UNICEF, in its bid to protect future generations, joins with TDR
UNICEF as a new TDR co-sponsor: strategy for shared success

The United Nations Children’s Fund (UNICEF) is the driving force that helps build a world where the rights of every child are realized. We believe that nurturing and caring for children are the cornerstones of human progress. UNICEF was created to work with others to overcome the obstacles that poverty, violence, disease and discrimination place in a child’s path. We advocate for measures to give children the best start in life, because proper care at the youngest age forms the strongest foundation for a person’s future.

This UNICEF mission, and the view that the survival, protection and development of children are universal development imperatives that are integral to human progress, links well with the TDR mission to help coordinate, support and influence global research to combat a portfolio of major diseases of the poor and disadvantaged. Anchored as they are in the United Nations system, both institutions share in the global authority that advises decision-makers, and both can rely on a variety of partners at grassroots level to effectively turn the most innovative ideas into reality.

Over the past few years, UNICEF has developed a collaborative working relationship with TDR and has intensified its participation in TDR’s discussions at policy level – as an observer since the fall of 2001 and as a host to the TDR Standing Committee meeting at UNICEF headquarters in April 2003. During this time, discussions were held regarding closer links between UNICEF and the Special Programme. This culminated at the TDR Joint Coordinating Board (JCB) meeting in June 2003, where UNICEF was officially welcomed as a new TDR co-sponsor. At this JCB meeting in New Delhi, board members and co-sponsors recognized and underlined the strengths that UNICEF brings to the partnership with regard to a strong country presence, particularly in relation to scaling up new and improved tools for child health.

What this means for UNICEF

UNICEF believes that the Millennium Development Goals (MDGs), and goals contained in the outcome document of the 2002 UN Special Session on Children: A World Fit for Children, provide a focus for scaling up programmes for child survival. Globally, nearly 11 million children under five years of age die every year due to preventable diseases such as pneumonia, diarrhoea, malaria, measles, malnutrition and AIDS, with 90% of these deaths occurring in just 42 countries, mostly in Africa and South Asia. UNICEF is therefore supporting countries to scale up cost-effective interventions to prevent child deaths, toward achievement of the MDG to “reduce by two-thirds the mortality rate among children under five” by 2015.

“Partnerships for shared success” is one of UNICEF’s strategies for implementing the World Fit For Children plan of action. Collaboration with energetic and diverse networks at global, regional, national and community level has long been a hallmark of UNICEF’s work. It has also been a source of UNICEF’s strength, as the wide and diverse network of our partners multiplies the impact of our efforts.

Becoming a TDR co-sponsor is viewed by UNICEF as another important “strategic partnership”, helping to facilitate evidence-based programming for children, leading to greater recognition of child health issues in the portfolio of TDR and facilitating specific collaborations of relevance to child health programmes.

In line with the TDR Strategic Emphases Matrix, it is clear that “new basic knowledge”, “new and improved tools”, “new and improved intervention methods”, and “new and improved strategies and policies” are required if the international community wishes to reduce significantly the current high levels of infant and under-five mortality. This is particularly important in the fight against the major child killers such as malaria, diarrhoea and pneumonia. UNICEF recognizes that a large proportion of the present TDR body of work is in the area of malaria, a priority for UNICEF country programmes in Africa as part of the Roll Back Malaria partnership.
UNICEF roles and responsibilities
One of the four key functions of TDR is to encourage “intervention development and implementation research”. With a strong field presence and over 6000 staff located in developing countries, UNICEF country programmes in support of national health system development can help to identify needed interventions and provide a large-scale programme base for implementation research activities at the country level.

There has already been active collaboration between UNICEF and TDR in the area of implementation research for home and community management of malaria and pneumonia, the results of which have direct relevance to a more effective community approach to the sick child. It is hoped that this specific collaboration will lead to expansion into other areas of mutual interest.

UNICEF is in the process of undertaking a comprehensive analysis of current involvement in public health research in general and collaboration with TDR in particular, at global, regional and country level, in order to better understand our role and contribution to the TDR partnership. This will include collaboration with key researchers and research institutions operating at the country level.

Working in collaboration with the other TDR co-sponsors, UNICEF can make use of the mechanism of the UN Country Teams to promote the work of TDR at country level, strengthen the link between health research and implementation, and raise the profile of the key role played by health research in improving health outcomes for children.

UNICEF is very pleased to join the Special Programme as a new co-sponsor, acknowledging the many major achievements that have been facilitated by TDR over the years and which have contributed significantly to improving child health. It is hoped that this partnership will continue to strengthen the impact of health programmes for children, advocate for the protection of children’s rights, help meet children’s basic needs, and expand the opportunities for children to reach their full potentials.

On behalf of the Joint Coordinating Board, I would like to warmly welcome UNICEF as a new co-sponsor of the Special Programme for Research and Training in Tropical Diseases (TDR).

UNICEF brings to TDR a unique field perspective on the infectious diseases that affect the poorest populations worldwide, and a growing technical expertise which will strengthen the Special Programme. At a time when TDR is consolidating its plans to develop improved solutions to diseases which continue to be neglected by the international community, the arrival of UNICEF as a co-sponsor is timely and promising.

Together with the other TDR co-sponsors (the World Bank, UNDP, WHO), JCB looks forward to collaborating with Dr. Pascal Villeneuve and other UNICEF friends.

Jean Larivière M.D.
Chairman, TDR/JCB
December 2003
Carlos Morel: an appreciation

As many readers will be aware, Dr Carlos Morel, TDR’s director since 1998, departed TDR in December 2003 and returned to Brazil. Below, Dr Asamoa-Baah provides an appreciation of Dr Morel’s significant contribution to TDR.

