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Keynote Articles

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www.who.int/tdr
Artesunate combinations are coming: partnership develops CDA

Three partners announced an agreement to develop a new combination treatment for malaria on 23 April 2004. The three partners — GlaxoSmithKline (GSK),1 Medicines for Malaria Venture (MMV),2 and WHO/TDR — will develop the three-drug combination of chlorproguanil-dapsone-artesunate (CDA).

The two-drug combination of chlorproguanil and dapsone, known as Lapdap, was approved last year by the UK Medicines and Healthcare Products Regulatory Agency (see TDRnews no. 70, October 2003). Since WHO strategy is to use new antimalarial drugs in combination with an artemisinin derivative in order to delay development of drug resistance, Lapdap is now being further developed in fixed-dose combination with artesunate for use in uncomplicated falciparum malaria.

“Partnership is essential to combine resources and expertise, and accelerate the process of providing safe, effective and affordable drugs. It is the best way to help ensure that a drug such as CDA gets to the people in need as quickly as possible”, explained Chris Hentschel, MMV’s Chief Executive Officer. The new treatment could be “an important development in the fight against malaria” commented Dr Nafo-Tisseyre, Director of the WHO Roll Back Malaria partnership. “Our hope is that it will prove useful in regions of Africa where resistance makes other antimalarials ineffective.”

Development of CDA was supported by an initial grant from the UK Department of International Development (DFID) to TDR, and is now receiving further significant funding through MMV. The product development team is chaired by Professor Peter Winstanley of the University of Liverpool. A broad network of clinical trial sites involving investigators from northern and southern institutions will be required to develop the drug, and a call for participation of sites is envisaged later this year, in preparation for phase 3 studies.

The agreement states that, if the development of CDA is successful as a result of this initiative, the therapy will be made available at preferential prices to the public sector in malaria endemic countries so as to maximize its availability to those in need. Currently phase 2 trials are ongoing at Malawi, if all targets are met, the drug should be ready for regulatory submission in 2006.

Following a series of TDR studies, several syphilis diagnostics are now included in the WHO Bulk Procurement scheme. This is in recognition of the vigour of the evaluation scheme developed by the Sexually Transmitted Diseases Diagnostics Initiative (SDI) in TDR, in which rapid tests are first evaluated at laboratory sites using well-characterized archived serum samples and the most promising then selected for further evaluation of performance and acceptability in field settings.

The decision to include rapid syphilis diagnostics in the bulk procurement scheme will be a tremendous boost to syphilis control programmes worldwide; the lack of effective tools for screening has been recognized as a major barrier to the prevention and control of this infection, especially in developing countries. The WHO Bulk Procurement scheme was originally set up for essential medicines, to enable countries and UN agencies to purchase medicines of assured quality at low prices.

The WHO estimates that, worldwide, 12 million new cases of syphilis occur every year. Since most infected individuals have no symptoms, diagnostic tests are needed to identify them. Syphilis is a major cause of adverse pregnancy outcome in developing countries; it can be transmitted to the fetus in utero resulting in stillbirth, preterm delivery, low birth weight and serious health problems in the infant, especially in the first year of life. Congenital syphilis is preventable if infected mothers are identified and treated appropriately by mid-second trimester Given the serious morbidity and mortality of congenital syphilis, antenatal screening is universally recommended; programmes are cost-effective even when the prevalence is low, and a number of countries are developing programmes for the elimination of congenital syphilis.

While excellent laboratory-based tests for syphilis do exist, they are often not available or accessible in areas of high disease burden; and although simple rapid tests that do not require laboratory facilities are commercially available, until now there has been little reliable information on their performance and operational characteristics. In the first round of TDR-sponsored evaluations, six tests were evaluated at eight SDI laboratory sites, selected by open competition. A report (see TDRnews no. 70, Oct. 2003) describing the results of this evaluation is available at www.who.int/std_diagnostics.

With these ASSURED diagnostics, innovative programmes to eliminate congenital syphilis through decentralized antenatal screening can now be a reality for many high burden countries.

The two-colour bands indicate positivity. 

1 The SDI, originally founded in 1990, has been housed within the Product Development Initiative at TDR since 1994. Its mission is to promote the development, evaluation and application of diagnostics for sexually transmitted diseases which are appropriate for primary health care settings in developing countries.

2 SDI has coined the term ASSURED (affordable, sensitive, specific, user-friendly, can be performed in a few simple steps requiring minimal training, rapid and robust, equipment-free and deliverable to end-users) to describe the ideal diagnostic test it is seeking for its three priority diseases, syphilis, chlamydia and gonorrhoea.
Integrating leprosy control: new challenges for Implementation Research

The issue of integrating leprosy services into the general health services was addressed at a TDR workshop co-organized with the Oswaldo Cruz Foundation, in Rio de Janeiro, March 2004. This had been identified as a major research challenge by the TDR Scientific Working Group on Leprosy in November 2002; it was reinforced by the WHO Technical Advisory Group in 2004 (see box 1). Participants at the workshop proposed a multi-country study with two research phases.

