Making a paradigm shift
The Bamako 2008 Global Ministerial Forum on Research for Health

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Liberia diary: ‘greening’ clinical trials in a remote site
Now, a drug trial of moxidectin, a potential drug for the eradication of onchocerciasis in Africa, to be conducted in Liberia and the Democratic Republic of Congo, is adding another dimension to the quest for sustainability – an environmental dimension.

The clinical trial site in Bolahun, Liberia, in a remote northern border region that was once the scene of civil war, offers the most dramatic example of the challenges involved (see page 19).

The trial site development in Bolahun has involved the construction of a major new research centre that will house the Phase III clinical trial activities. Capacity development at the Liberia trial site, as well as those in DRC, has largely been funded through a US$ 6 million donation from Wyeth Pharmaceuticals, owner of the moxidectin compound.

However, despite the generous donation, guaranteeing a power supply to the site has been an ongoing challenge.

The centre, soon to begin recruiting patients, currently is powered by diesel fuel. However, diesel power capacity could be unpredictable, due to the site’s remote location, (a 10-hour trip from Monrovia, partly over dirt roads in dry weather). Even though a backup generator has been installed, any interruption in fuel supply or failure of one of the generators could threaten the successful collection of data essential to the trial.

Also, once the trial is completed in three years’ time, there is no guaranteed budget for supply of fuel to continue powering the array of laboratory, clinical, ophthalmological and computer equipment, which could be used for further research or in the delivery of more routine health services.

In order to address such issues, TDR’s Annette Kuesel, who is coordinating the moxidectin research effort together with Fatorma Bolay of the Liberia Institute of Biomedical Research, developed a plan to provide solar power-based electricity to the centre.

Solar power generation capacity not only would assure the sustainability of the infrastructure investment in Bolahun for other trials for neglected tropical diseases, but it could potentially power existing facilities of a nearby health centre, and also Bolahun High School.

The high school, founded by monks in 1925 and a focus of Peace Corps volunteer activity in the 1960s and 1970s, has an interesting history. It had a national reputation for academic excellence before the war, and has recently been rebuilt thanks to the support of a network of distinguished alumni.

Kuesel recruited a master’s degree student to make detailed engineering plans for a photo-voltaic system sufficient to fuel the research and health centre and the school. Unfortunately, a donor has yet to be found.

The fact that the sturdy, modern centre was built with sun-dried mud bricks and that other “green” measures have been considered, such as solar-powered health waste disposal and re-use of biofuel waste from nearby banana and rice fields, make the Bolahun story a potential case study of efforts to “green” health research facilities in remote locales.

Charged by our Joint Coordinating Board to address climate change impacts and issues on neglected diseases, we find the Bolahun story one of the most palpable examples of how TDR can be a leader of innovation in the research sector. Learning from the Liberian experience, we can explore how to incorporate environmental and climate change mitigation features into our field and clinical research activities – supporting the global drive for sustainable development through our research work.

But becoming a model requires us to first complete our work in Bolahun. And that means locating donors for a 15KW solar power generation system.

Any takers, please tell us…

Elaine Ruth Fletcher
Managing Editor, TDRnews
Optimizing global health research ‘architecture’

Research policy actors are examining critical questions about how the global community can act on recent calls for massive new investment into a global R&D effort targeting neglected diseases.

The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPA), approved by the World Health Assembly in May 2008, has led to the creation of a major WHO task force on sustainable financing of research. This highlights the need to spend much more on such research.

Right now, only 3% of the US$ 160 billion spent globally on health research is invested in neglected diseases. Some argue this should quadruple to 12% over the next six years.

If funds of such an order of magnitude are to be leveraged then investors, whether private or public donors, need to be assured that the international organizations and NGOs engaged in research have coordinat ed mandates for action that optimize their efficient use of funds and can appropriately support regional and national efforts.

WHO-associated and other health research agencies have thus been called upon to improve coherence of programmes, or even consider a merger of certain international research efforts.1

This need to review global health ‘architecture’ was noted in the Bamako call for action at the close of the Global Ministerial Forum on Research for Health in November 2008.

In direct response to the Bamako call, WHO’s Executive Board, meeting in January, asked actors to “better align and coordinate the global health research architecture and its governance through the rationalization of existing global health research partnerships, to improve coherence and impact, and to increase efficiencies and equity.” 2

The matter is sure to also arise as the World Health Assembly considers approval of a new WHO research strategy in May. No single programme or agency can remain aloof to the questions being asked and the challenges posed. There are indeed multiple international research initiatives operating from WHO, involving other partners. And there are multiple NGO initiatives promoting research. Potential duplication in activities and administration needs to be examined. Just as donors are urged to “harmonize” activities, we need to examine ourselves and see how we are collaborating with our partners. However, any proposed reorganization must consider that the ultimate goal is to improve efficiency, responsiveness to scientific opportunity and the needs of developing countries – and not merely superimpose another layer of bureaucracy.

TDR is in a pivotal position in this debate. TDR’s special programme model of governance equally involves both developed and developing country governments. As TDR’s Joint Coordinating Board chairman has remarked, the co-sponsorship of TDR by several UN agencies makes the Programme responsive not to only WHO, but to the UN system more broadly. We believe that the maintenance of this governance model is crucial if developing countries are to play a pivotal role in global research for health, and if research is to remain accountable to high disease burden countries.

There will be furthered discussion of TDR’s position and role in research coordination and alignment at the next Joint Coordinating Board session, 15-17 June. It is important to bear in mind the good news inherent to this debate: that is the wave of interest in research for health, both at the global policy level and from developing countries. At the Bamako Forum, I spoke with the minister of health from Sierra Leone, a country recovering from civil war. He was adamant that development of research capacity was critical to health and development.

TDR is building such capacity on the ground. In this TDRnews issue, we feature efforts in Liberia and Uganda, where research investments are greeted with enthusiasm and involvement by policy leaders as well as local communities. Engaging and responding to country needs has to be kept in the forefront of our thinking. It is these efforts that will lay a good foundation for a research ‘architecture’ that is strong, stable and durable.

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**The Lancet** – Rectal artesunate can save lives of severe malaria patients

“A rectal application of the inexpensive antimalarial drug artesunate could save the lives of many people who develop severe malaria who live in the world’s remotest locations, e.g. rural Africa and Asia.”

NEW TB TREATMENT

**Drug trial meets patient enrolment target**

A pivotal Phase III trial of a shorter, 4-month course for tuberculosis (TB) treatment has taken a significant step forward after the enrolment quota of 1836 volunteer patients was reached at African study sites. The trial is testing a 4-month course of TB multidrug treatment including gatifloxacin against the standard 6-month multidrug TB course.

The trial, launched in 2005, aims to assess whether the new regimen is safe and as effective as the standard 6-month regimen. The achievement of the target sample size in October 2008 means that the final patients needed for the study will now complete treatment in the second quarter of 2009.

TB centres of the national TB control programmes in Senegal and Benin together with clinical and research institutions in Guinea, Kenya and South Africa are partners in the study, which is being conducted in collaboration with the European Commission (EC)-funded Ollotub Consortium. TDR provides co-sponsorship and funding, as well as technical oversight in collaboration with the Institut de Recherche pour le Développement (IRD), France.

In 2003, TDR and the Ollotub Consortium began a programme to develop and register a TB treatment containing gatifloxacin, an oral fluoroquinolone antibiotic with activity against Mycobacterium tuberculosis. In the Phase III trial involving adults under the age of 65, patients are randomly allocated to receive either the standard 6-month TB treatment or the shortened tested treatment (rifampicin + isoniazid + pyrazinamide + gatifloxacin for 2 months, followed by rifampicin + isoniazid + gatifloxacin for 2 months).

Because gatifloxacin has been associated with the problem of hypo- and hyperglycaemia, patients with a history of diabetes or abnormal blood glucose levels have been excluded from the trial. It is expected that the initial analysis of safety and efficacy will be conducted 1 year post-treatment, i.e. in mid-2010, followed by a final 2-year analysis. Should the initial 1-year analysis be positive, it is anticipated that a formal file for registration of a gatifloxacin-containing TB drug combination will be submitted to the United States of America’s Food and Drug Administration and other regulatory authorities in late 2010 or early 2011.


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TDR EVALUATION

**Does HMM reduce malaria mortality?**

TDR is to evaluate whether distribution of free artemisinin-combination therapies (ACTs) through home-based management of malaria (HMM) can reduce malaria mortality as well as morbidity.

The TDR research will be carried out in the context of a major US$ 20 million initiative to extend HMM, including ACTs offered free-of-charge, to some 10 million Africans in four countries. The initiative was launched 16 February in Nairobi, by the Canadian International Development Agency (CIDA) and Population Studies International (PSI), a Washington, DC-based NGO.

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These are the conclusions of a TDR-supported study published recently in *The Lancet*, “Pre-referral rectal artesunate to prevent death and disability in severe malaria: a placebo-controlled trial.”

The research was presented at the December 2008 meeting of the American Society of Tropical Medicine and Hygiene (for more details see page 30).
Over the next 2-3 years, the TDR scientists will monitor the impact of the home-based effort on ACT treatment to determine if indeed it reduces mortality from malaria.

What makes the TDR research ground-breaking is that the effectiveness of the home-based approach for delivering ACTs on child mortality has never before been monitored. ACTs also are not yet widely available in Africa, particularly for the most poor and vulnerable people.

Research has, however, demonstrated that prompt and effective treatment of uncomplicated malaria (usually with chloroquine) prevents an infection’s evolution to severe malaria and death.

If the health impact of delivering ACTs (free-of-charge) through HMM is significant, results would serve as a powerful catalyst for the expansion of such programs across sub-Saharan Africa.

The CIDA/PSI project will cover some 2.5 million people in each participating country. Community selection will be based on criteria such as high malaria burden and the existence of community-based health networks. TDR will evaluate impacts of the programme in a subset of the trial population in three countries. TDR scientist Franco Pagnoni, overseeing the evaluation, estimates that the project could potentially avert up to 11,000 child deaths in each of the four pilot areas.

HMM provides a regimen of pre-packaged, unit-dosed antimalarials along with associated health communication materials. WHO has adopted HMM as a cornerstone of disease-control efforts, particularly in Africa, where half or more of all malaria cases are treated at home.

Yet there remains “inadequate access to ACTs for such treatment,” according to the 2008 World Malaria Report.

Glossina Genome
Sequencing at 80% mark – completion planned in 2009

Researchers at the Wellcome Trust Sanger Institute have sequenced 80% of the *Glossina m. morsitans*, the tsetse fly species that is a vector of human African trypanosomiasis (HAT), in the context of a TDR-supported international genomics effort.

The International Glossina Genomics Initiative (IGGI) has now drawn up an implementation plan for complete sequencing of the *Glossina* genome by 2009, with sequence assembly to follow this year as well. The plans were discussed at IGGI’s sixth annual meeting in Mombasa, Kenya, during November 2008.

IGGI members have proposed that completion of the sequencing can be expedited by using a new sequencing technology that is more efficient and less expensive than conventional means, providing the estimated US$ 250,000 in funding needed for the effort is secured. The new 454 FLX sequencing technology was recently developed by Roche Diagnostics. IGGI is an international consortium that was convened by TDR in 2004 to accelerate genomics-based research on the *Glossina* genome.

HAT is estimated to infect about 300,000 people worldwide, with an additional 60 million people in 37 African countries considered to be at risk. The same species of tsetse fly also is a carrier of animal African trypanosomiasis (AAT), whose effects on agriculture have hindered economic development in rural areas and cost African farmers almost US$ 4.5 billion every year.

According to Yeya Touré, TDRs innovative vector control interventions leader, a fully sequenced genome would represent a significant contribution to current and future vector control efforts. This would happen in part by helping disease-endemic countries (DECs) to exploit the data to develop new vector control strategies. TDR aims to facilitate DEC involvement in genomics research through seed-funding of preparatory activities and support for regional training centers that would offer courses in bioinformatics and functional genomics.

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Eco-Bio-Social Research
Six countries test dengue interventions

A multi-country research effort in Asia designed to study dengue transmission and then test social and ecosystem-based interventions is launching its Phase II. Following the completion of the Phase I situation analysis, all six sites will initiate tests of various community-based management approaches in April. These are designed to address locally identified factors in disease transmission.

The initiative, funded by the EcoHealth Programme of the Canadian International Development Research Centre (IDRC), involves multi-disciplinary research teams at universities and research centres in India, Indonesia, Myanmar, the Philippines, Sri Lanka and Thailand.

The initiative has been designed to improve dengue prevention through better understanding of its ecological, biological and social (“eco-bio-social”) determinants.