I was privileged to be serving as Executive Director in WHO headquarters throughout the duration of Carlos Morel’s tenure and have a special attachment to TDR, considering myself ‘part of the family’, as prior to assuming my current post I had a close and rewarding relationship with TDR, serving on the programme’s Scientific, Technical and Advisory Committee for a number of years. Now, as I look back on Carlos’ duration as Director of TDR, I am reminded of the words of Henry Wordsworth Longfellow; “Let us then be up and doing; With a heart for any fate; Still achieving, still pursuing; Learn to labour and to wait”.

Carlos played an instrumental role in driving TDR forward in many areas. One of the elements that he oversaw was the realization of the need for a truly robust, evidence-based mechanism to add diseases to TDR’s portfolio – and to begin to drop those diseases that had been successfully overcome and that were rapidly diminishing in significance as global public health problems. This resulted in the development of a ‘sunrise’ and ‘sunset’ system for diseases which is beginning to be implemented. The programme embraced two new diseases, dengue and TB, into its disease portfolio, each bringing new challenges and new opportunities.

When resources are scarce it is necessary to limit and prioritize investments, in time, money and goals. Carlos undertook this challenge enthusiastically with characteristic Brazilian verve, skilfully guiding TDR through a challenging, and at times painful, restructuring process. Introducing a new strategy, better tuned to prevailing global needs and conditions, devising new administrative and management systems more appropriate to meet changing operational systems, and introducing innovative monitoring and evaluation mechanisms to help measure real progress. Moreover, research and development has a fundamental, ‘long-term’ essence about it, which does not fit well with the prevailing need for short-term, visible results demanded by politicians and those facing continuing health crises. Carlos rose to the challenge, ably convincing many that research and development must be an essential component, and an integral part, of most health interventions if they are to be truly sustainable.

TDR’s new prioritization framework was based on that devised by the Global Forum for Health Research (GFHR) – itself a spin-off from TDR in the late-1990s. TDR convened panels of leading interdisciplinary experts from around the globe to adapt the mechanism to TDR’s special and unique needs. The result was a progressive strategy based on a comprehensive review of needs and opportunities, one which was extremely well received within the scientific and tropical disease research communities and one which has already spawned several imitations.

TDR has played a pivotal role in establishing new agencies with specific mandates to tackle neglected diseases, such as the Medicines for Malaria Venture, Global Alliance for TB Drug Development and, most recently, the Foundation for Innovative New Diagnostics. TDR is working with these new entities to focus available resources and efforts towards the accelerated development of urgently needed new diagnostics and therapeutic drugs. Carlos also ensured that TDR continued to work closely with the control community, notably Roll Back Malaria, Stop TB, and the newly-established Global Fund to Fight AIDS, TB and Malaria.

Carlos’ time at TDR witnessed major scientific breakthroughs which offer tremendous promise for the future, such as the unveiling of the genomes of several parasites and vectors, which creates huge potential for the development of new and sustainable weapons and interventions against TDR target diseases. TDR-supported efforts also brought success in the field of drug development (the registration of new drugs for malaria and leishmaniasis), field-based intervention mechanisms (such as the hugely successful community-directed treatment for onchocerciasis, now being expanded to cover other diseases), and a markedly successful programme of institutional and human resource capacity building in disease endemic countries. In addition, TDR took pioneering steps in areas related to its core activities, such as the area of ethics in biomedical research.
As a valuable member of the WHO Communicable Diseases (CDS) Senior Management Group, Carlos helped to maintain a balanced view of research and control efforts. Whenever times were difficult or discussions became intense, Carlos almost invariably had a Brazilian anecdote or proverb that not only succinctly encapsulated the state of affairs, but usually helped meetings to flow smoothly onward.

With Carlos’ tenure at TDR unfortunately curtailed before his vision could really metamorphose into the reality that he was striving for, I wish him and his family well and every success upon their return to Brazil, together with the new ventures and enterprises that await them there.

Dr A. Asamoah-Baah.
ADG, CDS

### STOP PRESS

A selection process, involving all TDR co-sponsors and the Joint Coordinating Board, is under way to identify a successor to Dr Morel. Until this process is completed, Dr Rob Ridley will take up the position of Director ad interim.
There is a strong need for vaccines to complement drug therapy for schistosomiasis. This was the conclusion of a meeting on schistosomiasis research with special reference to vaccine development, convened by TDR and the Philippine Council for Health Research and Development (PCHRD), and held at the Research Institute for Tropical Medicine (RITM), The Philippines, October 2003. Mathematical models indicate that drug treatment in combination with a vaccine would be beneficial, and would contribute to savings for the health care system as a whole, even if the protection afforded by the vaccine were not absolute.

Chemotherapy is currently the cornerstone of schistosomiasis control, especially following the reduction in price of the drug praziquantel seen in the last decade. Use of this drug has already led to a dramatic reduction of morbidity in endemic areas. However, this very success has fostered the widespread misconception that schistosomiasis is less serious than other infectious diseases in tropical countries and that further research is not a priority.

It was felt that a far more complete assessment of the impact of the disease in endemic populations is needed, particularly with regard to school-age children, avoiding the narrow perspective of organ malfunction only. Estimations of impact of schistosomiasis are based on DALY (disability adjusted life year) analysis. Schistosomiasis has far greater impact on health status than current burden of disease estimates suggest, especially considering its sequelae such as anaemia, growth retardation and impaired cognitive development. In addition, a serious limitation of the chemotherapy-based strategy is “rebound morbidity”, following reinfection.

