CONTENTS

2 Lapdap: a new antimalarial for Africa

3 FIND: finding new diagnostics

4 SWG identifies focused research agenda for malaria

5 FAME: an initiative to promote medical research publishing in Africa

6 HINARI approaches major milestone

8 Partnership for Social Science in Malaria Control: five-year strategy envisages centres of excellence in Africa

9 Ethical, legal and social issues of genetically modified disease vectors in public health

10 TDR’s Co-artemether Product Development Team: a public-private partnership in action

12 WHO-Aventis Collaborative Working Group: one cornerstone of a global alliance for controlling and eliminating African sleeping sickness

13 Miltefosine: what next?

14 TDR meets the tropical disease research community in Germany

15 TDR trainee profile

16 New research awards

22 Publications

24 Deadlines

KEYNOTE ARTICLE

Lapdap: a new antimalarial for Africa | page 2 |
KEYNOTE ARTICLE

Lapdap: a new antimalarial for Africa

A new antimalarial treatment, a combination of chlorproguanil and dapsone known as ‘Lapdap’ which was developed by TDR and partners, has been approved by the UK Medicines and Healthcare Products Regulatory Agency (MHRA) for the treatment of uncomplicated Plasmodium falciparum, the most life-threatening malaria parasite, in adults and children more than three months of age. Lapdap is effective against drug-resistant parasites and is anticipated to be available in several African countries by the end of 2003, assuming that national approval is granted.

Affordable new antimalarials are badly needed in sub-Saharan Africa, where first-line treatments (e.g. chloroquine, sulphadoxine/pyrimethamine) are failing due to increasing parasite resistance. Lapdap is cheap to produce and has a short half-life, presenting a smaller ‘window’ for selection of resistance than drugs with a longer half-life, so the antimalarial efficacy should be retained for longer.

The safety and effectiveness of Lapdap will now be further assessed through surveillance of phase IV trials; so far, in the phase III clinical programme in sub-Saharan Africa, the most common adverse effect was anaemia, which occurred in only a small proportion of patients and was of limited duration. The safety of Lapdap will also be assessed in specific patient groups, e.g. very young children, pregnant women, those co-infected with HIV, those with a predisposition to certain kinds of anaemia. Since chlorproguanil-dapsone is pharmacologically similar to sulphadoxine/pyrimethamine, further work is also needed to understand how the useful therapeutic life of chlorproguanil-dapsone will be affected by the growing resistance to S/P.

To what extent chlorproguanil-dapsone will, by itself, find use in the treatment of malaria is, however, uncertain. WHO strategy is to use new antimalarial drugs in combination with an artemisinin derivative, and Lapdap has the potential to be used in this way as a ‘loose’ combination with an artemisinin. The development of a fixed-dose combination of Lapdap with artesunate (chlorproguanil-dapsone-artesunate or CDA) is already under way and is currently undergoing phase II clinical trials in Malawi. The creation of a public-private partnership to further develop this combination drug is at an advanced stage of negotiation.
An independent non-profit foundation based in Geneva and known as the Foundation for Innovative New Diagnostics (FIND)1 was launched in May 2003 by TDR and the Bill and Melinda Gates Foundation.

FIND represents an expansion of TDR’s ongoing efforts to find and develop new diagnostics for neglected infectious diseases; in particular it builds on the former TDR Tuberculosis Diagnostics Initiative (TBDI). With funding from the Gates Foundation (US$30 million for the first five years), FIND will be able to quickly turn methods into products, untested products into evaluated products, and promising tests into tools with demonstrated impact and feasibility.

Tuberculosis (TB) was chosen as the first target for FIND because of the magnitude of the TB problem (TB kills one person every 15 seconds) and because, once detected, cases can be ably treated by existing health systems. Ultimately however, other neglected diseases will be the focus of attention.

FIND and TDR have a jointly elaborated work-plan on TB diagnostics, which will be carried out through managing a portfolio of focused research activities rather than through open requests for investigator-initiated proposals. However, some investigator-initiated proposals will be funded each year, and two joint FIND/TDR requests for applications have already been issued, calling for research towards 1) an antigen detection system for case-finding or follow-up, and 2) improved sputum microscopy (this being the most widely available diagnostic test for tuberculosis, which has been in use for more than 100 years).

FIND will be directed by Giorgio Roscigno, the founding director of the Global Alliance for TB Drug Development, while TDR’s own Mark Perkins will become FIND’s scientific director. The FIND offices are located next door to TDR’s new premises (see page 11).

“The recent outbreak of SARS illustrates the need for easy-to-use and accurate diagnostics to aid in the control of tropical diseases” says TDR director Carlos Morel. “Great strides have been made in developing drugs and increasing patient access to good medicines, but diagnosis remains a stumbling block in public health. Public health needs can only be met by partnerships at all levels”.

1 www.finddiagnostics.org/
The Scientific Working Group (SWG) is one of the major tools for TDR, for bringing the disease emphasis back into the Programme. An SWG meeting takes place once every five years for each disease. It sets the research agenda not only for TDR but for the whole of the disease field, from basic science to policy-making. Experts from all geographic areas, including disease endemic countries, take part in the meetings, which are five-day exercises.

The focus of the SWG meeting held in March 2003 was malaria, which remains a major threat to human health despite considerable national and international efforts. The meeting brought together an interdisciplinary group of scientists, representing academic, government and non-governmental organizations, who reviewed the current state of knowledge and identified gaps and opportunities in research and training to address these gaps.

Recommendations for a focused research agenda included:

- Evaluation of treatment and access to treatment for uncomplicated malaria in children and during pregnancy, with an emphasis on home management of malaria.
- Evaluation of new approaches to preventing and managing severe malaria.
- Evaluation of artemisinin-based combination therapies.
- Development of new drugs with novel targets.
- New approaches to drug-based malaria prevention including intermittent preventive therapy in children and during pregnancy.
- Strategies for scaling up the use of insecticide-treated nets.
- Genomics for discovery and development of drugs, diagnostics, vaccines, insecticides, and anti-parasite effector molecules.
- Strategic and basic research in vector-parasite-host interactions.
- Assessment of mechanisms for drug and insecticide resistance.
- Development and field evaluation of transgenic methods for interrupting malaria transmission.
- Investigation of the pathogenesis of malaria, in particular of anaemia and mechanisms of immune response.
- Development and application of a common methodology for measuring socio-economic status.
- Policy and operational research on the impact, viability, sustainability, and optimal balance in public-private partnerships.
- Ethical, legal and social issues of new malaria-related tools.
- Continuation and expansion of capacity building and synergistic partnerships.

Scientific Working Group identifies focused research agenda for malaria
TDR supports major health research projects in Africa and other regions through a variety of grants. The results of this research are published in well-known biomedical journals rather than in national medical journals; repeated bibliometric analyses to assess the impact of TDR grants in published literature have shown that the vast majority of grant recipients publish in mainstream biomedical journals with a high impact factor. Since the same bibliometric analyses show that most of these research results are cited by scientists outside Africa, the impact of this research on local researchers, health professionals and policy-makers, all of whom have little access to major international health journals, is questionable. To give greater visibility to African medical research therefore, TDR/Research Capability Strengthening (RCS) has launched an initiative to strengthen local publication of health research conducted in or relevant to Africa. A postal survey, in July 2002, of 69 African medical and health journals found that the majority were under-funded, did not publish regularly, lacked high quality articles and standard peer review, and were mostly invisible to the rest of the international medical community.

In October 2002, 15 African medical journal editors, four mainstream medical journal editors, and representatives of international editors’ associations and other interested partners were brought together in a consultative meeting and workshop in Geneva. Setting up the Forum of African Medical Editors (FAME), a professional association and network, was the first step taken by the African editors in reviewing the problems faced by their journals and trying to find common solutions. The FAME secretariat is located at Kenya Medical Research Institute, Nairobi, Kenya, and a list-serv for FAME members and interested partners is now operational at fame@who.int.

The FAME steering committee met for the first time in Mombasa, Kenya, 22-24 April 2003. The meeting was attended by members from Ethiopia, Kenya, Mali, Mozambique, Uganda, and Switzerland (WHO/TDR/RCS). The work planning meeting, which was facilitated by a professional public health facilitator, was participatory, enabling all members to contribute their ideas to the establishment of FAME. The report of the meeting includes proposals, a workplan, and the draft constitution. The FAME general founding meeting will be held in Addis Ababa in September 2003.

It is expected that capacity building within existing African medical journals, and collaborative projects with interested parties, will lead to greater journal sustainability and publishing regularity, improved quality of peer review and contents, and higher regional and international visibility of African medical research through indexing in major bibliographic databases.

2. World Association of Medical Editors, Council of Science Editors.
HINARI, the Health Internetwork Access to Research Initiative, is approaching a major milestone: 1000 registered institutions. The Initiative has expanded in two phases; at the time of writing, a total of 945 institutions in 96 countries in all regions of the world are registered users.