Eco-bio-social research is a trans-disciplinary research concept that integrates research on environmental, vector-epidemiological (entomological) and social factors that make communities vulnerable to vector borne diseases such as dengue. The aim of such research is to develop inter-sectoral approaches to disease control, addressing issues that extend beyond traditional boundaries of health-sector activities.

In the current study, research teams are examining both effectiveness and community acceptance of locally developed vector control measures. For instance, in Yangon, Myanmar, teams will examine how use of natural predators and biological larvicides such as dragonfly nymphs and *Bacillus thuringiensis serovar israelensis* (Bti), as well as water covers, window curtains and waste control measures, may reduce vector densities. Stakeholder
drug safety

WHO/TDR establish Pregnancy Register

A new Global Pregnancy Register to collect epidemiological data on the impacts of new drugs for malaria, HIV and other major diseases on pregnant women is being established by the Making Pregnancy Safer Programme of WHO, TDR and several other WHO departments. The register will provide the evidence on drug safety in pregnancy from resource-poor settings of Africa, Asia and Latin America. The register will enable assessment of the risks and benefits of new drugs for HIV, malaria, leishmaniasis and other neglected tropical diseases, whose safety and efficacy in pregnant women have not been fully established.

Data on outcomes of such drug use are very scanty because pregnant women typically are excluded from clinical trials of new medications in order to protect them and their unborn children, says MO Islam, MPS director.

Thus for major and life-threatening diseases such as HIV or malaria, pregnant women are often treated with safe but potentially less efficacious medicines until cumulative evidence is gathered on the safety of newer first-line drugs, often over many years.

healthy pregnancies and their outcomes, along with data on pregnant women exposed to drug treatment,” Islam said. “The women not exposed to the drug of interest will act as controls, as it were, in comparison to women exposed to drugs of interest, enabling identification of any increased (or no increased) risk of birth defects due to a drug.”

The plans and funding for pilot testing of the register were approved at an informal consultation of the Malaria Pregnancy Register Protocol in Geneva, 7-8 November 2008. This was a joint meeting of TDR/MPS, the HIV Programme, the Quality and Safety of Medicines Programme and the Global Malaria Programme of WHO.

Pilot testing of questionnaires and methods to be used in the register are being implemented in 2009 in targeted health clinics of at least five African countries, prior to launching to scale. Development of systems for effective tracking of exposures to medicines, and awareness of its importance, are particularly challenging in countries where capacity of antenatal care programmes to conduct such monitoring is currently weak.

As part of the effort, WHO/TDR also are issuing calls to researchers worldwide for contributions of results from studies, reports and patient data sets on maternal outcomes and prevalence of birth defects in Asia, Africa and Latin America. These will be included in a planned WHO systematic review of the issue (Please see Calls on TDRnews back page).

>> See also TDR web link: safety of artemisins in pregnancy http://www.who.int/tdr/svc/research/antimalarial-policy-access/projects#_Safety_of_the

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80% of neglected disease research spending is for HIV, malaria and TB

Of the more than US$ 2.5 billion spent in 2007 on neglected disease R&D, almost 80% went to HIV/AIDS, malaria and tuberculosis (TB), a new report on global investment in new products for neglected diseases says.

The remaining neglected diseases and disease groupings, including diarrhoeal illnesses, helminth infections and bacterial pneumonia and meningitis, each received less than 5% of global funding, according to the G-Finder report by the Australia-based George Institute for International Health.

In terms of the types of research funded, the lion’s share of global investment went to R&D of drugs and vaccines, with very little dedicated to diagnostics. Over 80% of global funding was provided by only 12 organizations. The report recommends broadening funding so that all diseases receive the attention they deserve and more funders become involved in such R&D efforts.

The G-Finder report, supported by the Bill and Melinda Gates Foundation, surveyed 2007 R&D investments of 134 donors and private as well as public programmes/agencies (including TDR) in 43 countries. The report on funding trends aims to identify areas in which funding is lacking and where additional funding can potentially have a high impact.

Around 20% of global funding was invested by public institutions and private companies into internal programmes, the report found. The remaining 80% was granted to external organizations either directly or via “intermediary” organizations such as TDR as well as product development partnerships (PDPs).

Among the intermediary organizations, TDR ranks eighth in terms of funding.

STAC commends TDR’s strategy implementation

TDR’s Scientific and Technical Advisory Committee (STAC) met in Geneva on 23-26 February and commended TDR for the good progress attained over 2008. This was the first year of implementation of TDR’s new strategy, which aims to give disease endemic countries a pivotal role in research that addresses diseases of poverty.

Under the new strategy, approved by TDR’s Joint Coordinating Board in 2007, specific areas of TDR research focus include the early stages of “discovery” research for new drugs and diagnostics tools, as well as implementation research aiming to improve drug, diagnostics and health service delivery in real-life settings. Two key crosscutting TDR functions include “stewardship” of research priorities aiming to identify research needs and gaps and improve knowledge sharing, as well as “empowerment” of research leadership in disease-endemic countries. The STAC termed progress in TDR’s Stewardship function as “significant”, and commended the work of the other lines of TDR activity as “satisfactory” to “excellent”. However it noted the need to develop clearer strategies and indicators to ensure that disease-endemic countries play a pivotal role in global research, in TDR research in particular, and in setting the health research agenda. STAC also asked TDR to develop longer term indicators of the impacts of various TDR research activities on the success of disease control efforts.

“Issues that are now coming into focus include a need for TDR to not only better describe what we do but the processes we use, i.e. how we function,” said Director Robert Ridley, following the meeting. “There needs to be a particular emphasis on how we are going to help disease-endemic countries play a pivotal role for research. This means we will be looking very closely in the coming year at how we measure and evaluate the impact of our work with developing countries, and also how we talk about disease endemic country leadership.”

80% of neglected disease research spending is for HIV, malaria and TB
In making R&D investments, funders need to assess the likely health return against the cost of any investment, discounted for risk, the report emphasized. This is a complex process and factors include burden of disease, epidemiological trends, product shortfalls and the presence of other funders in a given space.


**ESSENCE tested in country pilot**

Efforts of the new TDR-based initiative Enhancing Support for Effective National Capacity Efforts (ESSENCE) advanced with the staging of a country pilot meeting hosted in March by the Commission for Science and Technology (COSTECH) of the United Republic of Tanzania.

ESSENCE is an effort by a number of international funders to strengthen research capacity in low-income African countries in the spirit of the Paris Declaration on Aid Effectiveness. The effort aims to harmonize their respective efforts and improve transparency while increasing the involvement of disease-endemic countries in combating neglected diseases.

The Tanzania pilot meeting in Arusha on 9-10 March established a dialogue between donors and country representatives about the undertaking’s collaborative aspects. The meeting, held under the leadership of Hassan Mshinda, director general of COSTECH, defined funder priorities and identified areas where activities may overlap. Participants also agreed on mechanisms that could lend synergy to future capacity-strengthening efforts, according to Fabio Zicker, coordinator of TDR’s Policy and Development (PAD) portfolio and a TDR liaison to the effort.

Members of the initial ESSENCE steering committee include the United Kingdom’s Department for International Development (DFID), Canada’s International Development Research Centre, the Ministry of Foreign Affairs of the Netherlands, the Norwegian Agency for Development Cooperation (NORAD), the Swedish International Development Cooperation Agency (Sida), the Bill and Melinda Gates Foundation, and the Wellcome Trust.

Subsequent to the pilot in Tanzania, the ESSENCE Steering Committee also met in concurrence with the Stakeholders Meeting on Strengthening Research Partnerships for Neglected Diseases of Poverty in Berlin March 16-19 to discuss a work plan and to agree on partners’ responsibilities.

An ESSENCE website is being developed, it will be unveiled at the meeting and launched shortly thereafter. This website will reinforce the fact that although ESSENCE activities are facilitated by TDR, ESSENCE was initiated during a meeting organized by the Sida, and it will extend beyond TDR’s existing sponsors and partners to involve other parties. Hannah Akuffo, formerly of Sida, has been asked to act as executive secretary of the initiative.

**Contact:** Professor Hannah Akuffo at Hannah.Akufo@sida.se

**Good clinical laboratory practice published by WHO/TDR**

From left to right, at the signing ceremony are Vanessa Grant (GCLP author), Joy Eldridge (BARQA Publications Committee), Juntra Karbwang-Laonthavorn (WHO/TDR), Andy Ramsay (WHO/TDR) and Tim Stiles (GCLP author).

TDR has obtained a copyright agreement from the British Association of Research Quality Assurance (BARQA), permitting WHO to publish and adapt BARQA guidelines on Good Clinical Laboratory Practice (GCLP). The agreement was signed at the Second Global Quality Assurance Conference in Edinburgh, 29-31 October 2008. GCLP provides guidance to laboratories analyzing samples from clinical trials. TDR will reproduce and adapt the guidelines as part of an overall effort aiming to help disease endemic country laboratories meet international good practice standards.

See web link to GCLP guidance in the Publications section (page 34).

**WHO Director-General congratulates China on LF elimination**

WHO Director-General Margaret Chan congratulated China for its success in having eliminated lymphatic filariasis (LF) as a public health problem in a recent ceremony in Beijing to celebrate the landmark effort.

Noting China was historically one of Asia’s countries with the highest LF burden, Chan said “China has acquired vast knowledge and experience over the last five decades and [the country] capitalized on new strategies and tools as it mopped up the remaining trouble spots in the country.”

CP Ramachandran, one of the key architects of TDR’s LF research initiative that led to the development of key new control tools and strategies in the 1980s and 1990s, was among those present at the ceremony on 7 October 2008. He provided an update on the ongoing Global Programme for the Elimination of LF, established by WHO in the wake of a 1997 World Health Assembly resolution (WHA 50.29) calling for worldwide LF elimination by 2020.

An estimated 120 million people globally are infected with the parasite that causes LF, which is often cited as the second leading cause of disability worldwide.

**Longtime TDR affiliate appointed WR in Gambia**

Dr Thomas TY Sukwa, a longtime TDR affiliate, has been named the WHO Representative (WR) for the Republic of the Gambia, one of Africa’s smallest countries with a population of approximately 1.6 million. The recipient of numerous TDR grants, Sukwa completed master’s and doctoral degrees in public health at Harvard University in 1983 and Johns Hopkins...
In the interim, Sukwa returned to his native Zambia to work as an epidemiologist with the Tropical Diseases Research Centre (TDRC), then sponsored by TDR. He focused on epidemiological and clinical research in schistosomiasis, human African trypanosomiasis and malaria, becoming director of the centre in 1994. In 1999, he became senior lecturer in community medicine at the University of Zambia’s School of Medicine.

In 2000, Sukwa joined the WHO Regional Office for Africa, where he served as the medical officer for malaria case management. There, Sukwa developed a framework to guide countries through the adoption of new anti-malarial treatment policies incorporating artemisinin-based combination therapies (ACTs). He also developed a regional antimalarial drug resistance database.

In 2005, Sukwa set up a Communicable Diseases Research Unit within WHO/AFRO, becoming Regional Advisor for Communicable Diseases Research. Following his involvement in TDR-sponsored high-level ministerial meetings in Abuja and Accra in 2006, he was re-assigned to head the WHO/AFRO Tuberculosis Unit, a position he held until his appointment as WHO Representative in the Gambia in July 2008.

Speaking on behalf of WHO last November, Sukwa applauded the Gambia’s support and collaboration with the organization. He cited Vision 2020, the recently revised National Health Policy and the new Health Master Plan as products of this collaboration, which he called evidence of the government’s commitment to strengthening the health sector.

TDR grantee lauded for TB research

TDR grantee Dr Saw Saw, a native of Myanmar and a newly minted PhD, was recognized last October for outstanding achievements in tuberculosis research with the Melbourne School of Population Health’s annual Knowledge Transfer Award. In order to be considered for the award, researchers must demonstrate that their work will change health outcomes, policy or professional practice; that it represents a novel approach or major discovery; and, that it embodies excellence in conceptualization, development, execution and application of innovative, high-quality knowledge transfer methods.

Through her doctoral work, Saw Saw examined the role of public-private partnerships in controlling tuberculosis in vulnerable low-income populations in Myanmar. Her research findings touched on several knowledge transfer issues, including the use of referral letters by general practitioners and the provision of health education on TB at the township level.

Several of her recommendations, such as disseminating health education methods through former TB patients and establishing links between all GPs and the township health department, have been adopted by Myanmar’s national tuberculosis programme for improving the delivery of DOTS care.

While a doctoral student at the University of Melbourne, Saw Saw worked with a longtime TDR adviser, Professor Lenore Manderson, and co-supervisor Mridula Bandyopadhyay, both of whom nominated her for the award.