At this point in time, there are only two serious vaccine candidates - Sh28-GST and Sm14-FABP. The former has reached the stage of large-scale clinical validation while the latter is in the process of industrial scale-up. Despite the considerable sums spent on developing and validating schistosome antigens, the current model vaccines are not perceived to be sufficiently protective and are characterized by irreproducible efficacy. Difficulties in scaling up production according to GMP standards have turned out to be a main obstacle, and the feasibility of GMP-grade production is now an important criterion in assessing vaccine candidates.

Most scientists in the field are, however, convinced that it is possible to develop a vaccine against this complex metazoan parasite. There are a number of reasons for this. Human populations in endemic areas invariably develop some degree...
of natural protection, while mice can be afforded 80% protection by immunization with irradiated cercariae. A transmission-blocking vaccine developed for use in Chinese water buffaloes was considered a short-cut to the human vaccine that could have an impact within the next few years. On the other hand, current antigens and prototype vaccine formulations induce <50% protection in model systems, though expectations of finding additional candidates through mining the expanding genomics databases1 and through proteomics analysis are justifiable.

Although there is lack of consensus regarding the desired type of immune response, and the protective responses evident in people are not necessarily those that would be elicited by a potent vaccine, the next research issues should be on the mechanisms of human resistance to the disease and the identification of antigens to which infected people respond. Identification of antibody isotypes and cytokine correlates of resistance and susceptibility in human populations is a key approach to establishing the acceptability of vaccine antigen candidates. Some antigens have been shown to require a Th2-type response, others a Th1-type response. We now have a basis for rational selection of the partially-protective antigens available, e.g. Sh28-GSTm Sm14-FABP, Sm97-paramyosin, Sm37-GAPDH, Sm-p80 calpain and Sm/Sj TPI. Of great interest in this connection is the new line of adjuvants becoming available, with well-characterized effects for modulation of human immune responses.

A vaccine would contribute to reduction of schistosomiasis morbidity through induced immuno-modulatory responses leading to reduced worm burdens, reduced egg production (anti-fecundity) and reduced viability of eggs (anti-embryonation). The objective should be to develop vaccines that can reduce or delay the development of morbidity after intermittent rounds of chemotherapy. Use of chemotherapy followed by vaccination would not only mitigate disease manifestations but could also result in reduced transmission. However, a strategy of chemotherapy plus vaccination would increase the total costs of disease control, at least initially.

Vaccine development should be re-emphasized using a coordinated approach to reposition vaccination within the totality of disease control. It was decided that a network be created to raise funds and act as a clearing house for work on all aspects of schistosomiasis vaccine development from genetic informatics to clinical trials.1

1 Two schistosome genomes have recently been sequenced:
Tsetse genomics: an international Working Group comes together

An international Working Group to investigate the status of *Glossina* genomics and initiate activities that might eventually lead to a full genome sequencing project was brought together by TDR in January 2004. A fully sequenced *Glossina* genome would make a very significant contribution to vector control efforts in African trypanosomiasis.

Vector control is a major element in the control of African trypanosomiasis (see box), a disease which is on the increase. Treatment consists of old, often dangerous, drugs, to which there is increasing resistance. No new drugs are likely to be in use in the next 5-10 years, and vaccines are unlikely to be developed. So vector control based on insecticides, targets and traps will be important in the control of African trypanosomiasis for the foreseeable future, and it is essential that this is supported by a strong scientific base that a *Glossina* genome sequence would contribute to.

The Working Group members’ expressed strong commitment to the genome sequencing project and expressed their willingness, as an International Partnership, to move such proposals forward. Other prominent members of the global vector biology community have also voiced strong support for an International Glossina Genomics Initiative (IGGI).

The mission of the IGGI is to:
- Enhance trypanosomiasis control by developing resources for research on the biology of *Glossina*, including studies on population genetics, host-pathogen interactions, and the genetics of vector competence.
- Stimulate new vector control initiatives such as development of targeted insecticides and studies on the host-seeking behaviour of *Glossina*.
- Increase the size and impact of the *Glossina* research community.
- Develop research resources including access to them.
- Train and build capacity in disease endemic countries.

The Working Group decided on a strategy based on the genomic resources currently available, which include 65 000 expressed sequence tags (ESTs) and a bacterial artificial chromosome (BAC) library for *G. m. morsitans*.

In phase I of the strategic plan, there will be a pilot feasibility study which will last until September of this year. Initial work will include constructing a BAC library, and BAC end sequencing and analysis, for *G. m. morsitans*; and identifying, and partially sequencing and analysing, B chromosome-containing BAC clones. Work will also begin on a physical mapping project, and on *G. palpalis*.

These phase I studies are intended to address comparative analysis between the two species using EST and full length cDNA data.

During phase II of the project, from 2004 to 2006, in-depth full length cDNA construction, sequencing and analysis will be undertaken for *G. m. morsitans* and *palpalis*. There will be further BAC work for *G. m. morsitans*, and the complete set of chromosomes and location of genes will be determined. Phase III of the project, 2005-2006, will see completion of the full genome sequence.

First however, funding for the IGGI has to be found. Initially, different members of the Working Group are seeking short-term funding through submission to a variety of possible funding bodies. For phase III of the project, the strategy and partnerships for funding will be discussed at the October 2004 meeting of the Working Group. In the meantime, activities will begin according to the roadmap developed at the January meeting.
For many years, researchers have assumed that an intervention deemed efficacious within clinical trials will be easily transmitted to the reality of control operations. Unfortunately, this is not the case; many examples can be given of effective disease control products which remain on the shelf, never reaching their full potential impact on burden of disease. Take the drug praziquantel for treatment of schistosomiasis, for example. Despite a new lower price, it is still not widely used in Africa, the continent with the highest burden of this disease.