HINARI was launched in 2002 as a public-private initiative aiming to enable access to international biomedical journals for scientists and health care workers in developing countries so they will be better able to participate in the global research agenda (see TDRnews nos. 64, 66, 69). A total of 39 publishers, including most of the major scientific presses, are now participating by providing free or low-cost access to their publications for universities, medical schools, research institutions, teaching hospitals, and government offices in low-income countries. While some WHO offices at regional and country level are providing support to help institutions equip themselves, many institutions now hold regular training courses on how to use HINARI. TDR also actively supports HINARI, and recently, for example, provided infrastructure support for connectivity of the largest hospital in Honduras and of the Armauer Hansen Research Institute in Ethiopia.

Users seem to be very happy with HINARI. “On behalf of our scientific team, I would like to express my deep gratitude and sincere thanks to HINARI. Access to the right information is of paramount importance if one wants to do good science. At this point, HINARI is unique, especially for the poor countries of the Third World, like Madagascar” (Philippe Rasoanaivo, Institut Malgache de Recherches Appliquées).

UPDATE

HINARI approaches major milestone

Barbara Aronson

Many institutions now hold regular training courses on how to use HINARI, as here in Bhutan at the Royal Institute of Health Sciences (RIHS), Health Literature, Library and Information Services (HEL-LIS) national focal point library.
Dr Howard Engers was at WHO in June. He dropped by the library to tell us how pleased he and his colleagues are with HINARI.

**Dr Engers, tell us about your institute.**

Armauer Hansen Research Institute (AHRI) is named for the Norwegian country physician, Gerhard Henrik Armauer Hansen, who first described the leprosy bacillus (*Mycobacterium leprae*) and who indeed was first to link a disease to a microorganism. AHRI is now part of the Ministry of Health ALERT – the All Africa Leprosy Rehabilitation and Training Center, a large hospital with both in-patient and out-patient services. These days the research scope of the Institute has been widened to mycobacterial research in general, mainly tuberculosis.

**I know that last year AHRI was not able to connect to HINARI. How have you solved this problem?**

In order to be able to use HINARI, we have installed a leased line. It costs us about US $500 per month. There are not many leased lines available in Addis Ababa, but we were able to get ours with the help of the Ministry of Health. Our line is not as fast as broadband – about half as fast – but it works. We have 12 workstations on line, with two in the library.

**How has HINARI been received at AHRI?**

We are all very excited about it. AHRI has graduate students - masters and doctoral level, and of course researchers. We have a bus service to transport staff to and from the Institute. They arrive on the 08:00hrs bus, and leave on the bus at 17:00hrs. We have one late bus at 19:30hrs. Since we have HINARI, there are always six or eight people staying for the last bus, so they can use HINARI. Staff also come in on Saturdays and Sundays. They set their experiment up, and then go to the library to use HINARI. Scientists are also coming from the University of Addis Ababa to use HINARI. They have their own password, but their connectivity is not always as reliable as ours.

**What impact is HINARI having on the work of AHRI?**

Research proposals coming from African institutions can be very out of date. You see it in the bibliographies – they are just not aware of what has been happening in the last year or so, because they don’t have ready access to the journals. So the ideas may be very good, but can be irrelevant. It’s hard to get funding this way. Now that we have HINARI, when I see a draft proposal – for a thesis chapter, for a grant - if I don’t see 2003 references, I send them back to the library to get 2003 and even pre-publication articles from HINARI. This changes things for us completely.

Dr Engers and his institute have recently been incorporated as part of the Ministry of Health. We asked if he intends to get HINARI working there and he assures us it will be one of his first priorities.

Nearly 1000 institutions in nearly 100 countries, including Bhutan as here at the RIMS HELS national focal point, are registered users of HINARI.
The Partnership for Social Science in Malaria Control (PSSMC), an organization whose membership comprises individuals from institutions committed to “the effort to Roll Back Malaria through building partnerships, and promoting quality social science contributions to developing and implementing evidence-based strategies,” held its third annual steering committee meeting 15-17 January 2003 at WHO headquarters in Geneva, Switzerland. Present at the meeting were members of the Steering Committee, representatives of partner organizations, and invited guests.¹

This year’s meeting was well represented by WHO personnel, including staff members from TDR and Roll Back Malaria. Dr Carlos Morel, Director TDR, gave the opening and welcome remarks, expressing a desire to see greater involvement of TDR in the activities of the PSSMC. During his remarks at the opening session, Mr David Alnwick, (then project manager of Roll Back Malaria; now director of WHO’s malaria unit) also commended the PSSMC on being at the “cutting edge” of effecting behaviour change in malaria control efforts.

One of the main accomplishments of this year’s meeting was the development of a five-year strategic framework, produced as a result of a highly participatory process incorporating input from all attendees. Major achievements of the organization over the past year were also reviewed, including:

- expansion of the Clearinghouse for Social Science and Malaria Literature, a PSSMC-created citation database that includes published literature, technical reports and oral/poster presentations from national, regional and international meetings. The Clearinghouse is hosted by the Malaria Foundation International on its website (www.malaria.org);
- support for four African social scientists to attend international conferences and meetings to present research and facilitate panel discussions;
- creation of a database of social science consultants that will be distributed to national malaria control programmes through the WHO Regional Office for Africa;
- development of an annotated bibliography of socio-behavioural issues related to malaria and pregnancy that was distributed through the US Agency for International Development and the Pregnancy, Malaria, Anemia Network;
- expansion of the PSSMC network of social scientists interested in malaria control in sub-Saharan Africa to 113 members representing 20 countries;
- development of a postdoctoral social science position within the US Centers for Disease Control and Prevention Malaria Fellowship Program.

As part of its strategic plan, the PSSMC is seeking funds to establish four regional resource centres to be located in the regions represented by the African members of the Steering Committee (Kenya, Mozambique, Ghana, Mali). These centres are envisioned to be centres of excellence for applied social science in malaria control and sources of technical expertise for the regions.

The next annual steering committee meeting is tentatively scheduled for January 2004 in Accra, Ghana. Plans are under way to host an “add-on” scientific day in order to bring together social science researchers, staff of national malaria control programmes, and local malaria stakeholders, to begin the process of establishing an open dialogue and sharing resources and expertise, and to develop approaches for social scientists to contribute to malaria control programmes in a more effective manner. ■

¹ Organizations represented:
- US Centers for Disease Control and Prevention
- TDR
- WHO Regional Office for Africa
- WHO Roll Back Malaria
- UK Department for International Development
- Malaria programme of the London School of Hygiene and Tropical Medicine
- Ghana Health Services
- University of Nairobi
- National Institute of Health, Mozambique
- Environmental Health Project
- Danish Bilharziasis Laboratory
- Multilateral Initiative on Malaria secretariat
- Malaria Consortium
- Gates Malaria Program, London School of Hygiene and Tropical Medicine
- Center for Health, Society and Culture, Emory University.
During the past seven years, TDR has led a number of efforts to develop the tools necessary for producing genetically modified insect vectors that are no longer able to transmit pathogens. A major focus, under its Basic and Strategic Research area (STR), has been to develop a genetically-modified mosquito that cannot transmit malaria. The concurrent publication of the malaria and mosquito genomes in 2002 brought this goal one big step closer. However, before any genetically modified organism can be released, important environmental and human health concerns must be assessed.

A recently published monograph on the ethical, legal and social issues (ELSI) involved,1 prepared under the auspices of TDR’s Steering Committee on Social, Economic and Behavioural (SEB) research (see publications page), helps to prepare the ground for this. The monograph introduces issues that are relevant not only to TDR but to anyone planning to utilize genetically-modified organisms in the environment for public health purposes. A number of issues need to be considered well in advance and prior to considering use of any transgenic organism in disease control.

The issues include:

- Assessing risk – taking up all the scientific and social issues that pose potential risks and developing safety precautions to address them.
- Evaluating risk – e.g. through setting up a specialized ethical review committee to offer advice to researchers on the ethics of their projects; carrying out environmental, medical and social studies prior to selecting a site for field trials; developing a contingency plan for aborting a field trial.
- Exchanging information – with community leaders, community members, and the mass media, including discussing intrinsic ethical issues such as whether gene transfer between species challenges the community’s concept of living organisms, and the ecological impacts of the genetically-modified organism on other animal species.
- Getting consent from the individuals and communities involved, including for the environmental and agricultural risks as well as the human risks of a trial, even though the exact cultural interpretation of the informed consent process may vary between countries.
- Making commitment to the local communities involved in the field trial such that they will be the first beneficiaries of more permanent use of a genetically-modified vector, if appropriate.
- Sharing information, technology, and data with all in order to benefit from global expertise and develop international consensus; and not letting intellectual property concerns become barriers to implementing public health measures using genetically-modified vectors.

Co-artemether is a fixed combination of two drugs, artemether and lumefantrine, which was developed in the 1990s by Novartis for the treatment of acute uncomplicated malaria. It is registered in developed countries as Riamet® and in disease-endemic countries as Coartem®. It is the first fixed combination of an artemisinin derivative and another antimalarial drug to be produced to international standards of good manufacturing practice. While Riamet® is priced by the normal commercial criteria and is thus unaffordable in the developing world, Coartem®, in a pioneering move, is being offered through WHO to the national malaria control programmes of developing countries by Novartis at cost.