“Saw Saw’s research brings together biomedical, social and cultural data and perspectives, ensuring its dissemination and translation into public health programs,” says Manderson. “She continues to work with the Myanmar Ministry of Health in controlling TB and has been very successful in securing further grants.”

The annual award by the Guatemala National Council of Science and Technology (CONCYT) was presented to Arana by the Vice-President of the Republic of Guatemala (Dr Rafael Espada), also the CONCYT President, at a ceremony at the Guatemalan National Congress on 18 November 2008.

The award is given to a researcher for his or her contributions to the development of the scientific knowledge and/or technology, based on the recommendations of an ad-hoc committee reviewing candidate nominations. Arana was nominated by the Institute of Research, Universidad del Valle de Guatemala, where he was co-director of the Centre for Health Studies prior to coming to TDR in May 2008.

TDR's Byron Arana receives top Guatemalan research award

Scientist Byron Arana, part of the TDR team on research to support visceral leishmaniasis elimination, was the 2008 recipient of Guatemala’s highest research award, the Science and Technology Medal.

Arana, a medical doctor who holds a PhD in tropical medicine, received the award for his work on the epidemiology of cutaneous leishmaniasis in Guatemala, studies on the search for treatment alternatives, and for his scientific contribution to national programmes for the control of onchocerciasis and Chagas disease.

– Compiled with contributions from Patrick Adams
TropIKA.net is a web portal that aims to foster innovation and knowledge application relating to the infectious diseases of poverty. In recent months, all the sections within TropIKA.net have expanded considerably. The first of our specially commissioned TropIKA Reviews, comprehensively addressing questions of key importance, will be published shortly.

Selections from recent TropIKA.net web news

News about TropIKA.net

More people are visiting www.TropIKA.net. There has been a steady rise in ‘hits’ over the last year; in a typical week there are now about 2000 visitors. However, we aim to improve on this figure, with the goal of making TropIKA.net the ‘one-stop shop’ for information and debate about infectious diseases of poverty. If you have not visited our knowledge platform yet, please do so. If you are already a regular user, please pass on the word to your colleagues.

TropIKA.net ‘knowledge hub’ expands activities

An important new initiative on TropIKA.net is our ‘knowledge hub’ designed to facilitate sharing of information in a large international health forum with potential impact on the battle against infectious diseases of poverty. The aim of this ‘knowledge hub’ is to provide information both to participants and to engage members of the broader community with a strong interest in the issues under discussion – so that even if unable to attend you may feel “virtually” present.

Before the meeting, background documents are made available online and dedicated collaborative workspace is offered to organizers, presenters and other interested parties/communities of practice.

During the meeting, daily overviews are posted by a special TropIKA.net team of journalists and rapporteurs. The team puts together session reports, comprising analytical summaries of issues and viewpoints, as well as links to the formal presentations, session conclusions and recommendations. Profiles, interviews and a meeting blog are also featured on the website, as are photographs. After meetings are over, TropIKA.net continues to maintain the ‘knowledge hub’ for ease of reference and further follow-up/perspectives on the event and the issues.

TropIKA.net at the 2008 Global Ministerial Forum on Research for Health

The Global Ministerial Forum on Research for Health, held 17-19 November 2008 in Bamako, Mali, was our latest and most extensive knowledge hub effort to date (http://www.tropika.net/svc/home/bamako2008).

Our special 22-member TropIKA.net team in Bamako included six journalists and twelve rapporteurs – from no fewer than ten countries. All rapporteurs were postgraduate research fellows from disease-endemic countries – this has been a strategic choice of TropIKA.net providing young researchers with an opportunity to participate in international policy fora.

“There is a lot of value in this approach,” said Nicole Biros, who coordinated the TropIKA.net ‘knowledge hub’ for Bamako. “It greatly benefits the team’s reporting that the rapporteurs are not only familiar with the science involved, but also with the social and contextual realities that are an integral part of the issues being discussed.”

The rapporteurs also build up new skills and diversify their interests as they experience these events not only as researchers but as professional communicators who have to provide information on research to a broader public. They thus lend a unique perspective to their collaborations with TropIKA.net’s journalists, who are in charge of the reports’ final writing and editing. The Bamako team also was well-served by these journalists’ diversity (half are based in Africa). Senior researchers from renowned institutions in Brazil, Ghana and Mali also worked with the knowledge hub, acting as arbiters on the review and editing of final reports. They, together with the knowledge hub’s collaborators from another cooperating agency, UNESCO, proved to be major assets to the undertaking, providing the team with valued regional perspectives and policy insights.

For the Bamako meeting, the team produced three daily overviews and 41 session reports. There were also seven news
stories, one profile, and four entries to the blog. The final Bamako Call for Action, adopted by 53 countries represented at ministerial level, is also available on the TropIKA.net website (http://www.tropika.net/svc/specials/bamako2008/call-for-action/call).

One impact of the ‘knowledge hub’ coverage was a tripling of the number of TropIKA.net website visitors during the period of the meeting and for days thereafter – evidence of the real need that the service was able to meet. The Bamako ‘knowledge hub’ section will remain on the TropIKA.net website as a readily accessible source of information on the event and a place where comments can still be posted. The regular TropIKA.net team continues to add information via the blog when reference is made to the meeting in the press or elsewhere. A CD-ROM compilation of all Bamako knowledge hub contributions will be produced and distributed to interested parties. Through the knowledge hub effort, TropIKA.net offers a space where health research forums can open up to real-time universal participation. On this site information and knowledge can flow back and forth, evolve and be stored, updated and easily retrieved. The network is an independent forum where issues can be debated and moved forward with equitable access by all stakeholders.

TropIKA.net plans more knowledge-hub participation at important health forums in 2009 and will post details of such forthcoming events. If you think this knowledge-hub approach could enhance a planned health forum event on infectious diseases of poverty in which you are involved, or if you are interested in participating on the knowledge hub initiative as a rapporteur, please contact: Edith Certain, certaine@who.int.

Selections from other TropIKA.net features

The world can well afford the malaria vaccine

A distinguished malaria researcher says that a shortage of funds should not stand in the way of developing an effective malaria vaccine. In an address to the Molecular Approaches to Malaria Conference, Lorne, Victoria, Australia – also published as an Editorial Opinion on TropIKA.net – Sir Gustav Nossal said that researchers have achieved things that 25 years ago would have been thought impossible. Research funding has also now reached a high level. He cautioned that it is not only money that is needed, “We need better and more benign governance structures in the developing countries.”

http://www.tropika.net/svc/editorial/gn/Nossal20080331

People at the top talk to TropIKA.net

Our profiles section (http://www.tropika.net/stakeholders/) features a monthly interview with a leading figure working against infectious diseases of poverty. Our interviewees have included researchers, clinicians, agency executives, academics and people in industry. We ask them about their work, achievements and outstanding challenges. These in-depth interviews often elicit surprising information and controversial comments. Experts profiled recently included Chetan Chitnis of the International Centre for Genetic Engineering and Biotechnology in India; Claire Panosian Dunavan, outgoing president of the American Society for Tropical Medicine and Hygiene; and Larry Geiter and Charles Wells of Otsuka Pharmaceuticals.

TropIKA.net news

The news section has expanded at a remarkable pace. At least ten new stories appear every month and we will soon be increasing this number. We have reported on developments from Cambodia to Colombia, and on diseases that range from dengue to dracunculiasis. Stories involving the innovative use of technology are also featured. So if you want to know the latest developments in the fight against infectious diseases of poverty, browse here: http://www.tropika.net/svc/collection/news/.

From the journals

We select for summary and comment articles in peer-reviewed journals that we regard as being of particular importance. Review and opinion articles are included as well as original research. Nearly 400 articles have been included in this coverage.

Reports

Journal articles are indexed on PubMed and other databases, and therefore specific topics are easy to search. However, when organizations produce reports these often go unread because there is no comparable index or register of such documents. TropIKA.net uses a variety of resources to identify new reports that relate to the infectious diseases of poverty.

In our reports section (http://www.tropika.net/svc/collection/report/) we publish a summary, with commentary on each report and include a link to the document itself. This could be one of the most important functions of our project. Examples of reports we have recently featured include:

• Meeting the Malaria Treatment Challenge, the Artemisinin Enterprise;
• Good Practices in Health Financing, International Bank for Reconstruction and Development (World Bank);
• The World Can’t Wait: More Funding Needed for Research on Neglected Infectious Diseases, Families USA;
• Cough up for TB! The Underfunding of Research for Tuberculosis and Other Neglected Diseases by the European Commission, Médecins Sans Frontières.

The TropIKA.net blog

The blog offers an opportunity to comment on articles that have appeared on TropIKA.net and on developments elsewhere. The editorial team also uses the blog to alert readers to interesting items published elsewhere on the internet. A surprising range of topics have been covered recently, from the inspiring (an Indian project to provide employment for leprosy-cured patients) to the bizarre (a campaign to ‘save the Guinea worm’). Responses to the blog entries are warmly welcomed.

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Health is the product of a complex social and environmental system that requires research and development spanning many fields – not simply the product of the presence or absence of disease and the medical ability to treat and prevent it. This was the message underlying the Global Ministerial Forum on Research for Health, 17-19 November 2008 in Bamako, Mali. The forum on the theme of “research for health” brought together researchers, policy leaders and civil society representatives from around the world, as well as leaders from other sectors ranging from environment and agriculture to security, sociology and economics.
BAMAKO – In a dusty health centre a few hours south of Mali's capital, Bamako, a health worker pricks the finger of a feverish little boy, squeezes blood into a malaria test strip, and waits until the result appears. It's a seemingly simple process – and yet 1 million African children still die every year from malaria because they do not get adequate diagnosis and treatment.

The tragedy of malaria is not a new story, rather an old one, that nonetheless illustrates the continuing failure of health systems to influence or manage the complex chain of social, cultural, environmental and economic factors required to transfer research knowledge to policy and practice.

Where health researchers and policy-makers have most often failed is in taking a holistic, systemic approach to fighting disease, says George Amofa, Ghana's deputy director-general of health services, speaking at the recent Global Ministerial Forum on Research for Health in Bamako.

It was out of this emerging awareness that an agenda for Strengthening Research for Health, Development and Equity was formulated as the focus of the Bamako discussions – bringing together for the first time stakeholders not only from the health sector, but also from science, agriculture, climate, food security, economics, politics, energy and trade. Some 1100 participants from 75 countries attended, including official delegations from 53 countries led by ministers of health, education and technology.

This broad base of involvement also was reflected in the joint organization of this year’s forum by six partners: the Council on Health Research for Development (COHRED), the Global Forum for Health Research, the World Bank, the World Health Organization (WHO), the United Nations Educational, Scientific and Cultural Organization (UNESCO) and the host country, the Republic of Mali.

In a keynote presentation, Luis Sambo, director of WHO’s Regional Office for Africa, called for “the right kind of research, now more than ever”. He cautioned that health research should not be considered a drain on resources but rather a producer of economic gains, citing a 2001 report of the Commission on Macroeconomics and Health. “We need research to guide health system reforms, as we have seen here in Mali. We need operational research to help give existing interventions a greater impact. Above all, we need research to persuade the world that investments in health must continue as one of the surest and best proven routes to a stable and prosperous global society.”

**Multi-disciplinary approaches to health**

The forum recognized that in order to fight priority diseases and improve the health of the world’s poor, policy-makers and researchers must address the determinants of health that lie beyond disease control, prevention and treatment. Sessions on the impacts of pandemics, global warming, food shortages and military conflicts offered insights into new approaches and models.

“Between 40% and 60% of health outcomes can be explained by forces from outside of the immediate health arena,” said Ok Pannenborg, a senior World Bank adviser and the World Bank Representative to TDR’s Joint Coordinating Board (JCB). These challenges range from weak supply chains that make it difficult for remote populations to access pharmaceuticals and other health tools to lack of reliable and affordable health services, unreliable food sources, poor environmental health conditions related to unsafe drinking water, inadequate sanitation and poor housing, and climate change threats related to increased patterns of drought and flooding.

“All these concerns transcend the boundaries of typical health sector parameters,” said Pannenborg. “Nevertheless, they strongly influence human health.”

“Malaria is an example of a health issue that requires a broader, systemic approach, just like HIV/AIDS,” said TDR Director Robert Ridley, chairman of a Bamako session on Pandemics and Infectious Diseases organized by TDR (see Box 1 on next page).
Considering the links between poverty and disease was the aim of a TDR-sponsored session on pandemics and infectious diseases at the Bamako 2008 meeting.

George Amofa of Ghana’s health service argued that the malaria pandemic has been largely ignored despite the fact that more than 1 million people annually die from the disease, with 90% of those deaths in sub-Saharan Africa.