The term ‘implementation research’ (IR) was first used by TDR in its strategy for 2000-2005 (see TDRnews, June 2000), to address the issue of how to effectively deploy specific tools/interventions within the real-world health services. A concept paper on implementation research has now been developed, for which TDR’s Scientific and Technical Advisory Committee (STAC) defined the framework, including the criteria (e.g. focus on process and outcome indicators) and general operating principles (e.g. rapid and active response to needs of disease control). STAC recommended that the issue of access be de-coupled from the question of health impact because, although both are important, they generally require different study designs and need to be measured over different time scales.

Basically IR will answer two types of research question. Firstly, the question of how to implement and ensure effective access by those in need; this is the next logical step for products in the TDR research pipeline that are ready for implementation. For example, TDR helped take rectal artesunate through to registration, and now is conducting research on strategies and impacts of deployment of this drug formulation in highly endemic malarious areas. Similarly, research to develop cost-effective delivery strategies for miltefosine, another recently-registered TDR product, for treatment of leishmaniasis, is ongoing.

Secondly is the question of how to bring interventions to scale within the context of the health system constraints in endemic countries. This question relates to tools that have been developed by TDR in the past and which, despite having become cornerstones of disease control, still face major obstacles to large-scale and sustained access. For example, among other things, IR is being conducted on drug delivery strategies for lymphatic filariasis elimination in urban areas (i.e. strategies for delivery of single dose DEC or ivermectin, with or without albendazole), and on strategies for improved delivery of praziquantel for schistosomiasis at community level.

IR can be used as a tool to optimize control appropriately, to contribute to the initiatives of many programmes, and to establish a closer relationship between scientists and control staff. For example, the initiatives of the Global Fund to Fight AIDS, Tuberculosis and Malaria, and of programmes related to the United Nation’s Millenium Development Goals can extensively benefit from implementation research.

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\text{Health workers carrying out implementation research on mass drug administration for lymphatic filariasis in India.}
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\[\text{WHO/TDR/Drump}\]

\[\text{1 Implementation Research in TDR: conceptual and operational framework. Document number: TDR/IDE/SP/03.1.}\]
The Vector Control Research Centre (VCRC) was established at Pondicherry in India in 1975, under the auspices of the Indian Council of Medical Research (ICMR). Coincidentally, this was the same year that TDR came into existence. Initially, the VCRC had a core group of about a dozen scientists, and its infrastructure was established with the financial and administrative support of the ICMR.

In the early days, the major work of the Centre was in integrated vector control with a focus on filariasis. This attracted some international recognition. A WHO team visited the Centre in 1976 and recommended studies on vector biology and control. Subsequently, in 1985, VCRC was designated as WHO Collaborating Centre for Research and Training in Integrated Methods of Vector Control. WHO supported the short and long-term training of 13 VCRC staff members in the fields of vector biology and control, parasitology, molecular biology, entomology, bio-pesticides and epidemiology. This helped the Centre to gain expertise and become self-reliant.

A particular strength of VCRC is its willingness to accept change in focus and priorities. Over time, its key performance areas have shifted to topics such as operational research (giving the opportunity to help solve problems in the control of vector borne diseases), molecular diagnostics, development of sustainable and cost-effective control tools, development of decision-making tools, and development of human resources. The Centre has directed its research activities towards developing products, methods and strategies to control vector borne diseases.

The relationship with WHO/TDR has covered a range of activities from research, human resources development, product evaluation and consultancy, to development of training materials and policy formulation. In the course of time, this investment has paid off handsomely, and today the VCRC is a leading partner of WHO/TDR. This is clearly manifest through:

- the wide range of research projects pursued by VCRC (to date, 40 with WHO/TDR support)
- the involvement of a number of VCRC scientists as consultants, advisors, and members of expert committees
- the nomination of VCRC as the first training centre for the International Course on Comprehensive Vector Control
- the great demand for VCRC as destination for WHO Fellows from other countries.

Apart from WHO/TDR, the VCRC has had close links with WHOPES (the WHO Pesticide Evaluation Scheme) and the WHO Regional Office for South-East Asia. Under WHOPES, 31 compounds have been evaluated in phase I and II trials for activity against disease vectors. Financial support for VCRC activities comes from a variety of sources (including ICMR and other national science agencies such as the Department of Science and Technology, and the Department of Biotechnology) and the Centre closely interacts with international agencies (including the Welcome Trust, London School of Hygiene and Tropical Medicine, Liverpool School of Tropical Medicine, Erasmus University, the US Centers for Disease Control) in carrying out research in the fields of epidemiology, modelling and filariasis elimination.

VCRC’s active role in filariasis elimination\(^1\) has been recognized and the Centre has now been designated WHO Collaborating Centre for Research and Training in Lymphatic Filariasis and Integrated methods of Vector Control.

Human resources development is an important activity for VCRC. Four regional/international training courses on Comprehensive Vector Control have been conducted with the support of WHO, and a total of 86 participants from eight countries have been trained. Thirteen national/international workshops on filariasis and vector control have been conducted in collaboration with WHO, strengthening the skills and performance of staff from various national control programmes. So far, 15 VCRC scientists have been trained outside India while eight VCRC scientists have served as members of WHO steering committees or as consultants and advisors to WHO in vector control.

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\(^{1}\) http://www.pon.nic.in/fil-free/vcrc/da5.html
An MSc course in medical entomology was offered by VCRC for the first time in India, and so far 83 students have successfully completed the course. Currently a diploma course in medical entomology is being conducted to benefit public health personnel in state and central government services.