Co-artemether is currently recommended to be given in two different dosage regimens:

- **A four-dose regimen** for partially immune patients, with four tablets given as a single dose at the time of initial diagnosis and then again after 8, 24 and 48 hours;
- **A six-dose regimen** for non-immune patients and for those who live in areas of multidrug-resistant malaria, with four tablets given as a single dose at the time of initial diagnosis, again after 8 hours, and then twice daily on each of the following 2 days.

However, both regimens are not registered in all countries and, during the discussions with WHO which led to the agreement for supply of Coartem® at cost, WHO indicated it would like to see the six-dose regimen as the sole global dosing regimen for co-artemether. In addition, WHO stressed the need in sub-Saharan Africa for the drug to be registered for treatment of infants as well as young children; at that time, it was only registered to treat individuals of 10 kg body weight and above.

Analysis of these two requirements quickly revealed the need for more R&D, especially for further assessment of the safety of the six-dose regimen of co-artemether in sub-Saharan African populations, and assessment of the safety and efficacy of the product in infants. WHO and Novartis senior managements agreed that this was best done in partnership, hence the establishment in 2001 of the Co-artemether Product Development Team (PDT), which includes representatives from Novartis, Roll Back Malaria (RBM) and TDR. The budget is mostly provided by Novartis, in return for guarantees about the ongoing supply of Coartem® at cost, though contributions have also been made by RBM and TDR.

The specific objective of the PDT is to obtain regulatory approval of the six-dose regimen of Coartem® for the treatment of acute uncomplicated malaria in patients down to 5 kg in body weight in all countries, mostly in sub-Saharan Africa, where only the four-dose regimen is currently registered. To facilitate this, permission
to extend existing Swiss regulatory approval of the six-dose regimen to include infants of 5-10 kg body weight will first be sought.

The design of the clinical study was challenging. For various reasons, a normal double-blind study would have been unethical and it was decided that an open label study would be done with the primary objective of assessing safety and the secondary objective of assessing efficacy. It was planned to enrol 300 male and non-menarche female patients of $\geq 5$ and $\leq 25$ kg body weight, with half of them in the $>5$-10 kg range. Three centres were used, one each in Kenya, Nigeria and Tanzania. Agreed enrolments were completed early in 2003.

The results were essentially the same in all three centres. The drug combination was well tolerated in all patient groups and cardiotoxicity was shown to not be a problem. A very high cure rate was achieved in all patient groups and an expert clinical report is now being prepared for regulatory purposes. Submission to Swissmedic, the drug regulatory authority in Switzerland, is planned for later this year. The Swiss submission will be followed by submissions to authorities in sub-Saharan Africa.

A debriefing with the PDT’s principal investigators will take place in October 2003 and will provide an opportunity for feedback. One issue has already emerged – the challenge of persuading infants to swallow antimalarial drugs! A positive response from Novartis is already on the table – a commitment to develop a paediatric formulation of co-artemether. The next challenge has also been laid down by WHO – what about pregnant women? Novartis have not said yes, but neither have they said no! Watch this space.

1 Principal Investigators: Michael Makanga, Kenya Medical Research Institute, Kilifi; Catherine Falade, University College Hospital, Ibadan; Zul Premji, Muhimbili University College of Health Science, Dar es Salaam.
An agreement signed between Aventis and WHO in May 2001 had clocked up a number of achievements by July 2003. Under the agreement, Aventis donates US$25 million over five years, including the drugs pentamidine, melarsoprol and eflornithine, to support WHO activities in management and control of African trypanosomiasis, and in research and development of drugs for this disease.

By July 2003, the WHO-Aventis Collaboration had:
- financed 31 active screening tours in which 200,000 people were screened
- financed reagents for diagnostic tests on 500,000 people in 15 countries
- financed equipment e.g. electric generators, centrifuges
- provided, via Médecins Sans Frontières (MSF), 183,295 vials of pentamidine for treating 26,200 patients in 16 different countries
- provided, via MSF, 227,403 vials of melarsoprol for treating 23,000 patients in 26 countries
- provided, via MSF, 92,500 vials of eflornithine for treating 10,000 patients in 17 countries.

Other achievements so far have included developing:
- activities (surveillance of drug resistance, implementation of research projects at field level) of the WHO Treatment and Drug Resistance Network in collaboration with TDR, Médecins Sans Frontières, the Drugs for Neglected Diseases Initiative, and many institutions in both developed and disease endemic countries;
- concerted vector control actions in collaboration with other UN agencies (International Atomic Energy Agency, the Food and Agriculture Organization) and the African Union;
- inter-country collaborations towards elimination by establishing sub-regional elimination programmes, standardized methods for screening, diagnosis and treatment, and training for heads of programmes and technicians;
- country/endemicity specific strategies to facilitate cost-effective and high-quality screening and treatment activities as well as sustainable surveillance.

In addition, national programmes for control of sleeping sickness in more than 15 countries have been revived and strengthened through ‘seed rehabilitation funding’ from the Aventis donation as well as through WHO organized screening which has leveraged funding from other sources (country governments, France).

Resurgence of sleeping sickness in the last 40 years followed cutbacks in vector control, surveillance and screening, and decreased access to drugs. Today, only an estimated 10% of those suffering from the disease receive proper treatment, yet the probability of cure is high if the disease is diagnosed and treated in its early stages.

TDR is working with the WHO Communicable Disease Control, Prevention and Eradication unit (W HO/CPE) and Aventis on technical aspects of ensuring sustainable drug manufacture at lower than current cost, with particular emphasis on eflornithine. This drug, which was first registered for treatment of late-stage African trypanosomiasis in 1990 by the United States Food and Drug Administration following its discovery in 1981 as an anti-trypanocidal agent by Cyrus Bacchi, Pace...
Following on from the registration of miltefosine (Impavido®) in India in the Spring of 2002 (see TDRnews no. 68), a phase IV clinical trial was launched. Currently almost 1200 visceral leishmaniasis (VL) patients are included in the trial, most of them from Bihar State, India, with others from Terai, Nepal. The results of the phase IV study will be of great importance for undertaking a large-scale evaluation of the levels of patient compliance and adverse events; the phase IV data will be analysed during a consultative meeting to be jointly organized by the ministries of health of India and Nepal, the WHO Regional Office for South-East Asia, and TDR and WHO in Geneva.

Based on results of the trial, the Ministry of Health of India may decide whether to recommend miltefosine as first-line drug for VL in India. The need to find a substitute for the pentavalent antimonials currently used as first-line treatment for VL is urgent since a growing proportion of patients (62% in 2002) no longer adequately respond to these drugs.

The Indian authorities are committed to a plan for elimination of visceral leishmaniasis. A window of opportunity now exists as a result of recent and substantial improvements in the tools available for VL control and prevention, including more field-applicable diagnostic tests, an oral drug (miltefosine), and long-lasting insecticide impregnated nets, which make the elimination goal more reachable than ever. Within an integrated control programme, these new tools should allow a drastic reduction in transmission, particularly in anthropoponic foci such as those of the Indian subcontinent (Bangladesh, India, Nepal) and East Africa (Ethiopia, Kenya, Sudan).

A quick assessment of the major anthropoponic foci to evaluate the devastating impact of VL on local populations and the exact burden in terms of morbidity and mortality is needed. Based on the real needs and corresponding costs (economic projections), WHO, together with several other institutions, could initiate a global public-private partnership for large-scale control of VL in these foci.

Simultaneously, TDR and Zentaris, the company which produces miltefosine, are looking towards registration of the drug in countries of East Africa and Europe, and in Brazil. To facilitate registration, studies on the efficacy of miltefosine will begin in these countries as soon as possible.

Other studies will look at the efficacy of miltefosine in treatment of post kala azar dermal leishmaniasis, and in HIV-positive patients and in children.

In order to prevent resistance, possible combination therapies are undergoing laboratory evaluation prior to their potential assessment in the field.

Finally, studies on more cost-effective drug delivery strategies, to secure full access of the most affected populations to miltefosine, are soon to begin in India.

Visceral leishmaniasis patient under miltefosine treatment: a phase IV trial is ongoing.

**UPDATE**

**Miltefosine: what next?**

University, New York, USA, in collaboration with TDR, is now registered in 12 disease endemic countries. WHO has been working with Hoechst Marion Roussel and now Aventis on sustained and affordable availability of eflornithine.

TDR has undertaken to identify and register a safe and efficacious oral regimen of eflornithine. The drug is currently approved only as an intravenous treatment, which limits its use on a large scale. Oral formulations would be preferred, but have lower bioavailability (of only 50%) than intravenous formulations and hence result in higher relapse rates. Thus a Product Development Team in TDR is clinically evaluating the safety and efficacy of oral eflornithine; the first study in Côte d’Ivoire has been completed. These development activities are supported by the Aventis donation.

**CONTACTS**

Dr Philippe Desjeux
Leishmaniasis research Coordinator, TDR
Tel: (+41) 22 791 3870
E-mail: desjeuxp@who.int

Dr Juntra Karbwang
Clinical Coordinator, Product Research and Development, TDR
Tel: (+41) 22 791 3867
Fax: (+41) 22 791 4854
E-mail: karbwangj@who.int
The Federal Republic of Germany is one of TDR’s major donor countries; it has a well established network of institutions specialized in tropical diseases and international health research. TDR is always exploring mechanisms for more and better collaboration with its donor countries, and a recent meeting in Berlin was aimed at fostering scientific and financial collaboration between German institutions and TDR.