Despite the impressive achievements of the World Health Organization (WHO) global elimination strategy, which is one of the most cost-effective interventions in the public health domain, WHO is concerned that leprosy prevalence still stands at around 4 per 10 000 in the six most endemic countries (which represent about 90% of the global leprosy problem), and that disease transmission continues in many low prevalence countries. Reasons for the continued high prevalence in six countries include, most importantly, the limited extent of geographical coverage with multi-drug therapy (MDT) services and therefore the poor access to leprosy diagnosis and treatment.

A major operational problem is that leprosy diagnosis and treatment remain highly centralized activities in many countries, and are often only conducted by specialized staff.

Participants at the workshop in Rio identified sets of variables related to the failures of leprosy elimination, and summarized the different challenges to integration in a diagram (see box 2). The first phase of the proposed multi-country study includes cross-sectional studies of the challenges to integration in countries where leprosy control is at different stages of integration; the second phase includes intervention studies for testing possible solutions to identified key problems.

In the first phase, standardized research methodologies and instruments will be developed in a proposal-writing workshop. The focus will be on:

- national decision-making, planning, resource allocation, reporting
- the appropriateness of actual procedures for early detection, diagnosis and treatment in leprosy patients
- the practice and impact of information, education and communication (IEC) activities
- improvement of the health information system regarding monitoring and evaluation of leprosy control.

The most efficient and equitable approaches to integration in achieving the objectives of leprosy control will be identified and fed into the intervention studies of the second phase.

**Challenges of Integration**

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The practice and impact of IEC activities have been identified as a focus on research. Here, a village chief sticks an MDT poster to his truck to help inform his remote community.
RESEARCH CAPACITY

TDR trainees at first La Trobe graduation ceremony in Myanmar

TDR in Myanmar

In Myanmar, TDR collaborates with the Department of Medical Research at the Ministry of Health, the Department of Medical Services at the Ministry of Defence, and the Institute of Medicine. Research that has been/is being supported by TDR includes studies on:

- operational and management issues related to increasing use of artemisinin and its derivatives
- drug compliance with respect to utilization of artemesunate and mefloquine (in specially prepared packets)
- interventions to counter the misuse of artemisinin and its derivatives
- mapping the geographical distribution of An. dirus sibling species complex and their behaviour/relaton to malaria transmission in Myanmar
- source reduction of well-breeding An. dirus and targeting of key wells to control malaria in coastal Myanmar
- efficacy of B. sphaericus in the field, against larvae of different species of mosquito in polluted water
- control-related issues such as assessment of malaria intervention strategies in Myanmar
- purine transport and metabolism in P. falciparum infected erythrocytes from individuals with genetic abnormalities
- adenosine transport in malaria infected erythrocytes
- an antibody-dependent cell inhibition assay to identify protective antigens and establishment of protective immunity
- the pharmacokinetics of mefloquine enantiomers related with efficacy, toxicity and resistance development
- assessment of self-care empowerment of women in the prevention and care of malaria
- preventing disability in persons with leprosy using a community-based self-care teaching approach.

At the first La Trobe University graduation ceremony in Myanmar, three TDR-funded students received their degrees.

The graduation ceremony was held on 9 February 2004 in the city of Yangon, and was the culmination of many years of cooperation between La Trobe University, Professor Pearson, and Myanmar. A number of La Trobe faculty members, and Steven Wayling from TDR, attended the ceremony, in addition to senior government officials and hundreds of colleagues, family and friends of the students. The assembly was addressed by the Rectors of the two nursing institutes in Yangon and by the La Trobe Vice-Chancellor and President.

UPDATE

Drug discovery from natural products: TDR focuses on Africa

In 2003, TDR launched an RCS-Plus R&D-driven initiative on drug discovery from natural products. Two centres of excellence in biological screening and phytochemistry were selected and funded and, at the end of the year, a workshop was held to develop a network for strengthening research capacity in these activities. Initially the focus is on malaria in Africa. TDR has been involved with natural products for some years already (see TDRnews no. 62, June 2000).

The initiative has two main objectives. Firstly, to advance drug discovery in disease endemic countries; it will do so by providing mechanisms for establishing and coordinating a network of collaborating investigators and laboratories to discover new leads for neglected diseases, based on natural products and using malaria as a model. Secondly, the initiative will support the strengthening of existing facilities for capacity building and R&D for drugs against neglected tropical diseases.

Of the two selected screening centres, one is in Nigeria and is a joint consortium between the College of Medicine at the University of Ilbadan and the National Institute for Pharmaceutical Research and Development (NIPRMD) at Abuja. The other centre is at the Kenyan Medical Research Institute (KEMRI) in Nairobi.

Developed during the workshop were plans for streamlining discovery, establishing state-of-the-art screening centres which adhere to good laboratory practices (GLP) and standard operating procedures (SOPs), and putting in place a network for streamlined supply of samples from investigators to screening centres. Sample supply, analysis and reporting will be bound by written agreements, taking into consideration intellectual property issues.