A seven-member team from TDR and its Joint Coordinating Board (JCB) visited the VCRC laboratories and field sites of TDR-supported projects in June 2003. This team especially appreciated the interaction between VCRC and the Directorate of Public Health and the Government of Tamil Nadu, and the utilization of research findings in the programmes. Team members acquainted themselves with the wide range of VCRC activities in research and human resources development through formal presentations by VCRC scientists and discussions in the laboratories. Possible lines of research in drug development, and the role of vector control in disease control programmes and modern diagnostics, were discussed. Visits to the field sites of research programmes supported by TDR gave an opportunity for the team members to interact with drug distributors for filariasis elimination, patients, and the community. The process of mixing diethylcarbamazine powder (antifilarial drug) with salt to eliminate lymphatic filariasis was demonstrated and discussions were held with members of a voluntary organization in a village setting on their participation in the programme.

JCB members expressed the view that TDR/VCRC collaboration has been a clear success, as indicated by VCRC’s competitiveness in generating funds, success in human resources development, and contributions to programme strategy and policies in the WHO South-East Asian region.

**Contributions of VCRC to research and control of vector borne diseases**
- 591 original research articles, 30 unpublished reports
- 9 vector control products developed
- 7 patents registered
- 9 strategies for disease vector control developed and transferred
- 4 disease prediction models developed
- 4 master plans for mosquito control developed and transferred to cities
- 4 reference cells set up at VCRC linking research with operational activities
- human resources developed: 32 PhDs, 83 MScs in medical entomology, 16 diplomas in medical entomology, 256 short-term trainees

**Services offered by VCRC**
- Mosquito identification
- Mosquito rearing and colonization
- Source of mosquito blood meal
The South-South Initiative (SSI) in tropical diseases research that began in 2001 has now launched its own website (www.ssi-tdr.net). This initiative is based on the rationale that, although many disease endemic countries (DECs) have cutting-edge expertise in different research areas, this potential is not fully exploited due to lack of opportunities for sharing information and expertise among DEC institutions.

So the overall aim of the Initiative is to promote interaction and collaboration between researchers in DECs in the application of scientific and technological advances to the tropical diseases in the TDR portfolio. More specifically, the aim of the SSI is to help develop/promote collaborative research proposals, training and capacity building in cutting-edge technologies, common protocols, the sharing of information and reagents, and a network for research groups in DECs. Now, with the website up and running, this will be much easier. The Site is a mine of information about bioinformatics resources, training opportunities and training centres, networks, databases, and links through to a host of handy protocols and tools, e.g. in molecular methods and sequence analysis, and to online training materials in bioinformatics.

How does SSI function? Whereas the Initiative is hosted by TDR, the website is hosted by the Regional Bioinformatics Training Centre at Mahidol University, Thailand, and the coordinating committee, which manages the Initiative, is drawn from three regions – Africa, Asia, and Latin America. This committee develops an annual plan of activities and identifies opportunities for research collaborations, training, networking and funding. Research proposals developed with the help of SSI are submitted by the principal investigators to the Pathogenesis and Applied Genomics (PAG) Committee in TDR, and applications for funding of training activities are also submitted to PAG, or to the Research Strengthening Group in TDR.

For further information, visit www.ssi-tdr.net.
TDR’s strategy for 2000-2005 places renewed emphasis on social research to help elucidate the social, economic, political and behavioural determinants that affect the emergence, resurgence, persistence, and control, of infectious diseases. There is increasing evidence that many of these determinants are “transnational”, and linked to large-scale changes which reverberate from global to national and subnational levels. “Upstream” basic social research is needed to reach a better understanding of the phenomena involved. TDR’s Steering Committee for Social, Economic and Behavioural Research has developed a research agenda (see TDRnews October 2001) and, for the third consecutive year, is calling for research proposals focusing on globalization, inequality of access and infectious diseases. While TDR-supported research on these issues is already ongoing in a number of sites, new grant applications have been invited, to be submitted before 26 February 2004.

A growing body of literature addresses the impact of globalization on health, but less is known about the linkages between globalization and infectious diseases. Globalization has been defined in a number of ways, including as a “set of processes changing the nature of human interaction across a wide range of spheres including the economic, political, social, technological and environmental”¹. There is growing concern that globalization may affect the epidemiology of infectious disease. Some of the linkages are obvious, others need to be established through well-designed social research. While it is clear that the increase in global trade and travel is bringing about marked changes in the distribution of people and pathogens, it is less well understood which large-scale forces lead to changes in infectious disease epidemiology among poor and marginalized populations. One sequence of interacting factors may be that, in a given society, globalization affects the distribution of wealth and power, thus leading to social inequalities. These in turn increase risk, which may eventually result in a higher burden of infectious disease, notably among the poor and marginalized.

Other TDR-supported activities complement this research agenda. A workshop focusing on the Latin American situation was held in Angra dos Reis, Brazil, in October 2003, prior to the 7th Latin American Congress of the International Forum for Social Sciences and Health (IFSSH). Funded by TDR and organized by the Laboratorio de Ciencias Sociales (LACSO, Universidad Central de Venezuela, Caracas) and the Fundação Oswaldo Cruz (Rio de Janeiro), the workshop brought together more than 20 scholars from across Latin America. Presentations on a wide range of topics were enriched by group discussions. The workshop produced a draft research agenda on the effects of globalization and social inequalities on infectious diseases. The proceedings will be published in a special issue of Cadernos de Saúde Pública, by the National School of Public Health of the Fundação Oswaldo Cruz, Brazil.

¹ This definition is found in Globalization and infectious diseases: a review of the linkages, a TDR commissioned review to be published in 2004, in the series on Special Topics in Social, Economic and Behavioural Research.
Latest Grants

Research in Pathogenesis and Applied Genomics

The TDR Committee on Pathogenesis and Applied Genomics (PAG) met in Recife, Brazil, in September 2003. The projects listed below were selected from among a large number of applications received from investigators worldwide.