The two-day symposium held at the new Gesellschaft für Technische Zusammenarbeit (GTZ) house in central Berlin was organized by GTZ (a German government-owned corporation for international cooperation), the German Society for Tropical Medicine and International Health, and TDR. The symposium brought together about 40 scientists working in tropical diseases research at German public and private research institutions.

The tightly-scheduled agenda included presentations related to research on: African trypanosomiasis, leishmaniasis, and viral haemorrhagic fever – categorized by TDR in its strategy for 2000-2005 as emerging or uncontrolled diseases; tuberculosis, malaria, and schistosomiasis – categorized by TDR as diseases where a control strategy is available but the burden persists; and onchocerciasis – a disease with a proven, effective control strategy, falling disease burden, and planned elimination.

The research presented ranged from identification of drug-resistant pathogen genotypes and development of drugs and vaccines to non-medical measures for disease prevention and the impact of national or international conflicts on infectious disease prevalence.

Much of the work presented is being conducted in collaborations between academic institutions in Germany and institutions in disease-endemic countries. Two examples of successful TDR-initiated public-private partnerships with German companies were presented: the development of miltefosine for treatment of visceral leishmaniasis with Zentaris AG (application for marketing authorization was recently submitted in Germany), and the ongoing development of a diagnostic patch for onchocerciasis with Lohmann Therapie Systeme AG.

The symposium was co-sponsored by four German ministries: the Ministry for Foreign Affairs, the Ministry for Health and Social Security, the Ministry for Education and Research, and the Ministry for Economic Cooperation and Development. Each of these ministries is involved in promoting tropical diseases research conducted in Germany, in collaboration with scientists in Germany or in disease-endemic countries, through policy-setting and/or funding. One of the goals in co-sponsoring the symposium was to initiate discussions on what can and needs to be done by German funding agencies, researchers, and TDR to enhance the development of effective control tools and strategies for tropical diseases and ensure their successful implementation in disease-endemic countries.

Improved information flow between research groups was identified as a prerequisite for more efficient research activities. One tool was introduced at the meeting by GTZ: the Scientists for Health and Research for Development (SHARED) website, designed to allow researchers and research institutions to network and easily retrieve information on research projects, personnel, and funding. TDR is preparing a website link to its own database on previous and current TDR-funded projects.

The German ministries, GTZ, and TDR will evaluate how cooperation between them can improve access to funding for research, development, and disease control implementation projects performed in collaborations between institutions in Germany and disease-endemic countries. TDR plans to have similar meetings in other countries.

1 www.shared-global.org
Mr Guo Jiagang successfully defended his PhD thesis on 16 May 2003 at the Swiss Tropical Institute (STI), receiving the distinction of cum laude from the University of Basel. His thesis, “Schistosomiasis control in China: Strategy of control and rapid assessment of schistosomiasis risk by remote sensing (RS) and geographic information systems (GIS)”, described the application of a compound model to identify snail habitats and determine high-risk areas for schistosomiasis transmission. The results, validated through ground-based snail surveys, showed that prediction has the same accuracy as surveying but at a significantly lower cost. This method will now be integrated into the Chinese schistosomiasis control programme particularly in monitoring the Three Gorges reservoir area where snail habitats will likely develop.

Dr Guo, head of the schistosomiasis programme at the China Center for Disease Control (CDC), China’s premiere research institute, joins another former TDR trainee, Dr Zhou Xiao-Nong, CDC Deputy-Director, who also completed his doctoral studies and subsequent research in the application of RS/GIS for schistosomiasis control.

Dr Guo’s training at the STI continues a long-standing collaboration between TDR, STI director Professor Marcel Tanner, and the schistosomiasis research and control programmes in China. Of interest, during his training Guo spent periods of time with other TDR collaborators including Professor Don McManus, Queensland Institute of Medical Research, Australia; Byron Wood and Louisa Beck of NASA’s Center for Health Applications of Aerospace Related Technologies; and his Chinese supervisors Professor Chen Minggang, CDC, and Professor Yuan Hong Chang, Fudan University. In effect, Guo’s training took place on four continents – not a common occurrence.

The use of remote sensing and geographic information systems for schistosomiasis control in China is well developed. In addition to Guo and Zhou’s work, Ms Yang Guojing, Jiangsu Institute of Parasitic Diseases, is currently registered at STI for a PhD in RS/GIS for schistosomiasis control with an emphasis on advanced spatial statistics, further moving forward this important tool for disease control. Another former trainee, Dr Luo Dapeng, applied similar approaches for malaria prediction in Yunnan Province, the only remaining province in China with significant transmission of Plasmodium falciparum.

These scientists and their collaborators are contributing their knowledge and experience to the Regional Network for Research, Surveillance and Control of Asian Schistosomiasis, (RNAS), a multi-country partnership between China, Philippines, Laos, Cambodia and Indonesia supported by collaborators from Australia, Denmark, Sweden, USA, Japan, Switzerland and Germany in addition to TDR and the WHO Regional Office for the Western Pacific. During the next meeting of RNAS, in Laos December 2003, the applications of RS/GIS to disease control will be the topic of scientific discussion.

Mr Guo (right) with STI Director Professor Marcel Tanner.
New awards

Research in Pathogenesis and Applied Genomics

The TDR Committee on Pathogenesis and Applied Genomics (PAG) met in Bangkok, Thailand, in September 2002, to deliberate and recommend projects for funding by TDR. The projects listed below were selected from among a large number of applications received from investigators worldwide.

New grants

The following projects were funded for one year in the first instance, and will be funded for an additional year if sufficient progress is made in the first year toward reaching the scientific objectives, and if sufficient funds are available.

- **A20369** OSCAR EDUARDO, Campetella Universidade N acional de General San Martin, Instituto de Investigaciones Biotecnologicas, San Matin, Argentina. Involvement of the transsilidase from Trypanosoma cruzi in the pathogenesis of Chagas Disease (budget: US$ 30 000)

- **A20264** CHRISTINE CLAYTON, Universitat Heidelberg, Zentrum fur Molekuleare Biologie, Germany. Arsenical resistance in trypanosomes (budget: US$ 22 000)

- **A20342** PATRICK C A DE BAETSELIER, Vrije Universiteit Brussel, Instituut voor Moleculaire, Belgium. Molecular characterization of macrophage activation states elicited during parasitic infections: the trypanosome model (budget: US$ 35 000)

- **A20380** ALAIN DESSEIN, IN SEKM, France. Immunogenetics of Schistosoma japonicum infection in China (budget: US$ 30 200)

- **A20393** WALDEREZ ORNELAS DUTRA, Universidade Federal de Minas Gerais, Instituto de Ciencias Biologicas, Belo Horizonte, Brazil. CD8+ T cells in human chagasic immunopathology. functional studies of CD28+ and CD28- populations (budget: US$ 32 000)

- **A20352** ANA MARIA C. FARIA, Universidade Federal de Minas Gerais, Departamento de Bioquimica e Imunologia, Belo Horizonte, Brazil. Aging and immunoregulation in chronic human schistosomiasis (budget: US$ 34 200)

- **A20305** ALBERTO CARLO S. FRASCH, Universidad Nacional de General San Martin, Instituto de Investigaciones Biotecnologicas, Buenos Aires, Argentina. RNA-binding proteins involved in post-transcriptional regulation of gene expression in trypanosomes (budget: US$ 35 000)

- **A20392** KENNETH J. GOLOBO, Universidade Federal de Minas Gerais, Instituto de Ciencias Biologicas, Belo Horizonte, Brazil. Determination of functional activity and TCR usage of CD4+CD8-T cells in human cutaneous leishmaniasis (budget: US$ 32 000)

- **A20382** GEORGES E. R. GRAU, Universite du la Mediterrane, Marseille, France. ABC A1 gene and cerebral malaria: role in the pathogenesis and relevance in genetic susceptibility (budget: US$ 35 000)

- **A20320** GARETH WYN GRIFFITHS, European Molecular Biology Laboratory, Heidelberg, Germany. Analysis and manipulation of mycobacterial phagosomal signalling networks (budget: US$ 35 000)

- **A20289** EMANUEL HAN MAN, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia. Characterization of a mucin-like proteophosphoglycan, a potential Leishmania major amastigote virulence factor (budget: US$ 35 000)

- **A20294** NADIRA D. KARUNAW EERA, University of Colombo, Faculty of Medicine, Dept of Parasitology, Colombo, Sri Lanka. Chemical and antigenic characterisation of bioactive parasite moieties involved in paroxysms of P. wax malaria (budget: US$ 35 000)

- **A20317** KRISTER KRISTENSSON, Karolinska Institute, Division of Neurodegenerative Disease Research, Stockholm, Sweden. The role of chemokines and chemokine receptors in trafficking of Trypanosoma brucei across the blood-brain barrier (budget: US$ 35 000)