Currently, under the guidance of TDR Product Research and Development experts, the two centres of excellence are developing SOPs and building laboratory capacity for in vitro and in vivo screening of natural products. It is expected that the centres will be up and running, with screening in progress, by the end of July 2004, and that at least one lead antimicrobial compound will be discovered by 2008.

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3 Vice-Chancellor and President, Professor Michael Osborne; Pro Vice Chancellor and Deputy President, Dr David Stockley; Professor Alan Pearson; International Programmes Officer, Barbara Green; Executive Assistant to the Vice Chancellor, Ms Karen Suy.
More and more these days, we learn from the headlines that access to health products by poor people, especially in developing countries, is often inadequate. The drugs, diagnostics or vaccines that could make the difference to their lives are too expensive or not available. Therefore solutions to guarantee access to existing products are needed. However, equally important is the stimulation of innovation to address the existing gaps in our knowledge and the lack of tools to address diseases of poverty. This issue is particularly acute for tropical diseases and other diseases of poverty where there is little market incentive. To work out a way to do this, WHO has set up a Commission to produce an analysis of intellectual property rights, innovation and public health.

The ten members of the Commission have a wide range of expertise. They are high calibre senior officials from developing and industrialized countries, from research institutions, governments, academia and industry. The Commission was established at the request of the World Health Assembly in 2003, which recommended that it should collect data and proposals from the different actors involved and produce an analysis of intellectual property rights, innovation and public health, including the question of appropriate funding and incentive mechanisms for the creation of new medicines and other products against diseases that disproportionately affect developing countries.

Ultimately the Commission will produce a global framework to ensure the invention of new medicines for diseases mainly affecting developing countries, TDR, as part of the WHO secretariat, had the opportunity to brief the Commission on the Programme has contributed to filling gaps through interacting with organizations from the public and private sectors during the past 25 years, and will actively support the work of the Commission.

A variety of environmental, economic, political and social factors have been linked to the resurgence of dengue/dengue haemorrhagic fever (DHF) as a major global health problem. These factors include population growth, climate change, rapid and unplanned urbanization, inadequate municipal services, increased use of non-biodegradable products such as bottles, drums, cans and tyres, vector adaptability, and inconsistent or fragmented national control programmes. Similar factors have been at play in the resurgence of epidemic dengue which has taken place in Latin America since the 1980s. Such etiological factors are triggered by large-scale stressors such as the social, economic and political transformations prevailing in Latin America.

Thus, in 1999, when TDR added dengue to its Disease Portfolio, research on the social, environmental and economic determinants of risk was viewed as crucial to a better understanding of existing challenges and alternatives for action and prevention. TDR has long had an interest in research requiring a trans-disciplinary perspective. Since the early 1990s, the Programme has funded a number of studies to look into the impact of environmental change, including reforestation, and agricultural and infrastructure development, on the risk for tropical diseases such as malaria and leishmaniasis and the resulting health and economic costs.

A new area of research has been defined taking into account the fact that communicable diseases emerge and persist in dynamic “eco-bio-social” contexts. Current approaches to ecosystems in relation to health theory the complex dynamics between the socio-economic and political (“social”) dimensions of health on the one hand, and its physical, biotic (“ecological”) dimensions on the other. Bridging both fields through cross-disciplinary research still represents a major challenge.

Two studies developed at a joint TDR/IDRC proposal development workshop in Recife, Brazil, October 2003, are under way. One study in Colombia, at the Fundacion Santa Fe de Bogota, in collaboration with the Universidad de los Andes, the Universidad del Valle, and the Colombiano National Institute of Health, is an investigation of the dengue problem in two endemic cities on the Magdalena basin river. The general goal is to identify the eco-social factors involved, in order to improve health promotion and disease prevention activities. A trans-disciplinary team including epidemiologists, anthropologists, meteorologists and social researchers is conducting this research project. Another study, at Ceara State University (Universidade Estadual do Ceara), Brazil, will research the eco-social factors responsible for re-emergence of dengue in the Brazilian city of Fortaleza, using a combination of survey research, ethnological assessment, and ethnographic research.

**Eco-bio-social research on dengue: a joint TDR/IDRC initiative**
The road towards a *P. vivax* malaria vaccine

In Colombia, a multidisciplinary group of young scientists dedicated to understanding * malaria and finding tools to prevent it is furthering a project of more than 20 years standing. The story begins modestly enough, with training in immunology of malaria for two key persons under TDR support, and leads ultimately, after establishment of the International Malaria Vaccine and Drug Testing Center (MVDC), to the award of a grant by the United States National Institute of Allergy and Infectious Diseases (NIAID) in 2001, to establish a Tropical Medicine Research Center (TMRC) that now employs about 100 scientists and technologists as well as many support staff.