New grants in Pathogenesis and Applied Genomics

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

- A30406 MARIANGELA CARNEIRO, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil. Longitudinal study of symptomatic Leishmania chagasi infection in urban area of Minas Gerais State, Brazil. (Budget: US$ 18 000)
- A30378 SUNGAE CHO, Yonsei University Medical Center, Seoul, Republic of Korea. Identification of HLA-A 0201 restricted CD8+ T cell specific peptide epitopes encoded from whole M. tuberculosis genome. (Budget: US$ 35 000)
- A30407 JOHN CHARLES KIBOKO ENYARU, Livestock Health Research Institute (ILRI), Tororo, Uganda. Evaluation of the epidemiological significance of an animal reservoir in gambiense sleeping sickness in NW Uganda. (Budget: US$ 34 020)
- A30408 GIOVANNI GAZZINELLI, Centro de Pesquisas Rene Rachou, FIOCRUZ, Belo Horizonte, MG, Brazil. Role of S. mansoni-derived antigens in the regulation of cell cycle progression and lymphoproliferation. (Budget: US$ 35 000)
- A30358 SUMALEE KAMCHONWONGPAISAN, National Center for Genetic Engineering and Biotechnology, Pathumthani, Thailand. Integrated genomic & proteomic studies for identification of potential targets of arte misinin and derivatives. (Budget: US$ 25 000)
- A30235 LUC JEAN G. VANHAMME, Free University Brussels, Brussels, Belgium. Characterization of trypanolytic activity of human apolipoprotein L1 and its neutralization by Trypanosoma rhodesiense and gambiense. (Budget: US$ 30 000)

New South-South collaboration grants in Pathogenesis and Applied Genomics

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

- A30380 IKRAM GUIZANI, Institut Pasteur de Tunis, Tunis, Tunisia. Post kala-azar dermal leishmaniasis (PKDL): molecular epidemiology and prognostic markers. (Budget: US$ 61 740)

Renewed grants in Pathogenesis and Applied Genomics

These projects were funded in 2002 and are being renewed for a further year following successful progress made towards meeting the objectives during the first year.

- A20369 OSCAR EDUARDO CAMPETELLA, Universidad Nacional de General San Martin, Buenos Aires, Argentina. RNA-binding proteins involved in post-transcriptional regulation of gene expression in trypanosomes. (Budget: US$ 32 850)
- A20393 WALDEREZ ORNELAS, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil. Characterization of trypanosomes. (Budget: US$ 30 000)
- A20392 KENNETH J. GOLLOB, Univers. Federal de Minas Gerais, Belo Horizonte, Brazil. Determination of functional activity and TCR usage of CD4-CD8-T cells in human cutaneous leishmaniasis. (Budget: US$ 28 000)
- A20382 GEORGES ER GRAU, Universite de la Mediterranee, Marseille, France. ABO1 gene and cerebral malaria: role in the pathogenesis and relevance in genetic susceptibility. (Budget: US$ 32 850)
- A20289 EMANUELA HANDMAN, Walter and Eliza Hall Institute, University of Melbourne, Australia. Characterization of a mucin-like proteophosphoglycan, a Leishmania major amastigote virulence factor. (Budget: US$ 35 000)
- A20294 NADIRA D KARUNANAYAKA, University of Colombo, Faculty of Medicine, Colombo, Sri Lanka. Chemical and antigenic characterisation of bioactive parasite molecules involved in paroxysms of P. vivax malaria. (Budget: US$ 35 000)
- A20317 KRISTER KRISTENSSON, Karolinska Institute, Div. Neurodegenerative Disease Research, Stockholm, Sweden. The role of chemokines and chemokine receptors in trafficking of Trypanosoma brucei across the blood-brain barrier. (Budget: US$ 21 250)
made towards meeting the objectives and if sufficient funds are available.

New grants in Molecular Entomology

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

A20363 MARIANO JORGE LEVIN, Instituto de Investigaciones en Ingeniería Genética y Biología Molecular, 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$ 43 000)

Research in Molecular Entomology

The projects listed below were selected by the TDR Committee on Molecular Entomology (BCV), at its meeting in Recife, Brazil, September 2003, from among a large number of applications received from investigators worldwide.

A20357 AHMED OSMAN EGIZA, State University of New York at Buffalo, Department of Microbiology, New York, USA. Mechanistic studies on male-induced female-specific gene expression in Schistosoma mansoni. (budget: US$ 33 000)

A20399 WILLIAM 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$ 15 000)


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

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Renewed grants in Molecular Entomology

The following projects were funded in 2002 and are being renewed for a further year following successful progress made towards meeting the objectives.