“We must take a systemic approach to malaria, looking at areas of research beyond the typical boundaries of health,” said Amofa. He proposed a range of measures to take, including developing a surveillance system for early detection of and response to outbreaks, designing better and more reliable diagnostics as well as communication strategies to promote behaviour changes, and improving supply chains for antimalarials, insecticide-treated bednets and diagnostic testing kits.

It remains important to ensure that research results are translated into policy and action, Amofa said. Citing Ghana as an example, he noted that it took many years for research demonstrating the effectiveness of bednets in preventing malaria transmission to be translated into policies promoting mass bed-net distribution.

TDR Director Robert Ridley said that for research to have an impact on diseases such as malaria, and thus on poverty, the global health community also must address the gap between scientific research and product development. Basic knowledge must be translated into usable products and strategies, particularly ones designed for poorly resourced environments. Countries also lack capacity to find solutions to their own specific problems, Ridley noted. One of the roles of TDR, he said, is to assist countries to build this national capacity.

Development of regional capacity for clinical R&D is also a priority, according to Mark Walport of the Wellcome Trust. Collaboration, including among countries in regions sharing common health issues, is essential to successfully overcome the challenges that infectious diseases and pandemics present, including scientific challenges (e.g. transmission routes and viral ecology or effective field diagnostics), logistical challenges (e.g. supply lines and location of stockpiles, large-scale delivery) and communication challenges (e.g. conveying the risks of the disease to the public).

Maria Guzman, virology chief at the Pedro Kouri Tropical Medicine Institute, spoke on how Cuba—a country with a low GDP—has found success in addressing the problem of pandemics. Currently, infectious diseases only attribute for 8.8% of mortality in the country. Cuba’s approach is anchored in the recognition of the universal right to health and education. Elimination campaigns for diseases such as polio, malaria and TB have involved mass immunization programmes and distribution of free medications, such as antiretrovirals for people with HIV/AIDS, by the public health system. The keys to success, she said, have been political will, adequate funding, strong surveillance and epidemiological monitoring, policy support for health and scientific research, and strong human research and medical staff capacity, as well as other features found in free-of-charge national health systems.

For more details and resources, see: http://www.tropika.net/svc/specials/bamako2008/session-reports/pandemics-and-infectious-diseases

He called for available tools and knowledge to be harnessed into workable delivery strategies designed for specific environments.

Meeting the maternal health Millennium Development Goal (MDG 5) will require an approach that extends beyond conventional health research, said Catherine Sanga, the United Republic of Tanzania’s assistant director for reproductive and child health in the Ministry of Health and Social Welfare.

“No only do we need to invest in health systems in order to see improvements, we need socio-cultural research to find out why home delivery rates are so high, and then how to better support women so that they come to hospitals for prenatal care and delivery.” This is where research can play a critical role by showing how systems impact on health, measuring problems and devising evidence-based responses, as well as monitoring and measuring those responses’ impacts and benefits.

Making ‘research for health’ a reality

For three days, the forum discussed and debated ‘research for health’ as a way of improving the health of the world’s poor. The challenge is to turn this “into a reality, not just a dream”, said Anthony Mbewu, president of South Africa’s Medical Research Council. The resulting Bamako Call to Action on Research for Health details the forum’s proposed solutions (http://www.tropika.net/svc/specials/bamako2008/call-for-action/call), some of which are briefly discussed below.

Funding – Many conference participants noted that while funding for research and control of particular
As part of this national research strategy, countries need to support local research institutions and develop their personnel’s capacity to “undertake, understand, translate and interpret research”, he said.

In Mali, for example, there are several centres of excellence for research in health and agriculture, with researchers working on important local issues such as drug resistance in malaria. However, most research for health in Mali is dependent on external funding, and thus at risk of being part of an external organization’s research agenda.

Suggestions from the forum included the creation of a national research centre that would set the national health research agenda and coordinate research efforts. In addition, the Malian government would need to significantly increase its budgetary commitment for research. Research receives 0.15% of GDP, well below the 2% of GDP recommended by the Bamako Call to Action.

The importance of expanding local health industries was also recognized. Initiatives like the Yaoundé Process are mapping health innovation activities in Africa by looking at specific needs of African countries in developing local R&D, manufacturing and distribution of vaccines, pharmaceuticals and diagnostic tests.

Monitoring/evaluation and implementation/operational research – Sometimes described as the “poor sister” of research, monitoring and evaluation (M&E) is a routine evaluation of programme performance based on pre-established indicators such as coverage, surveillance, lag time to action and distribution of drugs. A somewhat related field, implementation/operational research (IR/OR), typically examines how to overcome bottlenecks in programme performance and how to scale up programmes more effectively. Health policymakers increasingly recognize these efforts as key to the improvement of health systems. At Bamako, TDR and the Global Fund to Fight AIDS, TB and Malaria co-sponsored special sessions on implementation/operational research (see Box 3) and monitoring and evaluation (see Box 2).

The United Republic of Tanzania offers a relevant example of how research can lead to policy change, maternal health expert Sanga noted in a session on the Millennium Development Goals and health. Her government’s research examined whether Integrated Management of Childhood Illness (IMCI) improves paediatric care quality as well as this care’s affordability and child survival rates. IMCI typically is delivered as a package of interventions to address major childhood illnesses (e.g. malaria, pneumonia and diarrhoea). It includes assistance to health workers to improve case management, effective drug supply and management, and improved hospital care through better supervision and timely referrals.

The study found that districts using IMCI had a better quality of care with a lower cost per child and lower child mortality than districts that had not implemented IMCI. Sanga said, “Looking at these results, you could
argue that IMCI could save the lives of 28,000 children in Tanzania each year." She said the research already has resulted in rapid scale-up of IMCI.

Marie Ruel, Food Consumption and Nutrition division director at the International Food Policy Research Institute (IFPRI), noted the importance of using such tools to measure health system performance and to identify best practices. "Monitoring and evaluation and implementation research are the types of research where we can learn valuable lessons," she said. "This is the type of data can be used to scale up and replicate programmes elsewhere."

**Moving intersectorality**

‘Intersectorality’ was another buzz word at the forum. The importance of this theme was underlined in the Bamako Call to Action, which stated that "the nature of research and innovation for health improvement ... is not sufficiently inter-disciplinary and inter-sectoral."

The forum sought to improve dialogue between different government agencies (e.g. health, finance and agriculture) on common concerns, as well as between policy-makers, research leaders and civil society organizations. The Call to Action stressed the need for civil society and community participation in the research process, and in making key decisions to do with research and investment.

"Communities need to be empowered through research, and not disempowered, as often happens," said Thelma Narayan, a Society for Community Health Awareness, Research and Action (SOCHARA) public health consultant in India. "Our dependence on experts needs to give way to a more participatory form..."
of research, where communities are not just objects to be studied, but active participants and subjects in the research process”.

Mbewu of South Africa’s Medical Research Council suggested that national AIDS councils in South Africa, which mobilize and coordinate activities across all sectors of society in the fight against HIV/AIDS, could be used as an example of effective intersectoral coordination.

Innovation for health

The final Bamako communiqué stressed innovation for health – not only in the product R&D chain but also in developing systems, strategies and solutions to address issues ranging from gender equality to patient safety and health communications/education.

New ideas in the communiqué included the creation of “convergence centres” linking universities, start-up companies and venture capital, and the strengthening of e-health initiatives. Some of these are based on simple but innovative software technologies accessible through mobile phones.

New investments by the World Bank Group, the Bill and Melinda Gates Foundation and the Rockefeller Foundation may help engage the African private sector more fully to deliver services, train health workers, manage supply chains and manufacture health care tools and equipment. Yet the forum’s communiqué also appealed to the private sector to engage more proactively with other stakeholders. It called upon researchers to improve their translation of research results into commonly understood terms and messages, and for policy-makers to use research more effectively to guide decisions on health policy.

BOX 3. Implementation/operational research

This special session emphasized the increasing importance of operational and implementation research (OR/IR) in determining how well health programs are working and how they can be improved. As one presenter said, “You can distribute bednets, but if you don’t know what’s happening to them and if they are being used, your money and time is going to waste.”

The forum heard that OR/IR can help identify and solve problems in implementation, help policy-makers reach evidence-based decisions, improve program quality, strengthen public health efforts and help staff understand why and how well their programmes are working. OR/IR can also identify new directions in health programming.

Irene Akua Agyepong, Greater Accra regional director in Ghana’s Health Service, described recent operational research undertaken to find out why, in 2002, bed-net use across Ghana was very low. Initial research showed that bednets were not available for purchase in the markets, which led to their free provision. However, further research revealed that children under five, who are at high risk from malaria, were still not sleeping under the nets. This was a powerful indication of the need to understand the complex factors that influence bednet use and to adapt interventions accordingly, via education and other social measures.

TDR Strategic Alliances Coordinator Jane Frances Keyenga-Kayondo spoke about TDR’s role in building in-country research capacity. “This type of research is important,” she said, “because proven disease control tools fail, and often it’s not known why. You need evidence at every stage and in all settings to improve the quality of interventions.”

The session recommended that OR/IR play a more pivotal role in national health services and in donor-funded disease control programmes. The capacity of researchers to conduct this type of research also should be increased. The Global Fund has already encouraged the inclusion of OR/IR in the programmes it supports, and has produced a framework available on its and TDR’s websites to guide OR/IR researchers in good practices. ■

For more details and resources, see:
http://www.tropika.net/svc/specials/bamako2008/session-reports/implementation-operational-research
BOX 4. MRTC is African model for research training

MRTC Co-director Ogobara K Doumbo is also the head of a vaccine-testing programme, operated jointly with the NIH Laboratory of Parasitic Diseases. A staff of more than 50, nearly all from Mali, carries out research on malaria control, as well as on filariasis and leishmaniasis. From 1992-2008 the MRTC staff published, with international collaborators, more than 240 peer-reviewed articles in highly regarded journals.

Yéya Touré, currently leader of TDR’s vector control research activities, was MRTC’s founding director and remained there until 2001. The center is now co-managed by Doumbo and Sékou Fantamady Traoré.

The center was one of Africa’s first to develop a molecular biology unit and focuses on Anopheles gambiae, the region’s main carrier of malaria. There are 12 research groups with laboratories, all led by Malian PhDs and funded by research grants.

A bioinformatics unit was established with initial funding by TDR for two-week training sessions. The NIH now provides computers and sends scientists to teach the course. TDR funds 10 to 15 trainees, and then selects and funds two of the top research proposals coming out of this training. Other TDR contributions include support for development of mass treatment and vector control strategies, for characterization of filariasis transmission and for research into schistosomiasis and drug resistance. ■

― By Jamie Guth in Bamako, with a contribution from Beverly Stearns Peterson

“Research should not substitute for action,” said the World Bank’s Pannenborg. “We need to ensure that countries implement policies as a follow-up to research.”

Clearly, however, international and donor organizations also must play leadership roles. In light of that need, the Swedish International Development Agency (Sida) is leading ESSENCE, a new initiative supported by TDR to bring donors together in a more harmonized approach (see TDRbriefly, p. 8). A TDR-led stakeholder meeting 16-18 March is also addressing the all-important topic of donor coordination.

In November 2009, Bamako’s participants will review progress so far at the Global Forum for Health Research annual meeting, Forum 2009: Innovating for the Health of All, in Havana, Cuba. Mbewu of South Africa’s Medical Research Council said that until then, forum participants should continue the intersectoral dialogue launched at Bamako in the spirit of a common understanding that health is a critical investment in development. “All of the ministers of health, research, science and technology, education, food and agriculture, and environment here must continue their dialogue once they return home and coordinate their efforts in all programmes that affect health,” Mbewu said. ■
‘Greening’ a clinical trial site in a remote area

Reviving research in Liberia

The TDR-sponsored Phase III clinical trial for moxidectin, a new drug candidate and potential cure for onchocerciasis, is one of the largest undertakings in TDR’s history. Funded largely by a US$ 6 million donation from Wyeth Pharmaceuticals and contributions from the African Programme for Onchocerciasis Control (APOC), the initiative is not only testing a new drug for river blindness. It is building research capacity and stimulating sustainable development in countries recovering from conflict. In fact, mud brick construction of a modern clinical trial center in a remote corner of Liberia, as well as pursuit of clean solar and hydro-electric energy for the Liberian and Democratic Republic of Congo sites, make the trials potential models of environmental sustainability in the health sector. For TDR scientist Annette Kuesel, the project has been a journey down a road marked by unforeseen challenges and unexpected rewards.

Community manufacturing of the sun-dried mud bricks for the research centre.