The MVDC was established in 2000, after a program for introducing good laboratory practices (GLP) and good clinical practices (GCP), sponsored by TDR, had been set up at the Universi- dades del Valle in Cali. For nearly two decades previously, the scientists in this Centre had devoted their efforts to basic, preclinical and clinical research, taking care of the particularities of Colombia while following closely the philosophy and policies of national and international funding agencies. The goal of the TMRC is to accelerate the development of a *P. vivax* vaccine. The researchers are convinced that, to be useful and effective in the most endemic areas, a malaria vaccine has to include components of both *P. falciparum* and *P. vivax* due to their widespread co-existence. They have coordinated a first clinical trial conducted in 69 healthy, malaria naïve volunteers, to test the safety and immunogenicity of a *P. vivax* circum- sporozoite vaccine candidate developed by the group. This trial was successfully conducted at the Fundacion Clinica Valle del Lili, one of the Cali collaborators. The phase I clinical trial was based on the use of long synthetic peptides technology and the work was conducted in close collaboration with the group of Dr. Giampietro Corradin at the University of Lausanne, Switzerland.

Very rapid progress is being made in the assessment of new *P. vivax* vaccine candidates, and the group is currently developing a *P. vivax* sporozoite challenge system for the Phase II trials to be conducted in the near future. This work is supported by the WHO Initiative for Vaccines Research (IVR).

Today, the multidisciplinary group at MVDC is composed of about 100 scientists and technicans, including immunologists, molecular biologists and chemists dedicated to basic research (vaccine discovery). A group of biologists and veterinarians deals with preclinical analysis of vaccine candidates and antimalarial drugs in rodents and non-human primates, while epidemiologists and social scientists look at multiple malaria features in endemic communities. This sizeable team of biomedical scientists is supported by a large group of, amongst others, economists, engineers and lawyers.

Adhering to these principles, the Drs Herrera, during two decades, invested a great deal of effort in the training of young scientists and were instrumental in establishing graduate programmes (MSc and PhD) advanced postdoctoral training, and continuous education for health workers and communities at the Universidad del Valle.

Cali is a modern city with important hospital facilities and universities, located about 80 miles from the most endemic area for malaria. Like other projects of this type, the Colombian project was aimed at creating a facility to study malaria with special emphasis on new diagnostic tools, new and more efficient antimalarial drugs, and understanding the immune responses of endemic communities as a means to develop a malaria vaccine. Training and scientific interaction with peers are both integral to TDR’s philosophy.
MIM/TDR: Task Force begins charting a path for the future

A Multilateral Initiative on Malaria (MIM)/TDR Task Force meeting took place in Bamako, Mali, 17-19 March 2004. In addition to the usual business of reviewing reports and grant proposals, time was put aside for reflecting on past achievements and challenges, and charting directions for the future. At age seven, the task felt to be timely for MIM/TDR.

The MIM/TDR Task Force has, till now, served mainly as a review body for grant proposals, but members agreed it should play a more strategic advisory role in future. The Task Force’s mandate is today more relevant than ever since malaria remains a huge problem for Africa (antimalarial resistance to affordable drugs is widespread, preventive measures are not widely applied, and no vaccine is in sight), despite the greater visibility it receives now than when MIM was launched.

So far, 42 young Africans have completed postgraduate training through MIM/TDR, 25 at master’s level and 17 at doctoral level. The Task Force recommended an analysis to show how these researchers are taking up leadership roles, competing better for research funds, and generating other scientists. This analysis could be a powerful advocacy tool.

Three major gaps were identified: clinical research, vector research and social science research. With respect to the former, new and important questions regarding priorities for combination therapy, malaria in pregnancy, deployment of insecticide-treated materials, and malaria control in areas prone to epidemics, are being raised by Roll Back Malaria field operations. To enhance the safety, effectiveness and accessibility of public health interventions, opportunities at the interface of research and control need to be carefully explored. The discussion briefly touched upon the importance of genome sequencing for malaria research initiatives aimed at vaccine and drug development and vector control. For vector research, the MIM secretariat offered to define a strategic direction while, for social science research, the MIM/TDR secretariat will suggest practical ways for integrating this into its research and capacity building activities.

To advance its overall goal, the Task Force requires greater funding than is currently available. The TF will work with MIM partners and donors to at least double the funding for MIM/TDR within three years.

Implementation Research: case-detection and treatment of kala azar

A new drug for visceral leishmaniasis (VL) was developed with TDR support: miltefosine, an orally administered compound, short course, and a reasonable price (see TDRnews no. 68, June 2002). Is this the final solution of a severe public health problem in VL endemic areas? Anecdotal evidence from Bihar State in India, probably the most important focus of VL in the world, shows that the end of the tunnel has not yet been reached: most VL patients resort to the private medical sector where they may receive a delayed diagnosis and non-standardized treatment advice, and, even worse, many patients obtain the new drug over the counter, as long as they can pay for it. Increased human suffering and development of drug resistance are the foreseeable consequences.

Concern was expressed over the quality of many proposals and reports. The secretariat agreed to prepare a strategy for improving the quality of planning, writing, implementing and reporting on research projects, which should be coupled and integrated with the MIM mentorship programme. In order to evaluate, consolidate and build on what has been achieved so far by MIM/TDR, the Task Force requested an analysis of the research networks that have been established, with clear guidelines on how they can be reshaped to make them more effective and relevant.