- **A20310** MARCELA DE FREITAS, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil. Immunopathogenesis mediated by apoptosis in vivo blockade of cell death in experimental Chagas disease (budget: US$ 35 000)

- **A20349** DANI EL MASIGA, International Centre for Insect Physiology and Ecology (ICIPE), N arobi, Kenya. Expression of surface genes of T.b. rhodesiense in insect larvae for diagnosis and disease staging (budget: US$ 29 000)

- **A20379** FRANCINE N TOUMI, Hopital Albert Schweitzer Laboratoires de Recherches, Lambarene, Gabon. Polymorphism of FCyRIalpha receptor (CD32) and IgG2-mediated phagocytosis in children with sickle cell trait in Gabon (budget: US$ 10 000)

- **A20399** GUILLERME CORREA DE OLIVEIRA, Centro de Pesquisas Rene Rachou, Fundacao Oswaldo Cruz, Belo Horizonte, Brazil. Characterization of the genetic structure of Schistosoma mansoni populations in endemic areas with microsatellites (budget: US$ 13 000)

- **A20357** AHMED OSMAN EGIZA, State University of New York at Buffalo, Department of Microbiology, N ew York, USA. Mechanistic studies on male-induced female-specific gene expression in Schistosoma mansoni (budget: US$ 35 000)

- **A20285** ALEJANDRO GABRIEL SCHIJMAN, Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, Buenos Aires, Argentina. Role of the parasitic load and its genetic diversity in the incidence of congenital transmission of Chagas disease (budget: US$ 18 225)

- **A10337** MAURO TEIXEIRA, Instituto de Ciencias Biologicas, Departamento de Bioquimica e Imunologia, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil. Evaluation of the pathophysiological role of MIP-1 in human schistosomiasis. A biomarker of worse prognosis (budget: US$ 35 000)
New South-South collaboration grants

The following multicentre projects were funded for one year in the first instance, and will be funded for an additional year if sufficient progress is made in the first year toward reaching the scientific objectives, and if sufficient funds are available.

- **A20363** MARIA N. JORGE LEVIN, Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular (INGEBI), Buenos Aires, Argentina. Specific molecular mechanisms as targets of novel anti-parasitic drugs (budget: US$ 70 000)

- **A20308** HELMI MARDASSI, Institut Pasteur de Tunis, Tunisia. Comparative genomics and differential expression analysis of the PE-PGRS proteins of Mycobacterium tuberculosis (budget: US$ 50 000)

Renewed grants

Grants for the following projects, originally funded in 2001, were renewed for a further year following successful progress made towards meeting the objectives during the first year.

- **A00521** LEN A ASLUND, Department of Genetics and Pathology, Uppsala, Sweden. Functional analysis of Trypanosoma cruzi: expression profiling on cDNA microarrays of gene from genome projects (budget: US$ 5000)

- **A10422** ROBERT DOCAMPO, University of Illinois College of Veterinary Medicine, USA. Polyphosphate metabolism in Trypanosoma brucei and Leishmania major (budget: US$ 35 000)

- **A10329** ANA RODRIGUEZ, IB La Jolla, California, USA. Kinin receptors and their role in Plasmodium falciparum (budget: US$ 35 000)

- **A10328** MARY G WO-SHU LEE, New York University School of Medicine, Department of Pathology, New York, USA. Functional Genomics of African trypanosomes - proteins trafficking in Trypanosoma brucei (budget: US$ 35 000)

- **A10306** ROBERT LAZARUS MO D LIN, University of California School of Medicine, Division of Dermatology, USA. Analysis of Genomic toll-like receptors in mycobacterial infection by functional genomics (budget: US$ 35 000)

- **990559** MAOWIA MOHAMED MUKHTAR, University of Khartoum, Institute of Endemic Disease, Dept of Molecular Biology, Khartoum, Sudan. Parasite determinants associated with post kala azar dermal leishmaniasis (PKDL) (budget: US$ 15 000)

- **A10350** INGRID MÜLLER, Imperial College of Science, Technology and Medicine, Department of Immunology, London, UK. Influence of toll like receptor (TLR) activation on the innate immune response to Leishmania major (budget: US$ 35 000)

- **A00525** ERIC PEARLMAN, Case Western Reserve University, Division of Geographic Medicine, Ohio, USA. Pathogenesis of onchocercal skin diseases (budget: US$ 30 000)

- **A10308** ANA RODRIGUEZ, New York University School of Medicine, Department of Pathology, New York, USA. Role of dendritic cells in malaria-induced immunosuppression (budget: US$ 35 000)

- **A10325** EUZEN IR NUN ES SARN O, Fundacao Oswaldo Cruz, Laboratorio de Hanseniae, Rio de Janeiro, Brazil. Exploitation of novel genetic and molecular approaches to understand nerve damage in leprosy (budget: US$ 34 000)

- **A10341** JULIO SCHARFSTEIN, Univ Federal de Rio de Janeiro, Instituto de Biofisica Carlos, Rio de Janeiro, Brazil. Activation of kinin receptors by Trypanosoma cruzi: a modulatory role for kininase in cardiovascular pathology (budget: US$ 25 000)

- **A10440** W RACHART, Siripaborn Arpong, Mahidol University, Faculty of Science, Department of Biochemistry, Bangkok, Thailand. P. falciparum dihydroprotoaterase synthase (pfDHPS): optimization of enzyme expression in E. coli and development of a bacterial screening for new inhibitors (budget: US$ 35 000)

- **A10318** H.G. STO t, University of Nijmegen, Department of Molecular Biology, Nijmegen, Netherlands. Proteomic approach to identify novel drug targets and vaccine candidates in the human malaria parasite (budget: US$ 35 000)

- **A10332** THEODORE F. TARASC H I, Thomas Jefferson University Department of Pathology, Anatomy and Cell Biology, Philadelphia, USA. Evaluation of role of the Plasmodium falciparum AP endonuclease, pfApel, in DNA base excision repair (budget: US$ 35 000)

- **A10449** MARIE-TERESA TELLEZINO N, Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, (INGEBI-CONICET), Buenos Aires, Argentina. Biological functions and role in cell division of TzCRK1 and TzCRK3 and their associated cyclins (budget: US$ 19 000)

- **A10342** ESTHER VON STebuT, Johannes Gutenberg University Mainz, Department of Dermatology, Mainz, Germany. Vaccination against experimental cutaneous leishmaniasis with protein antigen-transduced dendritic cells (budget: US$ 35 000)
New research awards

Research in Applied Genomics to Drugs and Diagnostics

New grants

The following projects were funded for one year in the first instance, and will be funded for an additional year if sufficient progress is made in the first year towards reaching the scientific objectives, and if sufficient funds are available.

- **A20527 STEWART THOMAS, Institut Pasteur, Unite Genetique Moléculaire Bacterienne, France.** Post-genomic leprosy diagnostics (budget: US$ 33,500)

- **A20563 PIERRE DRIULHE, Institut Pasteur, Laboratoire de Parasitologie Biomedicale, France.** The malaria hepatic stage transcriptome: A seam for new drug and vaccine targets (budget: US$ 25,000)

- **A20519 LIAM GOOD, Karolinska Institute, Center for Genomics and Bioinformatics, Sweden.** Peptide-mediated delivery of antisense agents into mycobacteria for antimicrobial target identification (budget: US$ 27,000)

- **A20507 KASTURI HALDAR, Northwestern University Medical School, Department of Pathology, Chicago, USA.** A microarray approach to identify sphingolipid biosynthetic enzymes as targets for malaria chemotherapy (budget: US$ 22,000)

- **A20509 MARIAN E MARTIN DE ARAUJO STEFANI, Federal University of Goias, Instituto de Patologia Tropical e Saude Publica.** Characterization of novel M. leprae secreted proteins and potential diagnostic application for early leprosy infection (budget: US$ 21,000)

- **A20521 STEPHEN ANDREW WARD, Liverpool School of Tropical Medicine, UK.** A proteomic definition of aminoquinoline action and resistance: the search for new chemotherapeutic targets (budget: US$ 10,000)

Research in Molecular Entomology

The TDR Committee on Molecular Entomology (BCV) met in Bangkok, Thailand, in September 2002, to deliberate and recommend projects for funding by TDR. The projects listed below were selected from among a large number of applications received from investigators worldwide.

New grants

The following projects were funded for one year in the first instance, and will be funded for an additional year if sufficient progress is made in the first year towards reaching the scientific objectives, and if sufficient funds are available.