It was a muggy mid-November afternoon in 2008 when Kuesel arrived at Roberts International Airport, 35 miles south of Monrovia. In June 1990, Robertsfield as locals call it, had been the locus of a fierce battle between rebels and government forces. The badly damaged main terminal still stood vacant, while across the tarmac several UN planes unloaded supplies for the 14,000 peacekeepers still scattered throughout the country.

Kuesel had come with Varalakshmi Elango, a laboratory physician and TDR clinical monitor, to work with a team of researchers from the Liberian Institute of Biomedical Research finalizing preparations for the Phase III clinical trial of moxidectin. Moxidectin is a drug candidate for onchocerciasis (river blindness) eradication owned by Wyeth Pharmaceuticals.

The US$ 8.5-million Phase III clinical trial and capacity building effort, supported by the US$ 6 million Wyeth donation and contribution from APOC is due to begin this spring and summer and continue for three years. It is being carried out in remote areas of Africa not yet reached by the annual ivermectin treatments currently used to combat the disease in much of sub-Saharan Africa.

Of the study’s four sites, two are in the Democratic Republic of Congo, one is in Ghana, and one is in Boughun, Liberia. The latter is a small, battle-scarred village in Lofa County, just a few kilometers from Liberia’s northern border with Guinea and Sierra Leone.

Setting up a clinical trial in a remote setting is a common feature of much TDR-supported research. In fact, a conscious effort is made to conduct research in areas...
not well served by health or research facilities, so as to improve access to new tools and also strengthen capacity of health and research services. Still, Bolahun, as Kuesel would discover, embodied a kind of extreme.

During the war, Bolahun had been a point of passage for rebels to and from Monrovia. Like much of the area, it had been ravaged. Schools were burned, clinics were looted and once-bountiful farmland had been abandoned. Those who had remained in Bolahun had endured the daily misery of life in a war zone. Yet the area’s relative isolation in postwar Liberia was precisely what recommended its election as a moxidectin trial site. Lofa County’s residents had not had access to annual ivermectin (Mectizan®) treatments available in many onchocerciasis-endemic African regions.

These treatments have dramatically reduced onchocerciasis symptoms and intensity of infection over two decades. Ivermectin-naïve subjects thus represent the best test of moxidectin’s efficacy. Phase III trial findings here, as well as in similar communities in DRC and Ghana, would be of great scientific relevance (see box).

Getting there

In the years since the war, Bolahun has slowly begun to recover. Yet during the dry season, the 220-kilometer drive from Monrovia over mostly dirt roads can take up to 10 hours. In the rainy season, it can take twice that or longer.

Kuesel well recalls setting off from Monrovia to the village on her second visit there in September 2007. She was traveling with three Liberian colleagues: Fatorma Bolay, disease prevention and control officer in WHO’s Liberia office and acting director of the Liberian Institute for Biomedical Research (LIBR); Henry Salifu, national coordinator of the health ministry’s Onchocerciasis Control Programme; and Fred Sirleaf, the study coordinator.

“Our two-vehicle convoy had passed Gbarnga, where the paved road stops, and from there on you could hardly call it a road; it was more like a series of mud holes. After a few hours, near Zorzor, we came up on a massive mud hole, a small lake. A minibus traveling in the opposite direction had become stuck in the middle. We finally managed to pull the bus out with both of our 4x4s hooked one to the other. But before we could go through the hole ourselves, another oncoming car drove in and also became stuck. We pulled that one out too, and yet another blocked our way, and then another, and another. We pulled one vehicle after another out without getting a chance to go through ourselves. By then it was dark, we were not even supposed to be on the road, and Fatorma decided we should try going around the hole somehow. He hooked the winch to a tree at the top of a hill by the side of the road and tried to drive the car up, to no avail. We then considered returning to Monrovia and taking a helicopter the next day, but we weren’t sure we would make it back in time. So we stayed put.”

Four hours later, there was a break in the ‘flow’ of oncoming traffic, and the WHO convoy finally powered through. Kuesel, who had remained with the vehicle throughout the ordeal says, “that was quite a lesson for me. I’ll never again go in the rainy season without solid boots to wade through knee-deep mud to a ‘bathroom’.”

Capacity building in remote locales

As hard as it had been to get to Bolahun, the mud was merely a precursor of other hurdles to be overcome before the Phase III launch. On her very first visit to Bolahun in April 2007, Kuesel had encountered a place as devoid of infrastructure as any in which she had ever worked. Bolahun had no public transportation, no sewage system or sanitation, no phone service or source of electricity, and not a single concrete building.

“We didn’t realize when we planned the budget that we would actually have to build a research centre. We were truly starting from scratch.” When Kuesel asked how building materials would be supplied, Bolay and Salifu explained that sun-dried mud bricks would be produced locally. “Seeing a question about the durability of such a building plainly written on my face, they laughed and pointed to the mud-brick church next door,” she says. “It had been there, they observed, since 1942.”

By the time Kuesel made her third visit to Bolahun in November 2008, workers were putting the finishing touches on a clinical research centre complete with laboratories and examination rooms, meeting room and computers. The centre also included several “guest” quarters where, given the poor roads and transport, subjects could spend the night between daily examinations required by the protocol.

Outside were parked the three TDR-provided 4x4 vehicles to transport subjects and staff to villages, and two 20-foot containers filled with equipment and consumables, including 15 motorbikes to ease movement by research and health centre staff to surrounding villages.
(In one DRC site bicycles are being used due to inferior road conditions.) There was still a well to be dug and a water tower to be built, but those tasks would have to wait for the dry season.

**Setting the tone and training the staff**

On the day Kuesel and Elango arrived, Bolay called the first meeting in the new clinical research centre, where he introduced the TDR team to the Liberian study staff. But Bolay also had to deliver an important message: “He explained that this trial presents a unique opportunity for the team and for Liberia. Many of the trial’s staff members were making a sacrifice by moving to Bolahun from Monrovia, even those who were returning ‘home’ to this area after having fled during the war.

“And he stressed that every team member, from driver to physician, had been recruited because of their qualifications and capabilities. If they took advantage of the training, worked collaboratively, and established the right work habits and attitudes, the trial would be a personal success and a national one.”

An expert in transmission dynamics and control of onchocerciasis, malaria and schistosomiasis and a former TDR grantee, Bolay had stayed in his native Liberia throughout the war, passing up higher-paying positions in Europe and the USA to coordinate emergency health action for victims of violence. If there was anyone with the poise and experience to manage a major clinical trial in a place like Bolahun, it was Bolay.

“Officially, he’s the institutional principal investigator on the study. But in reality, he’s so much more,” says Kuesel.

“‘We wouldn’t be where we are now without him.’

After the meeting, Kuesel got to work. Along with Elango, she conducted staff training sessions on the research protocol, on Good Clinical Practice (GCP) and Good Clinical Laboratory Practice (GCLP), and on standard operating procedures (SOPs).

“Conduct of clinical trials according to GCP and GCLP ensures that data obtained are accurate, credible and comparable across different trial sites,” Kuesel observed. “And GCP safeguards the well-being of subjects and respects their rights. No matter how disadvantageous something might be for the study, if it’s better for the subject, it will be done.”

**Sites untouched by ivermectin are ideal sites for moxidectin trial**

Timing and location of the Phase III moxidectin clinical trial is critical to its success. For the study to provide reliable data on the safety and efficacy of moxidectin, it has to occur before the arrival of ivermectin from the Merck Mectizan® (ivermectin) Donation Program. Donated ivermectin has reached more than 55 million Africans in 34 African countries over the past two decades, largely through an innovative community-directed treatment strategy developed by TDR and implemented by the African Programme for Onchocerciasis Control.

In Lofa County, however, ivermectin distribution was delayed due to the civil war, and paradoxically as a result, its residents are ideal candidates for the trial of moxidectin. Kuesel explains: “Ivermectin is a very effective microfilaricide. It kills the small worms that cause the disease symptoms (blindness, skin rash, lesions) and disease transmission. However, the adult worms, which live in their human host for up to twelve years, continue to produce microfilaria. Therefore you have to provide for the mass distribution of ivermectin annually to residents of endemic areas in order to keep the number of microfilaria low.”

While low microfilaria levels eliminate or prevent progression of disease symptoms, they make it very difficult to measure the effect of moxidectin on the macrofilaria. This explains the importance of launching the study of moxidectin in areas like Lofa County, before ivermectin treatment is introduced.

From the research done so far, it appears that moxidectin is likely to be as effective a microfilaricide as ivermectin. “But it needs to be able kill or sterilize the adult worms, and be safe for large-scale use, to qualify as a potent tool for global eradication of onchocerciasis,” says Kuesel.

Should critical Phase III trials show positive results in three years’ time, that would be a big step towards the eradication goal – but not the final one. Larger Phase IV trials would then be initiated to ensure that the drug is safe and effective in mass treatment.
Setting up the equipment

“In selecting the equipment to be provided both to Bolahun and to the trial sites in DRC, we had to take their remote locations into account,” Kuesel explains. For instance, from Bolahun there is no way to get samples to a central, accredited laboratory. So the village research centre needed a laboratory with analytical equipment facilitating strict quality control and assurance. For that purpose, Kuesel had purchased some of the more sophisticated machinery on the market, “the kind that would leave minimal room for operator error.” As a precautionary measure, Kuesel also had ordered duplicates of all critical equipment. Getting an engineer to fix, say, a biochemistry analyzer would be a very time-consuming and expensive endeavor in Bolahun. Moreover, were refrigerators to malfunction, even for a short period of time, the loss could have devastating consequences for the study: “so we made sure to have backups.” Finally, since there was neither cell phone transmission in Bolahun nor a nearby courier service (common in less remote areas of Africa), satellite-based phones and internet had to be ordered.

“We had about 80% of the equipment and consumables that we had purchased for the study and the centre shipped to Bolahun in the two 20-foot containers,” she recalls. “And we spent the first two days of our November stay in Bolahun unpacking it all.”

Even so, the satellite dish for internet and phone access was yet to be installed. So Kuesel had a unique way of keeping in touch with the outside world. Together with her driver, Mr. Massalay, she would drive some two kilometers out of town every day and walk up to a hilltop where she could capture a faint cellular phone signal. At the pre-appointed time of 4 p.m., her colleague in Geneva would phone.

Yet even once the phone and internet connections, as well as other purchased hardware, are finally up and running this spring, the biggest barrier to a smooth successful clinical trial in Bolahun has yet to be entirely overcome.
Powering a future

That barrier does not involve recruiting subjects or importing equipment or even building a clinical research centre out of mud bricks. In fact, the trial sites located in the Democratic Republic of Congo are in places almost as resource-poor as Bolahun.

What sets Bolahun apart, however, is the fact that the village, like much of Liberia, lacks a stable source of electricity and thus a reliable source of power for the equipment essential to a study. “Thinking about how our convoy had become stuck in the mud on the way to Bolahun made me shudder at the thought of having to rely on diesel fuel generators for the research centre,” Kuesel says. “So when I suggested to Fatorma and Henry that we try to find a fuel-independent energy source, they loved the idea. They told me about Liberia’s ambitious pre-war plans to supply all of the country’s health centres with solar power. The war had stopped them from carrying out the plan, but it’s still alive.

“By installing solar power at the centre in Bolahun, we would not only increase the likelihood of success for this trial, but we would also lower the cost of future research undertakings here, leveraging even greater benefit from the investment made here in capacity building.”

In her efforts to secure solar power for the clinical trial site, Kuesel talked to Rolf Korte, then chair of TDR’s Joint Coordinating Board, who put her in contact with Dieter Uh, alternative energy head at the German Gesellschaft fuer Technische Zusammenarbeit (GTZ). Uh arranged for Matthias Bergmann, a consultant studying renewable energy sources in Berlin, to design a solar power system for the Liberian site.

He designed the system with three potential energy generation capacities: 1) to support only the study’s energy needs, 2) to support expansion of the research centre, and 3) to power the health centre and nearby Bolahun High School. The high school, founded by monks in 1925 and further developed by the Peace Corps in the 1960s and 1970s was the pride of the northern Liberian region prior to the war. Its graduates have included a vice-president of Liberia, university presidents, associate supreme court justices, lawyers, nurses and doctors, including Bolay. Recently, the school has been rebuilt thanks to the contributions of alumni.

“It was clear from the start that the price tag for solar power was too high for our clinical trial budget, despite the fact that it is relatively ample thanks to the Wyeth donation,” says Kuesel. “But we were optimistic about recruiting a donation of solar panels.”

Unfortunately, the company initially approached declined to make a contribution. For the time being, the clinic is running on conventional diesel generators, while other donors are sought.