Discussion also focused on the need for a mechanism to define research and capacity building priorities relevant to malaria in the coming 5-10 years. Immediate concerns included the balance of focus on basic, applied and policy research, the need to focus more on research that enables translation of results into policies and public health interventions was emphasized. Another concern was to expand the geographical range of MIM/TDR capacity building activities, which are currently concentrated in a number of countries. The Task Force recommended a more proactive approach for achieving better geographical balance, as well as continued consolidation of established teams and institutions, and collaboration between African researchers and colleagues in Asia and Latin America with similar research interests.

A conceptual framework of factors potentially associated with late diagnosis and treatment failures was developed and key research questions were formulated. On this platform, and under the umbrella of the overall research objective “to develop improved implementation strategies for early case detection and treatment of VL patients”, a set of specific research objectives was agreed. These focus on the knowledge, attitudes and actual practices of VL patients and on their health-seeking behaviour, as well as on organizational, managerial and policy issues of the health sector, including a large range of health care providers. After completing the first “formative” phase of research, a second round of inter-village studies will be conducted which will test new options of managing early VL diagnosis and rational treatment in a cost-effective way.

The four Indian research teams are composed of members from different disciplines in the social, medical and biological sciences; their close interaction with control staff and realistic view of what is feasible and sustainable will be essential for the success of this implementation research.
TO HELP EXPLOIT THE INFORMATION COMING FROM GENOME SEQUENCING ACTIVITIES ON INSECT DISEASE VECTORS, TDR IS FACILITATING THE DEVELOPMENT OF A NETWORK OF RESEARCH CENTRES ON INSECT DISEASE VECTORS. THIS WILL OPEN THE WAY FOR PROMISING YOUNG SCIENTISTS IN DISEASE ENDEMIC COUNTRIES TO LEARN THE SKILLS NECESSARY FOR USING GENOME DATA AND FOR DEVELOPING PARTNERSHIPS TO PRODUCE MORE EFFECTIVE TOOLS TO INTERCEPT DISEASE TRANSMISSION.

OVER THE PAST FEW YEARS, TDR HAS BEEN PARTICIPATING, THROUGH THE ACTIVITIES OF ITS MOLECULAR ENTOMOLOGY COMMITTEE AND ALONG WITH OTHER PARTNERS, IN THE SEQUENCING OF INSECT DISEASE VECTORS. THE ANOPHELES GAMBIAE GENOME IS NOW PUBLISHED, Aedes Genome Data Are Being Made Available, and Efforts Have Begun on Sequencing the Glossina Genome (See TDR News no. 71, February 2004), Providing Unique Opportunities to Increase Our Knowledge of These Vectors and Improve Our Tools for Their Control. Thus the Time Is Now Ripe to Ensure that This Genomics Knowledge Is Put to Good Use Where It Is Needed.

Under its RCS-Plus Initiative, TDR Will Help Strengthen Three Centres, Each One in Africa, Asia and Latin America. As Yet, the Centres Have Not Been Identified but the Plan Is to Begin by Strengthening Two Centres and Then, Hopefully, a Third One When Additional Funding Becomes Available. Each Centre Will Run One Two-Week Course a Year, on Molecular Entomology, Bioinformatics, and Functional Genomics, for Up to 20 Trainees. It Is Hoped the First Course Will Start in 2004. The Ultimate Goal Is to Establish Sustainable Basic Research and Training Facilities That Promote Utilization of Genomics in Developing Disease-Endemic Countries.

TDR extends its warmest congratulations to Professor Akintunde Sowunmi, who was recently awarded the Fellowship of The Royal College of Pathologists (United Kingdom) by examination of published works. Of 93 papers submitted for inspection, 77 were the results of studies financially supported by TDR.

With his earliest TDR support, Professor Sowunmi evaluated the in vivo and in vitro sensitivity of P. falciparum to mefloquine. In 1991, with TDR support towards his postgraduate training, Professor Sowunmi went on to examine the measurement and application of electrophysiological changes in severe and complicated malaria. Under a TDR entry grant, Professor Sowunmi was able to return to Nigeria to undertake this latter area of research to unravel pathophysiological changes in Nigerian children suffering from severe and complicated malaria. After he successfully competed for the prestigious TDR Career Development Award in 1994, and for the following five years, Professor Sowunmi looked at novel approaches to sequential and combination therapy of falciparum malaria. Under subsequent funding from TDR, Professor Sowunmi has undertaken studies for the Multilateral Initiative on Malaria in Africa (MIM/TDR) related to drug resistance in Africa and has taken part in TDR R&D committees reviewing new combination therapies for malaria including chlorproguanil-dapsone (Lapdap). Professor Sowunmi is head of the malaria research group at the Post-graduate Institute for Medical Research and Training (PIMRAT), University of Ibadan, Nigeria, one of Africa’s premier malaria research groups. He also sits on TDR’s Research Strengthening Group (RSG).