- **A20493 BARRY BEATY, Colorado State University, USA.** The Biology of Disease Vectors Course 2003 (budget: US$ 50,000)

- **A20353 GEORGE DIMITROLOUS, Imperial College of Science, Technology and Medicine, London, UK.** Genome expression analysis of mosquito salivary gland function and characterization of specific promoters (budget: US$ 40,624)

- **A20290 ABD ULLAYE DIO P, Institut de Recherche pour le Développement (ex-ORSTOM), Dakar, Sénégal.** Détermination du rôle d’peptides antifongiques dans la résistance du cycle sporogonique de Plasmodium falciparum chez Anopheles gambiae s.s. (budget: US$ 5,000)

- **A20259 Q I GAO, Jiangsu Institute of Parasitic Diseases, Wuxi, Jiangsu, China.** Identification of Anopheles sinensis and Anopheles anthropophagus and their role in malaria transmission in China (budget: US$ 27,500)

- **A20330 LIZETTE KOEKEMOER, National Health Laboratory Services, Johannesburg, South Africa.** The role of monooxygenases in insecticide resistant Anopheles funestus Giles (budget: US$ 37,800)

- **A20314 OSAVELDO MARINOTTI, University of California at Irvine, Irvine, CA, USA.** Microarray analysis of gene expression in the fat body of Anopheles gambiae mosquitoes (budget: US$ 25,379)

- **A20315 RO SEMARY SANG, Kenya Medical Research Institute, Nairobi, Kenya.** A comparative study of populations of Aedes aegypti in dengue endemic and non-endemic areas of Kenya (budget: US$38,950)

Renewed grants

Grants for the following projects, originally funded in 2001, were renewed for a further year following successful progress towards meeting the objectives during the first year.

- **A10390 MARTIN AKO GBETO, Centre de Recherche Entomologique de Cotonou, Bénin.** Etude des relations et des divergences écologiques des formes moléculaires et chromosomiques d’Anopheles gambiae s.s. (budget: US$ 13,530)

- **A10435 ALESSANDRA DELLA TORE, Università di Roma “La Sapienza”, Italy.** Molecular and cytological characterization of Anopheles gambiae molecular forms and evaluation of their role as malaria vectors (budget: US$ 38,000)

- **A00401 FOTIS KAFATO, European Molecular Biology Laboratory, Germany.** A method for inducible in vitro dsRNA inhibition in anophelines. Application for the study of a serpin gene complex (budget: US$ 37,000)

- **A00351 CHRISTOS LOUIS, Institute of Molecular Biology and Biotechnology, Greece.** Analysis of the ookinete invasion of Anopheles and subsequent transformation to oocyst using mRNA microarrays (budget: US$ 33,600)

- **A00914 CHRISTOS LOUIS, Institute of Molecular Biology and Biotechnology, Greece.** AnaDB, the Anopheles database (budget: US$ 51,000)

- **A00398 CHRISTIAN MATHIOT, Institut Pasteur de Dakar, Sénégal.** Rôle d’Aedes aegypti dans l’interaction des cycles selvatique et épidémique de dengue 2: aspects génétiques et moléculaires (budget: US$ 29,463)

- **990501 ROBERT SIN DEN, Imperial College of Science, Technology and Medicine, UK.** N atral role of xanthurenic acid in regulation of malarial gametogenesis: a logical basis for novel chemotherapy? (budget: US$ 40,800)

- **A00407 JO SEPH VINTZ, University of Texas Medical Branch, USA.** Expression of a Plasmodium falci paraum chitinase-neutralizing single chain antibody
within the Anopheles gambiae midgut (budget: US$ 33 500)

- **A10429** GUYIUN YAN, State University of New York, USA. Assessing the spread rate of introduced genes in Anopheles gambiae (budget: US$ 40 000)

- **A10402** LAURENCE ZWIEBEL, Vanderbilt University, USA. Isolation and characterization of odorant receptor genes from Aedes aegypti (budget: US$ 40 000)

- **A20536** DANIEL AGRANOFF, St George’s Hospital Medical School, London, UK. Diagnostic system for TB by identification of proteomic signatures in serum (budget: US$ 50 453)

- **A20551** HEIDI ALBERT, Biotech Laboratories Limited, Cape Town, South Africa. A rapid manual test for rifampicin resistance directly from sputum using phage amplification technology (budget: US$ 60 300)

- **A20554** JUDITH MYRIAM BADILLA-DEL VALLE, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico. Parsimonious use of established and novel test to diagnose TB (budget: US$ 30 000)


- **A20529** GERHARD JOHN MULLER, Institute of Medical Physics and Laser Medec., Berlin, Germany. Laser-enabled mass spectrometric TB diagnostics (LMtBD) (budget: US$ 100 000)

- **A20562** MIKHAIL VLADIMIRSKY, Moscow Medical Academy, Institute Sechenovs, Phthisiopulmonology Res., Moscow, Russia. Application of immunomagnetic separation of mycobacteria from sputum samples for improved fluorescent microscopy (budget: US$ 20 000)

- **A20548** JOHN W ELCH, State University of New York at Albany, New York, USA. Single chip serodiagnosticstic for M. tuberculosis infection based on NEMS (Nanoelectromechanical Systems) (budget: US$ 84 470)

- **A20552** KARIN W ELDING, Statens Serum Institut, Copenhagen, Denmark. Combined antigens for specific serodiagnosis of M. tuberculosis (budget: US$ 80 000)

- **A20565** ANTHONY WOODMAN, Cranfield BioMedical Centre, Silsoe, UK. Artificial intelligence and gas-sensor arrays for the rapid detection of mycobacteria in cultures, sputum and breath (budget: US$ 69 970)

**Research in Tuberculosis Diagnostics**

**New grants**

The following grants were announced in October 2002

- **A20536** DANIEL AGRANOFF, St George’s Hospital Medical School, London, UK. Diagnostic system for TB by identification of proteomic signatures in serum (budget: US$ 50 453)

- **A20551** HEIDI ALBERT, Biotech Laboratories Limited, Cape Town, South Africa. A rapid manual test for rifampicin resistance directly from sputum using phage amplification technology (budget: US$ 60 300)

- **A20554** JUDITH MYRIAM BADILLA-DEL VALLE, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico. Parsimonious use of established and novel test to diagnose TB (budget: US$ 30 000)


- **A20529** GERHARD JOHN MULLER, Institute of Medical Physics and Laser Medec., Berlin, Germany. Laser-enabled mass spectrometric TB diagnostics (LMtBD) (budget: US$ 100 000)

- **A20562** MIKHAIL VLADIMIRSKY, Moscow Medical Academy, Institute Sechenovs, Phthisiopulmonology Res., Moscow, Russia. Application of immunomagnetic separation of mycobacteria from sputum samples for improved fluorescent microscopy (budget: US$ 20 000)

**New grants**

The following projects will be funded for one year in the first instance. Funding for a second year will be considered if sufficient progress is made in the first year towards reaching the scientific objectives, and if sufficient funds are available.

- **A20536** DANIEL AGRANOFF, St George’s Hospital Medical School, London, UK. Diagnostic system for TB by identification of proteomic signatures in serum (budget: US$ 50 453)

- **A20551** HEIDI ALBERT, Biotech Laboratories Limited, Cape Town, South Africa. A rapid manual test for rifampicin resistance directly from sputum using phage amplification technology (budget: US$ 60 300)

- **A20554** JUDITH MYRIAM BADILLA-DEL VALLE, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico. Parsimonious use of established and novel test to diagnose TB (budget: US$ 30 000)


- **A20529** GERHARD JOHN MULLER, Institute of Medical Physics and Laser Medec., Berlin, Germany. Laser-enabled mass spectrometric TB diagnostics (LMtBD) (budget: US$ 100 000)

- **A20562** MIKHAIL VLADIMIRSKY, Moscow Medical Academy, Institute Sechenovs, Phthisiopulmonology Res., Moscow, Russia. Application of immunomagnetic separation of mycobacteria from sputum samples for improved fluorescent microscopy (budget: US$ 20 000)

- **A20548** JOHN W ELCH, State University of New York at Albany, New York, USA. Single chip serodiagnosticstic for M. tuberculosis infection based on NEMS (Nanoelectromechanical Systems) (budget: US$ 84 470)

- **A20552** KARIN W ELDING, Statens Serum Institut, Copenhagen, Denmark. Combined antigens for specific serodiagnosis of M. tuberculosis (budget: US$ 80 000)

- **A20565** ANTHONY WOODMAN, Cranfield BioMedical Centre, Silsoe, UK. Artificial intelligence and gas-sensor arrays for the rapid detection of mycobacteria in cultures, sputum and breath (budget: US$ 69 970)

**Capability Strengthening Grants for Malaria Research in Africa (MIM/TDR)**

The MIM/TDR Task Force on Malaria Research Capability Strengthening met in Maputo, Mozambique, in March 2003, to deliberate and recommend projects for funding. The projects listed below were selected from among a large number of applications received from investigators in Africa.

**New grants**

The following projects will be funded for one year in the first instance. Funding for a second year will be considered if sufficient progress is made in the first year towards reaching the scientific objectives, and if sufficient funds are available.