- A10435 ALESSANDRA DELLA TORRE, Università di Roma “La Sapienza”, Rome, Italy. Molecular and cytological characterization of Anopheles gambiae molecular forms and evaluation of their role as malaria vectors. (budget: US$ 35 000)
- A20338 GEORGE DIMOPOULOS, Imperial College of Sciences, Technology and Medicine, London, UK. Genome expression analysis of mosquito salivary gland function and characterization of specific promoters. (budget: US$ 34 624)
- A20269 QI 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$ 18 900)
- A20330 LIZETTE KOEKEMOER, National Health Laboratory Services, Johannesburg, South Africa. The role of mono-oxygenases in insecticide resistant Anopheles funestus Giles. (budget: US$ 35 900)
- 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$ 32 200)
- A10360 DOUGLAS NORRIS, Johns Hopkins University, Baltimore, USA. Population and genomic approaches to insecticide resistance in Anopheles gambiae s.l. in Mali. (budget: US$ 43 996)
- A10708 SCOTT LESLIE O’NEILL, University of Queensland, School of Life Sciences, Brisbane, Australia. Characterization of Wolbachia as a tool to modify insect vector competence. (budget: US$ 34 810)
- A10424 ANA MARIA PERALTA de MERIDA, Universidad del Valle de Guatemala, Guatemala City, Guatemala. Population genetics of Aedes aegypti in Chiapas (Mexico) and Central America. (budget: US$ 30 655)
- A10410 ANN SODJA, Wayne State University, Detroit, USA. Isolation and characterization of an antena-specific gene in Aedes aegypti. (budget: US$ 40 000)
- A10429 GUIYUN YAN, State University of New York, Buffalo, USA. Assessing the spread rate of introduced genes in Anopheles gambiae. (budget: US$ 40 000)
- A10402 LAURENCE ZWIEBEL, Vanderbilt University, Nashville, USA. Isolation and characterization of odorant receptor genes from Aedes aegypti mosquitoes. (budget: US$ 39 750)

Social, Economic & Behavioural Research (SEB)

The projects listed below were selected by the TDR Committee on Social, Economic & Behavioural Research (SEB), at its meeting in Recife, Brazil, September 2003, from among a large number of applications received from investigators worldwide.

- A030419 KAMOLNETR OKANU-RAK, Mahidol University, Faculty of Tropical Medicine, Bangkok, Thailand. Factors associating with completion & default among DOTS and self-administered therapy (SAT) for treatment of TB. (budget: US$ 24 999)
- A10399 QIAN WANG, Sichuan Institute of Parasitic Diseases, Chengdu, China. Access constraints of Tibetan herdsmen communities with respect to tuberculosis care. Sichuan, China. (budget: US$ 24 580)
- A30368 CHIARA I. ANUMUDU, University of Ibadan, Ibadan, Nigeria. Socio-economic factors in drug resistant malaria in Nigeria: linking molecular epidemiology with social analysis. (budget: US$ 5000)
- A30367 ANNE J. MILLS, London School of Hygiene and Tropical Medicine, London, UK. Understanding health seeking behaviour in South Africa: implications for improving health equity. (budget: US$ 26 329)
- A30339 QIANG SUN, Shandong Medical University, Jinan, China. Study on the patient’s adherence to directly observed treatment for tuberculosis in China. (budget: US$ 24 350)
- A303028 XIAO-NONG ZHOU, National Institute of Parasitic Diseases, Shanghai, China. Biosocial & environmental risks related to disease burden of schistosomiasis in the Yangtze river basin, China. (budget: US$ 40 300)
- A30276 YANG WANG, Chongqing Medical University, Chongqing, China. Comparing access to TB diagnosis between migrants and residents in Chongqing, China. (budget: US$ 24 890)

New grants in Social, Economic & Behavioural Research

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

- A10399 QIAN WANG, Sichuan Institute of Parasitic Diseases, Chengdu, China. Access constraints of Tibetan herdsmen communities with respect to tuberculosis care. Sichuan, China. (budget: US$ 24 580)
- A30368 CHIARA I. ANUMUDU, University of Ibadan, Ibadan, Nigeria. Socio-economic factors in drug resistant malaria in Nigeria: linking molecular epidemiology with social analysis. (budget: US$ 5000)
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Renewed grants in Vaccine Discovery Research

The projects below were selected from among the large number of applications received from investigators worldwide. TDR wishes to thank members of the Vaccine Discovery Research Committee and external reviewers for their critical assessments and contributions to the selection process. Unsuccessful investigators are encouraged to re-compete next year.

Vaccine Discovery Research

The projects below were selected from among the large number of applications received from investigators worldwide. TDR wishes to thank members of the Vaccine Discovery Research Committee and external reviewers for their critical assessments and contributions to the selection process. Unsuccessful investigators are encouraged to re-compete next year.

**New grants in Vaccine Discovery Research**

- **A30112 MICHELLE WYKES**, Queensland Institute of Medical Research, Brisbane, Queensland, Australia. Regulation of B and T cell memory to MSP1-19. (budget: US$ 38 208)

- **A30133 SEDDIKEH ZAKERI**, Pasteur Institute of Iran Tehran, I.R. Iran. The analysis of genetic variation in the malaria vaccine candidate P-MSP-1 gene and evaluation of its immune response. (budget: US$ 15 000)

**Renewed grants in Social, Economic & Behavioural Research**

These projects were funded in 2002 and are being renewed for a further year following successful progress made towards meeting the objectives.

- **A30093 CHAMPAKLAL CHAUHAN**, International Centre for Genetic Engineering and Biotechnology, New Delhi, India. Study of immunogenicity and protective efficacy of rodent homologs of P. falciparum merozoite surface protein-9. (budget: US$ 36 200)

- **A30125 LIM MIAO**, Fourth Medical University, National Defence University, Beijing, China. Protective immune response induced by the combination of P. falciparum MSP1 and AMA+ based protein, DNA and rMVA vaccine. (budget: US$ 23 000)

- **A30121 SUSILOWATI TANA**, Universitas Indonesia. Factors contributing to the resilience of IDPs, and how current social inequalities affect the persistence of TB. (budget: US$ 25 000)

- **A30144 BIAO XU**, Fudan University, Shanghai, China. Does TB care reach the poor? Study of the TB control programme in two counties in rural China. (budget: US$ 24 990)

- **A30158 ABHY SATOSKAR**, Ohio State University, Colombus, USA. Protective immunity from MSP1-2.9 and pre-erythrocytic stage antigen. (budget: US$ 37 700)