An international workshop on Intensified Control of Neglected Diseases was held in Berlin, Germany, December 2003. The workshop brought together experts from many fields—public health, economics, human rights, research, non-governmental organizations, industry; it was sponsored by WHO, several German government departments, and TDR.

Neglected diseases were presented from a variety of perspectives. TDR for instance focused on development of new control tools and refinement of existing ones, and the need for the research and control communities to work together. David Canning, Director of Population and International Health, Harvard University, USA, looked at health from the economic perspective. He reminded people that “health is not just a by-product of economic development, rather it fuels economic growth” and is, in fact, one of the best investments around. While some diseases should be neglected because they are too expensive to treat, others need to be prioritized, but every decision needs to be based on evidence. Paul Hunt, Director, Human Rights Centre, University of Essex, UK, looked at neglected diseases from the human rights perspective. Neglected diseases are at the core of human rights as they deal with issues related to poverty, discrimination and stigma, as well as the right to health. “We should look at neglected communities, and not just neglected diseases, and provide them with an integrated solution to their health problems.”

A publication is available that outlines the discussions, as well as a framework for future action, which is to be further developed in line with country specific needs and translated into concrete implementation plans.

The malaria community has lost a distinguished physician, scientist, researcher, teacher and friend. Professor Masamichi Aikawa passed away in May 2004. He will be remembered for his contributions to the understanding of the structure of the malaria parasite and of the pathogenesis of the disease, among others. TDR and the Multilateral Initiative on Malaria (MIM) have lost an important supporter. Between 1998 and 2002, Professor Aikawa was a member of the MIM/TDR Task Force on Malaria Research Capability Strengthening, encouraging African scientists to address essential research questions for reducing the malaria burden on the continent. The photograph above shows him making remarks at the March 2002 MIM/TDR Task Force meeting in Entebbe, Uganda. Through his efforts, his country, Japan, is one of the supporters of MIM.

1 German Technical Cooperation (GTZ); German Ministry for Development and Technical Cooperation, Kreditanstalt für den Wiederaufbau (KFW); German Ministry for Health and Social Security.

2 Document WHO/DTS/TDR/2004.45

AWARD

TDR grantees awarded Fellowship of the Royal College of Pathologists

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OBITUARY

Professor Masamichi Aikawa (MD Ph.D) 1931-2004

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1 German Technical Cooperation (GTZ); German Ministry for Development and Technical Cooperation, Kreditanstalt für den Wiederaufbau (KFW); German Ministry for Health and Social Security.

2 Document WHO/DTS/TDR/2004.45
Latest grants

Research in Applied Genomics to Drugs and Diagnostics

The TDR Working Group on Applied Genomics to Drugs and Diagnostics, established by the Committee on Pathogenesis and Applied Genomics, met in Boston, Massachusetts, USA, in October 2003, to deliberate and recommend projects for funding by TDR. The following projects were selected from among a large number of applications received from investigators worldwide and will be funded in the first year toward reaching the scientific objectives, and if sufficient funds are available.

A JOHN MANOJO DURASINGH, Harvard School of Public Health, Boston, USA. A forward genetics approach identifying molecular determinants of resistance to quinoline drugs in P. falciparum (budget: US$ 40 000)

A80032 PIETRO CALI, University of Florence, Italy. Mosquito resistance to insecticides and the potential to develop resistance to transgenic mosquitoes (budget: US$ 50 000)

Drug Discovery Research

The TDR Drug Discovery Research Committee met in Geneva, Switzerland, April 2003, 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

A20775 QUENTIN BICKLE, London School of Hygiene and Tropical Medicine, London, UK. Research on the interaction between malaria and Trypanosoma cruzi (budget: US$ 60 000)

A20776 FOAUD YOUFF, Theodor Bilharz Research Institute, Giza, Egypt. Screening and evaluation of compounds for schistosomiasis chemotherapy (budget: US$ 60 000)

A30732 JAN STREET, The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia. Discovery of new antimalarial drug candidates for tropical diseases targets (budget: US$ 50 000)

Renewed grants

A98012 RETO BRUN, Swiss Tropical Institute, Basel, Switzerland. In vitro/in vivo screening component of the JPMW malaria screening program (budget: US$ 216 494)

A00883 MARGARET NGOZI AGBAKO, University of Ibadan, Nigeria. Evaluation of antimalarial efficacy and second line treatment in TB clinics in Primary Health Care Zone A, Nigeria. (budget: US$ 25 000)

A11491 AHMED MOHAMED ASSAAD, Cairo University, Egypt. Integrated approach to antiparasitic drug discovery and development (budget: US$ 45 070)

A10879 MURIEL CHATELAIN, Institut de Recherche pour le Développement, France. Basic, drug resistance and antimalarial drug discovery in the context of the Onchocerciasis Research in Africa (OCRAD) (budget: US$ 80 000)

A11429 ANGELA ISABEL CALVO, Instituto de Salud Carlos III, Madrid, Spain. Discovery of novel antileishmanial drugs from marine invertebrates (budget: US$ 40 471)