- **A20536** DANIEL AGRANOFF, St George’s Hospital Medical School, London, UK. Diagnostic system for TB by identification of proteomic signatures in serum (budget: US$ 50 453)

- **A20551** HEIDI ALBERT, Biotech Laboratories Limited, Cape Town, South Africa. A rapid manual test for rifampicin resistance directly from sputum using phage amplification technology (budget: US$ 60 300)

- **A20554** JUDITH MYRIAM BADILLA-DEL VALLE, Instituto Nacional de Ciencias Medicas y Nutricion, Mexico City, Mexico. Parsimonious use of established and novel test to diagnose TB (budget: US$ 30 000)


- **A20529** GERHARD JOHN MULLER, Institute of Medical Physics and Laser Medec., Berlin, Germany. Laser-enabled mass spectrometric TB diagnostics (LMtBD) (budget: US$ 100 000)

- **A20562** MIKHAIL VLADIMIRSKY, Moscow Medical Academy, Institute Sechenovs, Phthisiopulmonology Res., Moscow, Russia. Application of immunomagnetic separation of mycobacteria from sputum samples for improved fluorescent microscopy (budget: US$ 20 000)
Research Strengthening Grants

Renewed capacity strengthening programme grants

- A00883 MARGARET N GOZI AGHAJI, University of Nigeria, Teaching Hospital, Nigeria. Evaluation of multi-drug resistance and second line treatment in TB cases in Primary Health Care Zone A, Nigeria (US$ 3000)

- A10493 ALI MOHAMED ASSABRI, Sana’a University, Faculty of Medicine & Health Sciences, Yemen. The epidemiology of severe malaria in children in Yemen (US$ 50 000)

- A00894 W EBER CHELI BATISTA, Centro de Pesquisas em Medicina Tropical, Brazil. Isolation & molecular typing of dengue virus circulating in urban & rural areas of Rondonia, Brazil (US$ 50 000)

- A11037 ADITYA PRASAD DASH, Centre for Research in Medical Entomology (ICMR), India. Community based dengue vector control under health system in one district (south India) and transfer of technology (US$ 35 000)

- A00786 PATTAMAPO RN KITAYAPONG, Mahidol University, Faculty of Science, Thailand. Suppression of dengue transmission by focal vector control (US$ 24 380)

- A10917 ABDOULAYE DJIMDE, University of Buea, Cameroon. Malaria pilot centre in rural setting of Mount Cameroon through multi-disciplinary approach studies (US$ 4 500)

- A00903 THELMA E. TUPASI, Tropical Disease Foundation Inc., Philippines. Community-based DOTS-plus programme for management of MDR-TB: pilot project, Makati (US$ 5 000)

- A10935 SAYERA BANU, International Centre for Diarrhoeal Disease Research, Bangladesh. Study on molecular epidemiology of tuberculosis and molecular mechanism of drug resistance of Mycobacterium tuberculosis (US$ 26 843)

- 990999 JEAN BICKII, Institut de Recherches Médicales et d’Etudes des Plantes Médicinales, Cameroon. Ethnobotanical studies and in vitro evaluation of activities of plants used against P. falciparum malaria (US$ 16 122)

- A10924 LUZIA HELENA CARVALHO, Fundação Oswaldo Cruz, Centro de Pesquisas René Rachou, Brazil. Molecular & immunological characterization of P. falciparum Duffy binding protein in endemic areas of the Brazilian Amazon (US$ 20 000)

- A10828 ALASSANE DICKO, Université du Mali, Faculté de Médecine, de Pharmacie et d’O donto-Stomatologie, Mali. Evaluation of malaria transmission target strategy based on periodic treatment with S-F vs early case management (US$ 18 200)

- A00847 ABDOULAYE DJIMDE, Université du Mali, Faculté de Médecine, de Pharmacie et d’O donto-Stomatologie, Mali. Toward a molecular tool for monitoring sulfadoxine-pyrimethamine (SP) resistance in Mali (US$ 2 500)

- A10830 DANIEL DODO, Noguchi Memorial Institute for Medical Research, Ghana. The role of cellular and humoral responses against the glutamate rich protein (GLURP) in malaria immunity (US$ 20 000)

- A10391 FANTAPPIE, Universidad Federal do Rio de Janeiro, Brazil. Cloning and functional characterization of high mobility group (HMG) proteins from Schistosoma mansoni (US$ 19 600)

- A10938 BEN ADU GYAN, Noguchi Memorial Institute for Medical Research, Ghana. Haptoglobin polymorphism, immune function and malaria severity (US$ 19 200)

- A10804 LE THANH HOA, Institute of Biotechnology (IBT), Viet Nam. Diversity in mitochondrial genomes of Asian & Indian Schistosoma species for evolutionary and genetic studies (US$ 19 406)

- A00751 ADITYA PRASAD, Chiang Mai University, Research Institute for Health Sciences, Thailand. Factors involved in development & lifespan of memory T cells in immunity to blood stage malaria (US$ 19 406)

- A10825 WANDEE YINDEE-YO UN GYE O, National Center for Genetic Engineering and Biotechnology, National Science and Technology Agency, Thailand. Identification of essential genes of Mycobacterium tuberculosis by antisense RNA (US$ 20 000)

New grants: R&D capacity in least developed countries

- A20785 LAURA ARCO S, Pontificia Universidad Catolica del Ecuador, Ecuador. Institutional capability strengthening in tropical disease research and training at Catholic University, Quito, Ecuador (US$ 53 300)

- A20766 VINO D JO SHI, Desert Medicine Research Centre, India. Studies on dengue and dengue haemorrhagic fever in Rajasthan, India (US$ 49 468)

- A20789 MATHIEU N'DOUNGA, Centre d’Etudes sur les Ressources Végétales, Congo. Chimiiorésistance de Plasmodium falciparum and alternatives thérapeutiques du paludisme non compliqué au Congo-Brazzaville (US$ 65 700)

- A20769 RAFAETRO HERINTSOA, Institut Malagache de Recherches Appliquées - Fondation Ratsimamanga, Madagascar. In vitro & in vivo antiplasmodial studies of compounds isolated from Madagascar & African antimalarial plants (US$ 49 000)
Re-entry grants

- **A20740** LAILA ABUBAKAR, University of Nairobi, Department of Biochemistry, Kenya. Functional genomics of tsetse-trypanosome interactions (US$ 18 100)

- **A20728** GIASUDDIN AHSAN, Ministry of Health & Family Welfare, In-Service Training Dept., Directorate General of Health Services, Bangladesh. Gender sensitive intervention study on tuberculosis control in the rural community of Bangladesh (US$ 18 598)

- **A20754** PEDRO EDUARDO ALMEIDA DA SILVA, Universidade Federal do Rio Grande, Brazil. Characterization of drug-efflux as potential mechanism of resistance to chemotherapeutic agents in M. tuberculosis (US$ 18 474)

- **A20741** RONALDO DA SILVA M. BORGES, Federal University of Rio de Janeiro, Instituto de Biofisica Carlos Chagas Filho, Brazil. Determination of the three-dimensional structure of dengue virus fusion peptide by nuclear magnetic resonance (US$ 20 000)

- **A20726** ANGELA ISABEL CALDERON, Universidad de Panama, School of Pharmacy, CIFLORPAN, Panama. Discovery of natural products against tropical diseases from Panamanian biodiversity (US$ 20 000)

- **A20743** ELWA LEED ELAMIN, University of Khartoum, Institute of Endemic Diseases, Sudan. Biotechnological characterization of Sudanese Leishmania isolates (US$ 20 000)

- **A20725** DENISE GOLGHER, Federal University of Minas Gerais, Department of Biochemistry and Immunology, Brazil. Role of regulatory T cells in the control of inflammatory process and immunopathology elicited by T. cruzi (US$ 20 000)

- **A20723** THEWARACH LAHA, Khon Kaen University, Faculty of Medicine, Thailand. Mobile genetic elements from the genome of schistosomes (US$ 22 000)

- **A20697** ROSETTE MEGNEKOU, University of Yaounde I, Biotechnology Centre, Cameroon. Malaria in pregnant Cameroonian women: changes in levels of circulating immune cells, plasma cytokines & hormones (US$ 20 000)

- **A20791** LUCIANO AN DRADE MOREIRA, Centro de Pesquisas René Rachou, FIO CRUZ, Brazil. Expression of a foreign antiparasitic gene in transgenic anopheline mosquitoes (US$ 23 500)

- **A20727** CHRISTOPHE ANTONIO NKONDJIO, Organisation de Coordination pour la Lutte contre les Endémies en Afrique centrale (OCEAC), Cameroon. Biology and genetic structure of the malaria vector Anopheles moucheti in Central Africa (US$ 24 300)

- **A20725** ABULLA HASSAN SHARIF, Tropical Medicine Research Institute, Sudan. Rapid assessment of patterns of L. donovani infection in western Sudan: immune surveillance and application of GIS (US$ 19 000)

- **A20733** SODIOMON BIENVENU SIRIMA, Centre National de Lutte Contre le Paludisme (CNLP), Burkina Faso. Etude comparative de l’observance et de l’efficacité de trois schemas de prévention du paludisme pendant la grossesse, Boromo (US$ 15 500)

New project development grants

- **A20759** AFEWORK KASSU, Gondar College of Medical Sciences, Department of Microbiology, Ethiopia. Research towards formulation of sustainable schistosomiasis control strategies in Ethiopia (US$ 10 000)

- **A20786** ABULLA BINGHOUTH, Hadramout University for Science and Technology, Faculty of Medicine, Yemen. Impact of malaria on pregnancy (US$ 10 000)
Publications

- Ethical, legal and social issues of genetically modified disease vectors in public health
  (Social, Economic and Behavioural Research, Special Topics No. 1, TDR/STR/SEB/ST/03.1).