Diesel generators can’t offer peace of mind. “We lose a lot of sleep worrying that both the generator and back-up generator will simultaneously break down,” says Kuesel. And these provide only enough energy to run the research centre.

As the search for a donor of solar technology continues, Kuesel has realized that in fact, what the team has been developing in Bolahun, out of practical need rather than any deliberate ideology, is a field health research facility that also has the potential to become a model of environmental sustainability in the health sector.

“We have built the centre for clinical trials to international standards using mostly mud-bricks manufactured locally. We designed the building with features that keep the temperature in the rooms relatively low without air conditioning. This was a cheap yet durable method of construction that also has a minimal ecological footprint,” she says.

“We also have sought ways to dispose of the centre’s health waste in a manner that is safe and sanitary, although we would still like to go further here in terms of developing a waste disposal system that is more environmentally friendly. For the diesel power generators, we have explored the possibility of using scrap waste from surrounding rice fields and banana plants as a source of biofuels. And then, of course, there is our quest to develop solar power generation...”

On one of their first nights in Bolahun, Kuesel and Elango were preparing the next day’s session when they saw a teenage boy carrying two chairs to the street-light newly installed for the research centre’s security. He sat down on one and placed his books on the other, and Kuesel snapped a picture. “He was doing his homework,” she says with a smile. “It drove home to me the impact a fuel-independent energy source would have, way beyond clinical research. I know that somebody out there will want to be a part of this.”

As with any drug undergoing clinical trials, there is the chance that moxidectin may not succeed. Even so, the investment in human and infrastructure capacity will remain. “We’re not just building capacity for this clinical trial. We’re helping Liberia recover from war, revive its research track and stimulate sustainable development – and we’re starting in Bolahun.”

- Written by Patrick Adams

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Clinical trials in northern Uganda

TDR explores shorter HAT treatment options

TDR is conducting clinical trials for two new drug treatment regimens for human African trypanosomiasis (HAT). If successful, these would significantly reduce length of treatment for both early and late stages. In 2008, a TDR expert team visited clinical trial sites in northern Uganda. They observed how the trials have strengthened human and infrastructure capacity as well as underlining the need for greater community awareness of HAT symptoms so that people can be treated early.

While prevalence is generally on the decline, human African trypanosomiasis (HAT), or sleeping sickness, remains an important public health risk in many remote areas of Africa, where it is endemic in 36 sub-Saharan countries (see box: About HAT).

Yet there are a very limited number of drugs available for HAT treatment. And their unwanted side effects, as well as the lack of prospects for the development of new products, have prompted TDR-supported researchers to examine innovative new modes of treatment using existing drugs. These include a new therapeutic drug combination for the late stage of the T.b. gambiense form of the disease as well as a shortened drug regimen for its early stage.

The two treatment regimes hold the potential to reduce unwanted side-effects of drug toxicity and to simplify and lower costs of treatment. Also, in the case of late stage disease, there is a potential to blunt the emergence of resistance to the current monotherapy treatment with eflornithine®, where an increased rate of patient relapse has been observed.

For late-stage T.b. gambiense, the Uganda trials are comparing a nifurtimox+eflornithine combination with the standard eflornithine regimen to see if the combination drug treatment can be as at least as safe and effective, while being delivered in only 10 days, as compared to the current 14-day regimen. The shortened regimen being tested also would require only two infusions daily plus oral medication, as compared to the present regimen of four infusions. The trial involving 109 patients is due to finish in June, after which results will be analyzed.¹

A second study, launched in February 2008, assesses a three-day course of pentamidine for early-stage HAT (T.b. gambiense) against the current 7-10 day regimen.² The
Article | Research on new HAT treatment regimens

A shorter drug treatment course would not only vastly simplify treatment and lower its costs, but it would also lessen the risk of pentamidine accumulation in the body and related adverse effects. The trial is of particular importance now in light of the fact that the only other drug candidate in the pipeline for early stage HAT, pafuramidine (DB289), was placed on clinical hold in late 2007 by its pharmaceutical developer.6

In this trial, however, recruitment of HAT patients has been a particular challenge. Identification of HAT victims at early stages of the disease is often difficult, and symptoms may be confused with other ailments. Access to area villages, where early-stage cases of HAT may be found, has proven to be a challenge. It is even difficult for the health centres at Adjuman and Moyo to communicate; even though they are quite close together, they are separated by the Nile.

To illustrate the complexity and high resource demands required, Moyo’s principal investigator, Jimmy Opigo, took the TDR team to observe a mobile screening activity in one of the area villages. The village was in a very remote area with poor roads and difficult access. But upon arrival, the TDR observers found that hundreds of villagers had already been screened without a single case of HAT being found. Although HAT certainly lurks in this region, communities themselves are generally not aware of the signs and symptoms, and therefore fail to seek treatment early. To support this observation, Dr Opar of Adjuman’s hospital talked of a divorced patient who had been abandoned by her family and declared as either suffering from HIV or mental illness. When the patient went to the hospital, she was diagnosed with very late-stage HAT and was under treatment at the time of the team’s visit. The doctor promised to step up the sleeping sickness awareness campaign to ensure that patients seek treatment early and avoid the complications of late-stage disease and its consequences. It was also observed that lack of awareness may account for the slow rate of recruitment into the study. Some 80 patients have been recruited, while the target is 200.

Late-stage gambiense disease

Study of the nifurtimox-eflornithine combination for treatment of late-stage HAT is taking place at two clinical trial sites in northern Uganda: Omugo Health Centre and Moyo District Hospital.

The two sites were selected based on their track record as HAT treatment centres and the availability of staff that could be trained to undertake the study. The study is part of a broader collaborative effort with the Drugs for Neglected Diseases initiative (DNDi) and Epicentre, a Paris-based clinical studies group, to seek alternative treatments for gambiense disease. The drugs used in the study are donations from Sanofi-aventis (eflornithine) and Bayer AG (Nifurtimox - Lampit).

During the visit to Omugo, the TDR team attended a formal handover to the health centre of facilities made available for the trial. TDR had helped to renovate and equip a 22-bed clinical trial ward at the centre as well as a laboratory, noted the site’s principal investigator, Freddie Kansiime. With patient recruitment finished and the study nearly completed, these facilities were handed back to the health centre for routine uses. This illustrates how the human and infrastructure capacity developed for the trial will have long-lasting impacts on health services.

At the ceremony, a local member of Parliament, E Wadri, described HAT as a major public health problem in that area and emphasized the need to develop new diagnostics for early diagnosis and treatment as well as more effective drugs.

“HAT patients who go undiagnosed only to be treated in the late stages of the disease often suffer from permanent physical, neurological, intellectual and/or mental disabilities, and they may become a burden to their community,” he said.

Diagnosing and treating HAT (gambiense) in its early stages

In Moyo and Adjuman, another remote Nile River village in northern Uganda, a clinical trial of a three-day course of pentamidine for early-stage HAT is also under way.

Launched in February 2008, the trial is examining whether the current 7-10 day regimen of daily intramuscular injections with pentamidine could be reduced to just three days.5 The shorter course is based on pharmacokinetic evidence indicating that pentamidine has a prolonged elimination period; the drug remains at therapeutic levels in the body for over 29 hours after a single IV administration.
Rhodesiense HAT endemic in south migrates towards gambiense zone

While new drug treatments for the gambiense form of HAT are sought, another trend is causing concern: the possibility of an intermingling between the T. b. gambiense species endemic in the north and T. b. rhodesiense, which is endemic in the south but appears to be migrating slowly northward, largely due to the unchecked movement of cattle.

In order to discuss this issue, the TDR team also visited the Namungalwe Health Centre in southern Uganda. There, Dr Kakembo, director of the National Sleeping Sickness Control Programme, and his deputy Dr Wamboga, described how the health centre, which functions as a referral centre for patients with sleeping sickness, was built to treat patients during the last large T. b. rhodesiense epidemic in the 1980s.

He also explained that Uganda is the only country in Africa where both T. b. rhodesiense and T. b. gambiense coexist. The intermingling of the two species in the same geographic region, however, could greatly complicate diagnosis and treatment. If the two diseases converge, a drug treatment effective against the two forms would be required. Potentially, the usefulness of a nifurtimox + eflornithine combination could be examined in a site such as Namungalwe.

Kakembo also observed that while prevalence of the rhodesiense form of HAT that is common in the south appears to have declined markedly, this also could partly be due to lack of active screening and mobilization of communities. This underlines again the need to stimulate grassroots awareness of the symptoms of early-stage HAT to facilitate treatment that can lead to a full recovery.

Along with testing new drug combinations, the TDR trials have helped improve the skill levels of the collaborating medical teams, stimulating them to think about needs for such improved outreach and diagnosis of HAT in remote areas, according to Deborah Kioy, the TDR scientist who has been managing the drug trials. However, there needs to be further follow-up by control officials at country level, and in coordination with WHO, to ensure that activities instituted for the studies continue following their conclusion.

- With reporting from Deborah Kioy in Uganda

About HAT

Transmitted by tsetse flies, HAT occurs in two forms: a generally acute form caused by Trypanosoma brucei rhodesiense and a usually chronic form caused by Trypanosoma brucei gambiense. Each form of the disease presents as Stage 1 (also called early or haemolymphatic stage) or Stage 2 (late stage or meningo-encephalitic phase).

Uganda is the only endemic country where both the acute form and the chronic disease coexist. T. b. rhodesiense is endemic in the south, while T. b. gambiense is endemic to the north.

The treatment of HAT is dependent on the form and stage of the disease: early stage gambiense disease is treated with pentamidine and late stage with eflornithine or melarsoprol; while early stage rhodesiense disease is treated with suramin and late-stage with melarsoprol.

Although molecular methods are available that can distinguish between the two species, diagnostic tools routinely used in the field cannot. As a result, mingling of the two parasite species in the same geographic locale would create a difficult situation for making decisions regarding treatment options.

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1 “Clinical study comparing the nifurtimox-eflornithine combination with the standard eflornithine regimen for the treatment of trypanosoma brucei gambiense human African trypanosomiasis in the meningo-encephalitic phase”: ISRCTN03148609 (see http://www.controlled-trials.com/ISRCTN03148609)

2 “Assessing three-day pentamidine for early-stage human African trypanosomiasis”: ISRCTN35617647 (see http://www.controlled-trials.com/ISRCTN35617647)

3 Expert group meeting, 14-15 April 2004, WHO/TDR

4 Priotto et al. Clinical Infectious Diseases 2007;45:1443-1445

5 ISRCTN35617647

6 Immetech Pharmaceuticals. Script No 3340, p 22, February 2008


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Stewardship’s Strategic Advisory Committee meets

TDR’s newest area of work – the Stewardship function – held its second Strategic and Scientific Advisory Committee (SAC) meeting 12-14 January. One of Stewardship’s key products is the new global report on infectious diseases research. This is a major new undertaking planned for draft review by the end of 2010. The report sets out to highlight the top research priorities among infectious diseases of poverty that can assist policy makers, researchers, funders and other stakeholders. In the recent SAC meeting, committee members discussed the initiatives under way that would contribute to this report. These range from the 10 new disease and thematic reference groups being established by TDR’s Stewardship function to examine global research gaps and needs in specific areas, to the expansion of TropIKA.net as a ‘one stop shop’ platform for research on infectious diseases of poverty.

The first such thematic reference group (TRG), on Environment, Agriculture and Infectious Diseases, initiated its activities in October 2008, and will be developing its first annual report in late 2009. That group has already developed a structure for its activities that the SAC recommended as a model for the nine other reference groups being established as part of the initiative. The annual reports of the reference groups will be consolidated as a technical document that will be used to produce a top level overview of challenges, opportunities and research priorities in infectious diseases by a “think tank” with cross-cutting activities and harmonized approaches. The think tank will include representatives from the reference groups. The SAC also recommended inviting people from outside the scientific groups with diverse backgrounds who can help identify fresh ideas and approaches to framing the challenges identified by each of the reference groups in a global context – including socioeconomic, political, national and regional perspectives.

Stewardship is also developing a high-level advocacy group to help communicate recommendations emerging from the global report. The SAC co-chaired by professor Eyitayo Lambo, former minister of health of Nigeria and Gillian Samuel, president of the Foundation Council, Global Forum for Health Research, recommended that the high-level advocacy group be developed in partnership with other organizations. Possible categories of members include ministers of health, science and technology, education, opinion leaders and philanthropists.

Environment, Agriculture and Infectious Diseases

Thematic Reference Group launches activities

Changes in global environmental and agricultural systems are among the major overlooked factors in the persistence, emergence and re-emergence of infectious diseases. These also interact with trends of economic development, population growth, urbanization, migration and pollution. Climate change and variability add new factors to this conglomerate of driving forces, as do related trends of over- and under-nutrition.

