications and research proposals relevant to TDR’s scientific work plans are reviewed by TDR Steering Committees at their regular meetings. To guarantee review, documents should be received by TDR in Geneva at least two months before the meeting date. For more information see: [www.who.int/tdr/grants](http://www.who.int/tdr/grants)

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### 30 years of TDR activities

We are celebrating the 30th anniversary of the establishment of TDR’s Joint Coordinating Board (JCB). If you have any stories about TDR-supported research that made a difference to public health and to TDR history, please send us your contributions for consideration in special anniversary web and print publications. The stories should be 500 words or less and clearly describe 1) the TDR link 2) the work or personality in question and 3) the broader relevance to public health and tropical disease research in the setting of a particular community, a country, a region or globally. We apologize that we cannot individually acknowledge every contribution. E-mail: tdr@who.int

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Establishing the effectiveness of community-directed distribution of ivermectin to control onchocerciasis (river blindness) – one of many TDR successes.

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**Global health research activities at the Wellcome Trust: support for developing country researchers**

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- Training
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For details see: [www.wellcome.ac.uk/international](http://www.wellcome.ac.uk/international)