  This monograph is for anyone planning to use genetically-modified organisms in the environment for public health purposes. It introduces the ethical, legal and social issues involved in assessing the environmental and human health concerns of such activities (see page 9).

- Research capacity building in developing countries: investing in health and development
  (TDR/RCS/GEN/03.1).

  For many years, TDR has been helping to develop core leadership and research capacity in disease-endemic countries to enable researchers and institutions to be more responsive to their public health needs and to participate more effectively in the global research agenda. This document features some of the outstanding individuals and research institutes who/which have received TDR grants to strengthen research capacity.

- Méthodes qualitatives en recherche sociale sur les maladies tropicales. Rapport du matériel didactique
  (TDR/RCS/MQRS/02.1, available in French only).

  Le présent document aborde les méthodes de recherche sociale employées dans l’étude des maladies tropicales: Il introduit et expose brièvement des méthodes de recherche qualitative adaptées aux besoins des chercheurs dans le domaine de la santé en tenant compte d’un engagement dans la lutte contre les maladies tropicales et l’amélioration de la santé des populations dans les pays du Sud.

- Méthodes qualitatives en recherche sociale: eau et hygiène du milieu. Rapport de recherche
  (TDR/RCS/MQRS/02.2, available in French only).

  Ce n’est que récemment que l’importance des méthodes qualitatives pour l’étude de la réalité sociale a été prise en considération par les sciences sociales. Elles sont de la plus grande utilité dans: 1) l’étude des expériences, des perceptions et des attitudes de la population, 2) le domaine médical, la logique des acteurs, les perceptions et attitudes aussi bien des malades que des spécialistes.

- Research Capacity Strengthening Strategy 2002-2005
  (TDR/RCS/SP/02.1)

  This document sets out the new TDR strategy for research capacity strengthening, which aims to increase the involvement of scientists in developing disease-endemic countries in all stages of the R&D process.

- Guidelines for the evaluation of dengue vaccines in populations exposed to natural infection
  (TDR/IVR/DEN/02.1)

  These guidelines are intended to help public health officials make decisions about dengue vaccine trials in their countries.

- Four-drug fixed-dose combinations (4FDCs) compliant with the WHO model list of essential drugs.
  (TDR/TB/4FDC/02.1; WHO/CDS/TB/2002.299)

  This report discusses the current state of development of 4FDCs for treatment of tuberculosis, and makes recommendations in four areas: implementation in TB control; improving quality assurance and safety testing; facilitating registration; expanding the evidence base for use.

- Scientific Working Group report on African trypanosomiasis, 4-8 June, 2001
  (TDR/SWG/01)

  This report provides a review of the present epidemiological situation and actual control needs for African trypanosomiasis. It is expected to guide TDR and others interested in research on this disease and to provide data that can be used in advocacy to convince policymakers and donor agencies to place control of the disease higher on their agendas. The research priorities set out are closely linked to control needs and open to the opportunities that science and technology can provide. Recommendations are made in three broad areas: epidemiology, and disease surveillance and control; drug development and drug resistance; pathogenesis and applied genomics.
**Assessment of the safety of artemisinin compounds in pregnancy**

(WHO/CDS/MAU/2003.1094
WHO/RBM/TDR/Artemisinin/03.1)

This is a report of two informal consultations convened by WHO in 2002; it presents WHO's current position on use of artemisinin compounds during pregnancy. With the increasing amount of interest in artemisinin combinations and artemisinin compounds in general, more studies - preclinical and clinical - are being envisaged and have been undertaken, so it was time to re-evaluate existing data and policies on use of the compounds in pregnancy.

**Tropical disease research: Results portfolio no. 3**

(TDR Final Report Series 2001/02, document no. TDR/GEN/02.1)

A collection of final reports selected by independent scientific experts from TDR-supported research projects. Copies of results portfolios no. 1 (1998/99; TDR/GEN/00.1) and no. 2 (2000/01; TDR/GEN/01.2) still available.

**The Sexually Transmitted Diseases Diagnostics Initiative (SDI) report. Laboratory-based evaluation of rapid syphilis diagnostics: results from eight SDI sites**

(Diagnostics Evaluation Series no. 1, TDR/SDI/DE/03.1)

Evaluation of the performance and utility of simple rapid tests for sexually transmitted diseases in primary health care settings in developing countries is a priority for SDI. Over 20 rapid treponemal tests for the diagnosis of syphilis are commercially available but reliable information on their performance characteristics is limited; this report details the laboratory performance of six such tests, of which four were selected to undergo further evaluation in the field.

**Drugs against parasitic diseases: R&D methodologies and issues. Discoveries and drug development.**

Eds: Fairlamb A H, Ridley RG, Vial HJ

(TDR/PRD/03.1)

Available at:

This is a report of a meeting on drugs against parasitic diseases held in Montpellier, France, in 1999, the goal of which was better coordination and guidance for research and development of antiparasitic drugs. The 21 papers published in the report (and presented at the meeting) cover: economic and patent issues; discovery of novel targets for pharmacological intervention; compound acquisition and rationale for drug development; methods for screening drugs and evaluating pharmacological activity.

**Support groups for women with lymphatic filariasis in Haiti.**

Jeannine Coreil, Gladys Mayard, David Addiss

(Social, Economic and Behavioural Research, Report Series no. 2, TDR/STR/SEB/RP/03.1)

This monograph describes the implementation and evaluation of a self-help programme for women with lymphatic filariasis in Haiti, when the feasibility and impact of support group participation in this low-income filariasis-endemic community was assessed. The benefits of participation were evident in the areas of illness knowledge, home care practices, quality of life and illness symptoms. The results contribute to our understanding of how community resources can be utilized for the control of filariasis and other tropical diseases.

**The behavioural and social aspects of malaria and its control: an introduction and annotated bibliography.**

H. Kristian Heggenhougen, Veronica Hackenthal, Pramila Vivek

(Social, Economic and Behavioural Research, TDR/STR/SEB/VOL/03.1)

The intention of this monograph is to highlight the importance of sociocultural factors in malaria control and to make clear that the fight against malaria and other infectious diseases is inseparable from the striving for socioeconomic and political equity. The authors show that human behaviour is related to risk for malaria, and that such behaviour is influenced by a range of cultural and social factors which it is crucial to consider. The monograph provides a valuable social science starting point for designing and evaluating anti-malaria interventions.

**Neglected diseases: under-funded research and inadequate health interventions. Can we change this reality?**

Carlos M Morel,
EMBO reports, 2003, 4:S35-S38.
Steering Committee meetings

Research proposals and reports submitted to TDR are reviewed by the relevant committees. To guarantee review at a given meeting, your proposal should in general be received in Geneva two calendar months before the date of the meeting, or earlier in the case of Research Capacity Strengthening. Proposals received later than this may be reviewed at the following meeting of the relevant committee. When preparing your research proposal, it is important to bear in mind that TDR supports goal-oriented research and that your proposal should be consistent with the plans of the relevant committee. Therefore please study the priorities of the relevant steering committee before submitting your proposal and, if you are applying for the first time, please contact the relevant research manager in TDR with an outline of your proposed research before developing a full proposal.

### DEADLINES

#### BASIC AND STRATEGIC RESEARCH
- **Molecular Entomology**
  - Meeting date: 26-31 May 2004*
  - Deadline: 5 Mar 2004*
- **Pathogenesis and Applied Genomics**
  - Meeting date: 26-31 May 2004*
  - Deadline: 5 Mar 2004*
  - Working Group on Applied Genomics for Drugs and Diagnostics
  - Meeting date: 01-03 July 2004*
  - Deadline: 2 April 2004*
- **Strategic Social, Economic and Behavioural Research**
  - Meeting date: 26-31 May 2004*
  - Deadline: 5 Mar 2004*

#### PRODUCT RESEARCH AND DEVELOPMENT
- **Chemotherapy Portfolio Review**
  - Meeting date: March 2004*
  - Deadline: Dec 2003*
- **Vaccine Discovery Research**
  - Meeting date: May 2004*
  - Deadline: Feb 2004*
- **Diagnostics Research and Development**
  - Meeting date: Sept 2004*
  - Deadline: July 2004*

#### INTERVENTION DEVELOPMENT AND IMPLEMENTATION RESEARCH
- **Implementation Research**
  - Meeting date: 29 Jun-02 July 2004
  - Deadline: 14 May 2004
- **Proof of Principle**
  - Meeting date: 08-11 June 2004
  - Deadline: 30 Mar 2004

#### RESEARCH CAPACITY STRENGTHENING
- **Research Strengthening Group**
  - Meeting date: Feb 2005*
  - Deadline: Oct 2004*
  - Only pre-selected letters of intent are invited to submit full proposals by 31 Oct
- **Malaria Research Capacity Strengthening in Africa**
  - Meeting date: March 2004*
  - Deadline: 30 Nov 2003*
  - letters of intent
  - full proposals, progress reports and renewals requests

* tentative date

** Replaces Drug Discovery Research.

TDR will hold a Chemotherapy Portfolio Review Meeting in March, 2004, to review all projects in TDR that concern drug discovery and development. A call for Letters of Interest related to drug discovery and development will be made in December 2003.