These are among the issues to be addressed by a new Thematic Reference Group (TRG) of international experts on Environment, Agriculture and Infectious Diseases (TRG-4), which held its first meeting 22-23 October 2008 in Beijing, China.

The expert group is one of 10 such thematic and disease-specific reference groups being launched by TDR in 2009 and 2010 as part of its Stewardship function for infectious diseases of poverty. The TRG/DRGs aim to evaluate and synthesize scientific information on specific global health issues, providing guidance on priority research gaps and needs that should be addressed.

Appearing at the Beijing meeting, Ayoade MJ Oduola, TDR’s Stewardship leader, stressed that the new China-based effort reflects TDR’s increasing commitment to addressing how global environmental change, including climate change, impacts the epidemiology and control of infectious diseases of poverty.

He noted that the expert group will be based in China for a minimum of four years (2008-2012). It will operate in collaboration with the WHO Representative Office in China and with approval of the Chinese Ministry of Health.

While the group will focus on global issues and trends, its outputs are also expected to address public health challenges in China. “Collaborations with Chinese research institutions and China-based international agencies will be of critical importance to the expert group’s analysis and findings,” says Johannes Sommerfeld, TDR manager of the reference group.

Stakeholder consultation paves way for meeting

A stakeholders’ consultation convened in Beijing on 21 October to discuss the planned framework for the TRG’s activities. The consultation, co-organized by the WHO Representative Office in China, TDR and the Chinese Center for Disease Control and Prevention (China CDC), brought together Chinese health officials and regional representatives of in-
international agencies. Presentations were made by the China Council for International Cooperation on Environment and Development and the United Nations Food and Agriculture Organization. Chris Tunon described WHO activities on behalf of the WHO Representative in China.

Stakeholders stressed the need for prospective, systemic and ecological approaches to the issues. Interdisciplinary and inter-sectoral research are needed to address complex linkages that exist between environments, agriculture and infectious diseases, and those linkages to poverty. TRG analysis and recommendations should be expressed in practical terms relevant to policy-makers’ actions.

The expert meeting featured overview presentations on how environmental change, climate change, agriculture, food security and disease prevalence/transmission interrelate. Discussion also focused on the need to also consider poverty linkages and economic systems that better incorporate relevant “externalities.”

Chairperson Anthony McMichael, an Australian National University professor, described some of the environmental and agricultural factors enhancing infectious disease emergence and spread, including intensified livestock production, live animal retail markets, changes to ecosystems (e.g. dam construction, deforestation) and global climate change. “Often factors act in concert in changing the range, seasonality and intensity of infectious diseases transmission;” he said. “Climate change, for example, is amplifying environmental stresses from human pressures on water systems, land cover and displacement of reservoir host species.”

Co-chairperson Xiao-Nong Zhou, a professor at the China CDC’s National Institute of Parasitic Diseases in Shanghai, also discussed trends related to climate change and agriculture with Lin Erda of the Chinese Academy of Agricultural Sciences.

Although China has made significant progress in combating infectious diseases, many persist and re-emerge, noted Kai JianLi director, Office for Epidemiology, China CDC. Public health challenges include dysentery, gonorrhea, viral hepatitis, HIV/AIDS, malaria, measles, schistosomiasis, syphilis, tuberculosis and typhoid and paratyphoid fevers. Emerging diseases include SARS (2003), avian influenza (2004), angiostrongyliasis (2006) and EV71 (2008).

Why China?

As China is undergoing rapid economic, agricultural and environmental changes, it is well placed to harness the TRG’s findings to challenges of infectious diseases of poverty, observed Zhou, an internationally recognized expert on schistosomiasis, a disease with multiple environmental dimensions. China has recently been challenged by both human-caused and natural environmental changes, including flooding and drought as well as the 2008 Sichuan Province earthquake. Climate change impacts on agricultural productivity and vector-borne disease transmission also are of concern.

Earlier in October, McMichael also chaired a meeting of experts on climate change and public health convened by the WHO and hosted by Spain’s Ministry of Health. The meeting, 6-8 October in Madrid, agreed on a research agenda to develop an evidence-based framework for action on the human health implications of climate change.*

Members of the Thematic Reference Group (TRG)

- Dr Anthony McMichael, TRG chairperson, National Centre for Epidemiology and Population Health, The Australian National University, Canberra, Australia.
- Dr Xiao-Nong Zhou, TRG co-chair, CDC National Institute of Parasitic Diseases in Shanghai, China.
- Dr Corey Bradshaw, Research Institute for Climate Change & Sustainability, School of Earth & Environmental Sciences, University of Adelaide, Australia.
- Dr Stuart Gillespie, Agriculture and Health Research Platform, International Food Policy Research Institute (IFPRI), Geneva, Switzerland.
- Dr Felipe Guhl, Centro de Investigaciones en Microbiología y Parasitología Tropical - CIMPAT, Bogota, Colombia.
- Dr Anthony Okon Nyong, Agriculture and Agro-Industries Department, Environment and Natural Resources Division, African Development Bank, Tunis, Tunisia.
- Dr Suud M Sulaiman, Environment Advisor, Khartoum, Sudan.
- Dr James A Trostle, Anthropology Department, Trinity College, Hartford, USA.
- Dr Jürg Utzinger, Department of Public Health and Epidemiology, Swiss Tropical Institute, Basel, Switzerland.
- Dr Bruce Wilcox, Center for Infectious Disease Ecology, Asia-Pacific Institute for Tropical Medicine and Infectious Disease, John A. Burns School of Medicine, University of Hawaii, Honolulu, USA.
- Dr A Lee Willingham III, WHO/FAO Collaborating Center for Parasitic Zoonoses, Faculty of Life Sciences, University of Copenhagen, Frederiksberg C, Denmark.
- Dr Yang Guojing, Jiangsu Institute of Parasitic Diseases, Wuxi, China.

Related resources:
- WHO Department for Public Health and Environment (PHE)
  http://www.who.int/phe/en/
- WHO/UNEP Health and Environment Linkage Initiative
  http://www.who.int/heli/en/
- IFPRI Agriculture and Health Research Platform
  http://www.ifpri.org/ahrp/ahrp.asp

* WHO Expert Meeting on Climate Change and Public Health
  http://www.who.int/phe/climate/meeting_madrid/en/index.html

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Empowerment SAC reviews ‘centres of excellence’

At least ten health research institutes are to be designated centres of excellence in infectious diseases research as a result of TDR’s Empowerment function (BL2) activities.

Empowerment’s Strategic and Scientific Advisory Committee (SAC) endorsed the plans in a meeting, 6-7 November 2008 in Geneva. The SAC also urged that TDR will develop criteria for the selection of candidate centres of excellence, as well as indicators to determine if centres meet research excellence goals. TDR also plans to develop cross-cutting indicators measuring progress on the broader strategic goal of having “disease-endemic countries play a pivotal global role in research on infectious diseases of poverty.”

In terms of other specific Empowerment activities supporting research, training, networks and quality management, SAC recommended the following:

**Research:** New funding should be sought to support research empowerment grants to scientists and institutions, particularly in small, poor countries that have a high disease burden. More emphasis should be given to translation of research results into policies and practices, including strategies for publications and packaging of results for various audiences.

**Training:** Significant progress had been made on harmonization and standardization of short courses and development of indicators and mentorship systems for TDR’s new stepwise programme of leadership training including: Leadership Training Grants, Leadership Development Fellows and Career Development Fellows.

**Networks:** Progress also was made on development of a data base of previous TDR grantees. SAC encouraged TDR to further explore how its range of networks could be harnessed to support training, mentorship and grooming health researchers and research leaders as well as centres of excellence.

**Quality management:** SAC commended the progress made by Empowerment on developing programmes for Quality Management training, coordination and institutional recognition in 2008. As of 2009, quality management activities are to be transferred to TDR’s team on Neglected Research Priorities, operating there as an independent function. This is to ensure that quality management cuts across all TDR health research and training activities. Links between TDR’s quality management activities and those of internationally recognized accreditation programmes also are being deepened and developed.

ANDI Task Force plans follow-up to Abuja launch

A Task Force of the new African Network for Drugs and Diagnostics Innovation (ANDI), held its first meeting on 10 February to plan concrete actions for turning the R&D initiative into a reality. This follows the launch of ANDI in October 2008 at a stakeholders’ meeting in Abuja, Nigeria.

The ANDI Task Force is charged with developing a strategic blueprint and business plan for the network. Meeting in Geneva, the group reviewed the potential scope of ANDI’s work, options for organizational structure and selection criteria for African countries interested in hosting the secretariat.

The proposed scope of work for ANDI include activities related to:

**Product R&D coordination and management:** e.g. a framework for scientific coordination and R&D priority-setting; collaboration with regional and western partners; management of intellectual property to protect local knowledge and promote innovation; and linkages of investors with entrepreneurs.

**Funding:** e.g. encourage African governments to support R&D; provide the platform for African product R&D funding and investment; promote establishment of venture capitalists that focus on health innovations; establish and manage an African Innovation Fund.

**Advocacy for product R&D at all levels:** e.g. advocate for increased investment in product R&D by various stakeholders including African governments, philanthropic agencies, and international/ development bodies; establish a mechanism to take African traditional medicines to international market standards; seek recognition of diagnostics/drugs registration among African member states.

Task Force participants agreed to recruit a consultant to aid in developing a five-year strategic and business plan. The group scheduled two more meetings, as well as teleconferences, in order to prepare for delivery of a business plan in the fourth quarter of 2009.

Those will be at the African Development Bank in Tunis, 7-8 May, and the WHO/AFRO regional office in Brazzaville, Democratic Republic of Congo, 3-4 August. A second stakeholders meeting is scheduled for the week of 5 October 2009 in Cape Town, South Africa, where the Task Force final report will be presented.

The first ANDI stakeholders’ meeting and launch of the initiative in October 2008 drew over 200 participants from Africa and around the world, including health ministers and private sector and intergovernmental organization representatives.

ANDI aims to promote African-led R&D innovation, and to support capacity and infrastructure development, according to Solomon Nwaka, TDR’s leader of drug discovery and innovation. It follows upon WHO’s recent approval of a Global strategy and plan of action on public health, innovation and intellectual property (WHA 61.21).

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Standardized protocol for PCR analysis of Chagas disease

A workshop and symposium on the use of polymerase chain reaction (PCR) for T. cruzi DNA detection has resulted in a single standardized protocol for PCR-based clinical analysis of the disease.

Sponsored by TDR, INGEBI-Conicet UBA and the United Nations University’s BIO-LAC programme, the workshop involved 32 biomedical researchers and medical practitioners from 14 countries – whose convening in a single forum also represented a significant achievement.

Most of the participants at the meeting, 17-22 November 2008 in Buenos Aires, Argentina, were from Latin America where Chagas remains endemic. Over four days, the group defined PCR best practices, outlining their applicability in a clinical setting and establishing the limitations of PCR technology as a diagnostic tool.

While PCR has been employed for clinical diagnosis and assessment of T. cruzi infection for more than a decade, there exist numerous and widely varying laboratory protocols for its use. The effect has been to render unreliable comparisons of PCR-based findings between groups, thereby slowing the pace of research.

Recognizing the need for a standard PCR protocol for T. cruzi DNA detection, a consortium of researchers from Brazil, Colombia and Argentina drafted a project proposal in 2007 and sought TDR support. Months later, the research began. Blinded blood samples with a known number of parasites, purified DNA from T. cruzi strains of different lineages and relevant controls were prepared by the coordinating center and sent to 29 participating laboratories.

Those laboratories that achieved a minimum of concordance with the blood samples were invited to participate in the workshop and symposium in Buenos Aires. The information gathered over the course of that week allowed for the establishment of a standard operating procedure (SOP) for the use of PCR as a diagnostic tool.

“In the absence of a validated commercial product, we have this,” says Janis Lazdins-Helds, TDR’s leader of research on drug development for helminth and other neglected diseases and one of the Buenos Aires workshop’s planners. “It has to be made in one’s own laboratory, but it’s a start. And it’s a wonderful example of how basic biomedical research findings can be used clinically for the benefit of both practitioners and patients.”

According to INGEBI-Conicet’s Alejandro Schijman, the initiative’s coordinator, the new SOP can serve as a point of reference not only for medical practitioners interested in disease diagnosis but also for clinical researchers using PCR to evaluate new therapies for Chagas in clinical studies.

Rectal artesunate session draws big turnout at American Society of Tropical Medicine and Hygiene (ASTMH)

Tropical medicine experts discussed results of randomized controlled trials of a life-saving, one-dose regime in rural African and Asian communities. The 57th annual meeting of ASTMH in New Orleans also covered logistics, ethics, adherence to referral advice and clinical research practices.