- **A30161 MICHAEL FRANCIS GOOD**, Queensland Institute of Medical Research, Brisbane, Australia. Targets for malaria cell mediated immunity from MSP1 and other proteins. (budget: US$ 45 000)

- **A30177 WEIQING PAN**, Second Military Medical University, Shanghai, China. Construction and immunogenicity of combined malaria vaccine containing PfCP-2.9 and pre-erythrocytic stage antigen. (budget: US$ 37 700)

- **A30177 WEIQING PAN**, Second Military Medical University, Shanghai, China. Construction and immunogenicity of combined malaria vaccine containing PfCP-2.9 and pre-erythrocytic stage antigen. (budget: US$ 37 700)

- **A30181 VIRANDER SINGH CHAUHAN**, International Centre for Genetic Engineering and Biotechnology, New Delhi, India. Study of immunogenicity and protective efficacy of rodent homologs of P. falciparum merozoite surface protein-9. (budget: US$ 36 200)


- **A30204 BIAO XU**, Fudan University, Shanghai, China. Does TB care reach the poor? Study of the TB control programme in two counties in rural China. (budget: US$ 24 990)

- **A20029 CHAMPAKLAL CHAUHAN**, International Centre for Genetic Engineering and Biotechnology, New Delhi, India. Study of immunogenicity and protective efficacy of rodent homologs of P. falciparum merozoite surface protein-9. (budget: US$ 36 200)

- **A20107 B. FOLASADE IYUN**, University of Louisville, Pan African Studies Department, Kentucky, USA. The growing crisis of tuberculosis in Nigeria: a case study of Oyo State. (budget: US$ 37 906)
Publications

• Report of the Scientific Working Group on Insect Disease Vectors and Human Health, 12-16 August 2002 (TDR/SWG/03.1).

TDR Scientific Working Group meeting reports provide up-to-date reviews of the present situations and actual control needs, with recommendations for the overall strategic and scientific directions of research, capacity and partnership building for the next five years. Each meeting is attended by 30-40 scientists, including many from disease endemic countries.

• Drugs against parasitic diseases: R&D methodologies and issues. Discoveries and drug development. Eds: Fairlamb AH, Ridley RG, Vial HJ (TDR/PRD/03.1). Now available in hard copy (see TDRnews No. 70, October 2003)

• The involvement of community-directed distributors of ivermectin in other health and development activities

(Report of a multicountry study; TDR/IDE/CDD/03.1).

Community directed treatment with ivermectin (CDTI) is currently the principal drug delivery strategy for onchocerciasis control. In this multicountry study, four research teams investigated the use of CDTI structures for other health interventions, such as for Expanded Programme of Immunization, and water and sanitation activities. Most health programmes were interested in building on the experiences and structures of CDTI and everyone was very much in favour of greater involvement of community directed distributors of ivermectin in additional health and development activities.

• Handbook on non-clinical safety testing

(TDR/PRD/NCT/04.1).

This Handbook is designed as an aid for scientists undertaking nonclinical safety testing for regulatory purposes during product development; it is broadly based on current safety testing guidelines including those of the Organisation for Economic Cooperation and Development (OECD). The Handbook will provide laboratories in disease endemic countries, and trainers throughout these nations, with the necessary technical aid for planning and implementing nonclinical safety testing programmes. The Handbook attempts to highlight the differences between drug, vaccine and traditional medicine development programmes.
• Implementation research in TDR: conceptual and operational framework (TDR/IDE/SP/03.1). See article on page 9.


A practical training manual covering the basic concepts and principles of scientific research, from the selection of objectives and study design, through the execution of studies and trials, to the analysis of data and presentation of results. The manual, which can be used in training courses or for self-instruction, is designed for young health scientists who are getting started in research and need to understand the basic steps in research design, including the way a research idea is translated into a feasible research proposal and the steps that must then be taken to implement the proposed study. Throughout the manual, principles and methods are illustrated with real data from research projects concerned with common problems in the health sciences. The core of the manual consists of eleven training modules, moving from an explanation of the basic principles of the scientific method through advice on the design of epidemiological, experimental and clinical studies, to chapters dealing with bias and confounding, the measurement of reliability, significance tests, and the establishment of association and causation.

• Schistosomiasis in the post-transmission phase (Acta tropica, Special Issue, 2000, 77 [1]; Giboda M, Engels D, Bergquist NR, eds).

Schistosomiasis is not always cured by treating the infection, and people may be left with the pathological effects of infection, e.g. fibrosis of the liver, for the rest of their lives. This ‘post-transmission’ schistosomiasis occurs in areas where transmission of the disease and re-infection is not a threat any longer – millions of people continue to suffer in formerly endemic areas where the infection has been eliminated as a public health problem. This volume contains global distribution figures and some fascinating historical notes on schistosomiasis; it paints a broad picture of post-transmission schistosomiasis, putting the challenges of elimination in perspective with pathological studies of late schistosomiasis.


This document summarizes the outcomes of 63 operational research projects conducted during ten years under the Small Grants Scheme funded jointly by the WHO Regional Office for the Eastern Mediterranean and TDR.

• Scaling up home management of malaria: from research to implementation (WHO/HTM/MAI/2004.1096; TDR/IDE/HMM/04.1)3

Large-scale research studies and pilot studies on the implementation of home management of malaria (HMM) have shown that scaling up HMM is both feasible and effective, and is already being practised on a limited scale in some African countries. The experiences and lessons learnt have been compiled in this handbook, which is intended to be a reference document to help define the mechanisms for scaling up HMM in the African region. The handbook is aimed at malaria control programme managers, malaria interagency coordinating committees, international donor organizations, nongovernmental organizations (NGOs) involved in malaria control, and research and training institutions.

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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.

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