A10364 ALI MOHAMED ASSAAD, Cairo University, Egypt. Integrated approach to antiparasitic drug discovery and development (budget: US$ 30 000)

A00883 MARGARET NGOZI AGBAKO, University of Ibadan, Nigeria. Evaluation of antimalarial efficacy and second line treatment in TB clinics in Primary Health Care Zone A, Nigeria. (budget: US$ 25 000)

A20769 LAURA ARCO, Pontificia Universidad Católica del Ecuador. Ecuador: Institutional capability strengthening in tropical diseases research and training at Catholic University, Quito, Ecuador (budget: US$ 42 450)

A99000 COLIN GREEN, Northumbria Park Institute of Medical Research, Harrow, UK. Discovery and development of a new drug for schistosomiasis (budget: US$ 216 494)

A10124 SATOSHI OOMURA, The Kitasato Institute, Tokyo, Japan. In vitro screening component of the PAMM malaria screening program (budget: US$ 113 000)

Capacity Strengthening Programme Grants

New grants

A30837 NICOLAS MBOGNO, Laboratoire National de Santé Publique, Congo. Research capacity strengthening for anti-trypansomosal compounds from medicinal plants (budget: US$ 50 000)

A30930 ISA NIEBE, Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso. Etude de l’activité antipaludique des plantes utilisées traditionnellement dans une région humide de BPA (budget: US$ 53 343)

A99048 BARBARA JUDITH MINDIKI MARTINEZ, Instituto de Tropical Medicine and Public Health, Belgium. Malaria research in Rwanda: Predictive model of potential risk for schistosomiasis after construction of the Three Gorges Dam (budget: US$ 15 000)

A00891 EDITH SANOGO, Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso. Resistance of the Three Gorges Dam to chemotherapeutic agents in M. tuberculosis (budget: US$ 20 000)

A30849 MOISÉS LUTAOME JOLOBA, Makerere University Medical School, Department of Medical Microbiology, Uganda. Evaluation of various methods for rapid detection of multidrug resistant tuberculosis (budget: US$ 13 200)

A10274 RENATO DA SILVA M. BORGES, Federal University of Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Brazil. Determination of the three-dimensional structure of dengue virus fusion peptide by nuclear magnetic resonance (budget: US$ 20 000)

A10382 ANGELA ISABEL CALDERÓN, University of Panama, School of Pharmacy CIFLORPAN, Panama. Discovery of potential therapeutic products against tropical diseases from Panamanian biodiversity (budget: US$ 20 000)

A30877 HEINRITZO RAFATRO, University of Antananarivo, Faculty of Medicine, Madagascar. Bionomics and molecular characterization of rodent malaria strains of Aedes aegypti (budget: US$ 12 000)

A10381 MARIAM ATTA EL BAKRAOUI, Faculty of Medicine, University of Asmara, College of Medicine, Eritrea. Research on neglected diseases in Eritrea (budget: US$ 25 000)


A30821 ABDOULAYE DIABATE, The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia. Discovery of new antimalarial drugs from marine invertebrates (budget: US$ 40 471)

Renewed grants

A81051 JOSÉ Mª MARÍAS, Instituto de Investigaciones Moleculares A. Mendiola Martinez, Instituto de Salud Carlos III, Madrid, Spain. Molecular and behavioral basis of reproductive isolation in natural populations of Anopheles gambiae (budget: US$ 24 000)

A30882 CLARA BEATRIZ OCAMPO-DURAN, Centro Internacional de Entrenamiento e Investigaciones Médicas, Cนามical. Differential gene expression in dengue-2 infected & non-infected midges of susceptible An. gambiae (budget: US$ 25 000)

A30878 MARIO EDUARDO MENDIOLA MARTINEZ, Institute of Tropical Medicine, Tanzania. Functional analysis of putative nuclear receptors of the Three Gorges Dam to chemotherapeutic agents in M. tuberculosis (budget: US$ 20 000)

A30810 MARIAM ATTA EL BAKRAOUI, Faculty of Medicine, University of Asmara, College of Medicine, Eritrea. Research on neglected diseases in Eritrea (budget: US$ 25 000)

A10287 RENATO DA SILVA M. BORGES, Federal University of Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Brazil. Determination of the three-dimensional structure of dengue virus fusion peptide by nuclear magnetic resonance (budget: US$ 20 000)

A10379 HEINRITZO RAFATRO, University of Antananarivo, Faculty of Medicine, Madagascar. Bionomics and molecular characterization of rodent malaria strains of Aedes aegypti (budget: US$ 12 000)

A30894 EDITH SANOGO, Centre National de Recherche et de Formation sur le Paludisme, Burkina Faso. Resistance of the Three Gorges Dam to chemotherapeutic agents in M. tuberculosis (budget: US$ 13 200)

A30849 MOISÉS LUTAOME JOLOBA, Makerere University Medical School, Department of Medical Microbiology, Uganda. Evaluation of various methods for rapid detection of multidrug resistant tuberculosis (budget: US$ 13 200)

A20745 RENATO DA SILVA M. BORGES, Federal University of Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Brazil. Determination of the three-dimensional structure of dengue virus fusion peptide by nuclear magnetic resonance (budget: US$ 20 000)

A10382 ANGELA ISABEL CALDERÓN, University of Panama, School of Pharmacy CIFLORPAN, Panama. Discovery of potential therapeutic products against tropical diseases from Panamanian biodiversity (budget: US$ 20 000)

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A10274 RENATO DA SILVA M. BORGES, Federal University of Rio de Janeiro, Instituto de Biofísica Carlos Chagas Filho, Brazil. Determination of the three-dimensional structure of dengue virus fusion peptide by nuclear magnetic resonance (budget: US$ 20 000)

A10382 ANGELA ISABEL CALDERÓN, University of Panama, School of Pharmacy CIFLORPAN, Panama. Discovery of potential therapeutic products against tropical diseases from Panamanian biodiversity (budget: US$ 20 000)
• A30791 LUCIANO ANDRADE MOKIRA, Centro de Pesquisas René Rachou, FIOCRUZ, Brazil. Expression of a foreign antiangiogenic gene in transgenic anopheline mosquitoes (budget: US$ 16 500)
• A30727 ANTONIO CHRISTOPHE, NORDJEO, Organisation de Coopération pour le Lutte contre les Épidémies en Afrique centrale (OCEAC), Cameroon. Biology and genetic structure of the malaria vector Anopheles mochita in Central Africa (budget: US$ 15 700)
• A30733 ABDULLA HASSAN SHAREIF, Tropical Medicine Research Institute, Sudan. Rapid assessment of patterns of Plasmodium infection in western Sudan. immune surveillance and application of GIS (budget: US$ 19 500)

Project Development Grants

New grants
• A30596 PAOLO ABEL, Caritas de New grants Project Development Institute, Uganda. Molecular epidemiology of vaccine antigen-encoding P. falciparum infections in mothers and neonates
• A30597 ALBERT LUKUKA KILAUIZI, Instituto National de Recherche Bio-médiQues, DRC. The impact of war and migration on schistosomiasis distribution in DR Congo (budget: US$ 10 000)
• A30597 SIENI KOJANDA, Institut de Recherche en Sciences de la Sante, Burkina Faso. Tubercolusis monitoring project in Burkina Faso (budget: US$ 10 000)
• A30597 S. ALBERT KUOJAMA, Instituto National de Recherche Bio-médiQues, DRC. Aga-dependent dynamics of P. falciparum alleles in children with normal haemoglobin and with sickle cell trait
• A30734 JOUJOUKAN KEUL ROUSSEAU, Centre de Recherche entomologique de Cotonou, Benin. Identifying factors selecting each type of mechanism of resistance in Anopheles gambiae
• A30670 AINAPA RUTENDO B.L., Blair Research Institute, Zimbabwe. Expression of genetic markers associated with susceptibility to HIV infection: impact of co-infection with schistosomiasis
• A30729 KERAH HINZUMBE C., Programme National de Lutte antipaludique, Tchad. Sensibilité des vecteurs de paludisme aux pyrithrines dans la zone de Bongor au sud du Tchad
• A30746 MARTINS NELSON, University of Dili, Timor TB treatment in East Timor
• A30752 MATONDO MAYA, Malaria Research and Training Institute, Uganda. Molecular epidemiology of Rhodesian sleeping sickness (PKDL) in the western region of Uganda
• A30752 VALERO MARIA VICTORIA, Instituto Superior de Ciencias de la Salud, Cuba. Predicting the occurrence of malaria transmission in Yamen (budget: US$ 16 500)
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 |

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### Deadlines

#### BASIC AND STRATEGIC RESEARCH
- Molecular Entomology: May 2005* - Feb 2005*
- Pathogenesis and Applied Genomics: May 2005* - Feb 2005*
  - Working Group on Applied Genomics for Drugs and Diagnostics: 08-10 July 2004 (Apr 2005*)
- Strategic Social, Economic and Behavioural Research: May 2005* - Feb 2005*

#### PRODUCT RESEARCH AND DEVELOPMENT
- Drug discovery and Drug Development (Chemotherapy Portfolio Review Committee): Apr 2005* - Jan 2005*
- Vaccine Discovery Research: May 2005* - Feb 2005*
- Diagnostics Research and Development: (26-27 May 2004)

#### INTERVENTION DEVELOPMENT AND IMPLEMENTATION RESEARCH
- Implementation Research Steering Committee: 06-09 July 2004 (14 May 2004)
- Proof of Principle Steering Committee: 08-10 Sep 2004 - 15 July 2004

#### RESEARCH CAPACITY STRENGTHENING
  - Letters of intent: 31 Oct 2004
  - Progress reports, renewal requests, full proposals
- Malaria Research Capacity Strengthening in Africa**: Mar 2005
  - Letters of intent: to be announced
  - 30 Nov 2004* Full proposals, progress reports and renewals requests

* Tentative date.
** Only pre-selected letters of intent are invited to submit full proposals.