A rectal application of an inexpensive drug could save lives of patients with severe malaria in some of the remotest locations of rural Africa and Asia.

A TDR-supported study promoting the treatment, Use of rectal artesunate at the community level in African rural settings, was presented to a packed session at the 57th American Society of Tropical Medicine and Hygiene (ASTMH) annual meeting in New Orleans, USA, 7-11 December 2008.

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Researchers from all over the world gathered to hear the conclusions from a panel including TDR coordinator of the research Melba Gomes and researchers Emran Bin Yunus from Bangladesh, John Gyapong from Ghana, Marian Warsame from Tanzania, and Tom Peto, Rita Baiden and other colleagues from the Study 13 Research Group.

That same morning, The Lancet published the study online.¹ Lorenz von Seidlein and Jacqueline L Deen also wrote in a commentary there, "If there are a handful of important papers every decade that will influence the way malaria is treated, this study is one of them."

That same enthusiasm was evident at the ASTMH session, which drew supportive comments and questions about how to move forward with the results.

The study sought to determine in very remote settings whether rectal artesunate plus referral to a clinic reduced mortality and permanent disability compared with rectal placebo plus referral. The multi-country study included over 17 000 patients, and showed that a single dose given rectally can be safe and effective as an initial treatment for patients with severe malaria who are too sick to take medication by mouth, and who do not have immediate access to an injectable treatment. Rectal artesunate is administered at a rural health centre or by a trained community member or caregiver in order to "buy time" while the patient is referred for definitive treatment.

What is new?

The trial was the first randomized-controlled study to assess the value of rectal artesunate in community-based settings in remote rural areas. It was undertaken in malaria-endemic areas of Bangladesh, Ghana and the United Republic of Tanzania.

In their Lancet commentary, Seidlein and Deen said that the trial results provide "a strategy for patients with severe malaria who cannot access parenteral drugs quickly." The survival benefit is significant in the communities where travel to get care takes at least six hours. Mortality was halved in longer travel, a particularly acute problem in Africa.

The study noted remarkably high compliance with the advice to go immediately to a clinic, partly because there was a recruiter in each village and communities received sustained malaria education. Before the study began in communities in urban settings and integrated disease management. See also: http://www.who.int/tdr/research/antimalarial-policy-access/ppt/HMM-Antwerp-Apr08.ppt

Other TDR sessions at ASTMH

TDR sponsored a total of five major symposium sessions, several papers and posters on malaria, and a presentation on TDR’s Helminth Drug Initiative at the 57th ASTMH meeting in New Orleans. In addition to the session detailed above, TDR’s major sessions discussed:

- Accelerating the development and deployment of diagnostic tools into the developing world: promises and challenges. Due to the lack of laboratory capacity in the developing world, high-quality diagnostic tests for infectious diseases are neither affordable nor accessible to the majority of patients. Moreover, owing to the lax regulatory oversight of diagnostics, those tests that are available are often sold and used with little evidence of their effectiveness. This symposium described the path from diagnostic target discovery to test development and deployment, identifying challenges and opportunities along the way.

TDR contact: Dr Rosanna Peeling, peelingr@who.int

Use of fluorescent probes and transgenic parasites to enhance drug screening. This symposium highlighted progress made by a network of investigators from disease-endemic and non-endemic countries using new genomic technology for drug screening.

TDR contact: Dr Ayoade MJ Oduola, oduolaa@who.int

Home Management of Malaria (HMM) in 2008: Improving access to ACTs and diagnostics at the community level in sub-Saharan Africa. This session provided a summary of how HMM is incorporating new tools like artemisinin-based combination therapy (ACT) and rapid diagnostic tests (RDT) for malaria and addressing new challenges posed by communities in urban settings and integrated disease management. See also: http://www.who.int/tdr/research/antimalarial-policy-access/ppt/HMM-Antwerp-Apr08.ppt

TDR contact: Dr Franco Pagnoni, pagnonif@who.int

Measurement and prediction of malaria treatment outcomes: Parasite, drug and host factors. Leading experts reviewed the protocols for in vitro and molecular measurements of antimalarial drug resistance, their limitations, and how these relate to treatment outcomes

TDR contact: Dr Olumide Ogundahunsi, ogundahunsi@who.int. ■

![For more information and The Lancet article, see www.who.int/tdr/svc/news-events/news/rectal-artesunate-lancet](http://www.who.int/tdr/svc/news-events/news/rectal-artesunate-lancet)

For archives of ASTMH meetings, see: www.astmh.org

Contact: Dr Melba Gomes
gomesmn@who.int
DEEP discusses costs of ineffective diagnostics

The fifth annual meeting of the Diagnostics Evaluation Expert Panel (DEEP) 3-4 November 2008, offered TDR scientists a chance to engage potential collaborators in estimating the human and economic costs of low-quality diagnostics for infectious diseases.

Owing to the lack of regulatory oversight in the developing world, many diagnostics are sold and used without evidence of effectiveness. There is usually little information available on test performance. As a result, cost is often the overriding consideration in test procurement. This situation has led to the marketing of cheap tests with low performance characteristics, which has in turn discouraged reputable manufacturers of high-quality diagnostics from competing in these markets.

Assembled in 2004, DEEP has a mandate to advise TDR and the Foundation for Innovative New Diagnostics (FIND) on recommendations for best practices in diagnostic trials. According to TDR scientist Rosanna Peeling, leader of TDR’s business line on accessible quality-assured diagnostics, results from work on the human and economic costs of low-quality diagnostics could generate advocacy materials about their consequences.

The meeting in Geneva opened with an overview of the global diagnostics landscape and the process by which diagnostics are regulated and approved in South Africa, Thailand, the United States of America and India. Speaking on behalf of the European Diagnostics Manufacturers Association (EDMA), Jean-François de Lavison stressed the need for international cooperation in the regulation of diagnostic tests. He called for the establishment of an International Diagnostics Manufacturers’ Association to comprise companies from developed and developing countries.

Advocacy recommendations included the use of case studies of problems or benefits associated with poor-quality or improved diagnostics; the use of mathematical models, such as those currently used for sexually transmitted infections (STIs), to estimate the costs/benefits of poor quality/improved diagnostics, including tests for drug resistance; the encouragement of regulatory authorities to work with health ministry and control programmes; the establishment by TDR of a session on diagnostics regulation at the annual International Conference for Drug Regulatory Authorities (ICDRA); and greater collaboration with partner organizations in advocacy efforts.

A website devoted to diagnostic tests for priority diseases was also proposed as an effective means of disseminating information to health authorities, funders and the public. The website would include information on product evaluation, including unpublished evaluations by WHO, FIND and FDA, among others, and toolkits describing how to evaluate diagnostic tests.

Contact: Dr Rosanna Peeling peelingr@who.int

Biosafety course in vector control launched in Mali

The year was 2002, the setting was Notre Dame University in the USA, and a young Malian PhD student named Mamadou Coulibaly was engaged in research related to the genetic modification (GM) of mosquitoes.

As he considered both the potential of such research to fight disease and also the social and environmental issues it inevitably raised, Coulibaly recalls asking his professor and mentor, “Isn’t it better to start talking about ethics issues now?”

Now, Coulibaly believes, that dialogue is advancing, thanks partly to several new initiatives by WHO and TDR.

Coulibaly was a member of the first TDR-supported course for Africa on Biosafety for human health and the environment, 17-28 November 2008 at the University of Bamako, Mali.

On 29 November - 2 December, coordinators of three new TDR-supported biosafety training centres in Africa, Latin America and Asia also met in Bamako to develop material for further biosafety training and assessment of GM research in Africa, Latin America and Asia. That was followed by a TDR-supported “train the trainers” course on laboratory biosafety and biosecurity, 3-8 December, aimed to consolidate and expand the initiative in Africa, Asia and Latin America.

Standing on an open concrete terrace at the University of Bamako on a break from the first African training course, Coulibaly described how his PhD studies had stimulated questions that he and other researchers now seek to address more systematically.

“I have a lot of theoretical knowledge in the technology,” Coulibaly said, “but the most interesting thing to me is: what do countries and ethics boards think about the release of transgenic mosquitoes into nature? How do neighbouring countries interconnect with each other? And what is the response of communities where GM deployment is planned?”
Sudan to develop a national HMM strategy

Sudan’s national malaria programme is developing a large-scale home management of malaria programme (HMM) for its malaria-endemic zones in the country’s northern region as a result of implementation research stimulated by TDR.

Sudan, the country in WHO’s Eastern Mediterranean Region (EMRO) with the highest malaria burden, will thus become the first country in the region to develop and implement such an effort. In preparation for the new initiative, the national malaria control programme organized a two-day policy development workshop in Khartoum, 3-4 February.

The workshop follows in the wake of a TDR implementation research project testing HMM strategies adapted to the country’s epidemiological and socio-cultural context.

The study was carried out in 2006 in the state of South Kordofan, in collaboration with TDR/EMRO, Roll Back Malaria/EMRO and the Istituto Superiore di Sanità in Rome, Italy. It was led by Khaled Elmardi of the National Malaria Control programme. A second such project was then initiated in 2007-08 in North Kordofan state, funded by the Federal Ministry of Health. Positive results of these two projects inspired the Ministry to convene the workshop to develop a national HMM strategy across Sudan’s northern region in zones where malaria is endemic.

The February workshop was facilitated by Hoda Atta, regional adviser for malaria in EMRO, Marian Warsame of WHO’s Global Malaria Programme and Franco Pagnoni of TDR.

The approximately 50 participants included representatives of high malaria-burden states as well as health officials from South and North Kordofan, where the two pilot projects had taken place, and several high level officials from the Federal Ministry of Health. The workshop was preceded by a field visit to North Kordofan, where participants were able to see first-hand how the home management of malaria project had been implemented.

Contact: Dr Franco Pagnoni

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Field visit to community medicine distributor in North Kordofan state, Sudan. Foreground, left to right: Mai M Alihilo, coordinator, Malaria Control Programme, North Kordofan, Sudan, Franco Pagnoni, TDR; Tarig Abdelgadir, coordinator, National Malaria Control Programme, Federal Ministry of Health; Marian Warsame (WHO/GMP); and Hoda Atta, regional advisor for malaria in WHO’s Eastern Mediterranean Regional Office. In background, left to right: Khalid A Elmardi, case management director, National Malaria Control Programme, Elrasheed M Ali, Partnership desk in National Malaria Control Programme.
Evaluation of commercially available anti-dengue virus immunoglobulin M tests

Diagnostics evaluation series, No. 3
52 pp., 2008

Serological assays that can detect virus-specific immunoglobulin antibodies to dengue virus are widely available and can provide an alternative to more costly, labour-intensive methods of diagnosing dengue fever. However, due to the wide variety of IgM response patterns to infection, there is a need to evaluate the sensitivity and specificity of available tests. This report describes the results of a TDR-sponsored laboratory-based evaluation of nine commercially available anti-DENV IgM tests.

Good clinical laboratory practice (GCLP)

Web version only
28 pp., 2008 (ISBN 978 92 4 159785 2)

In 2006, WHO/TDR convened a meeting of organizations engaged in clinical trials in disease-endemic countries to discuss the applicability of GCLP guidelines to their work. It was agreed that GCLP would be a valuable tool for improving quality laboratory practice. In line with that agreement, TDR/WHO recently acquired copyright to GCLP guidelines that were originally published in 2003 by a working party of the Clinical Committee of the British Association of Research Quality Assurance (BARQA), with the aim of disseminating them widely in developing countries and developing related training materials. These GCLP guidelines are presented here. Compliance with them will allow clinical laboratories to ensure that safety and efficacy data is repeatable, reliable, auditable and easily reconstructed in a research setting. GCLP guidelines set a standard for compliance by laboratories involved in the analysis of samples from TDR-supported clinical trials.

To download: http://www.who.int/tdr/svc/publications/tdr-research-publications/gclp-web

Second edition: Good laboratory practice (GLP) handbook and training manuals (Trainer and Trainee)

Web version only

First published in 2001 to assist countries in conducting non-clinical research and drug development, the GLP series, including a GLP Handbook and GLP Training manuals for trainers and trainees, has been revised and updated in line with World Health Assembly Resolution 61.21, Global strategy and plan of action on public health, innovation and intellectual property. Since the publication of the first GLP series, TDR-fostered GLP training efforts have resulted in a network of GLP trainers whose input shaped the development of this second edition. This revised GLP series will support TDR in empowering disease endemic countries to develop and lead research activities with internationally recognized standards of quality.

To download: http://www.who.int/tdr/svc/publications/tdr-research-publications/glp-handbook09-web

Available through TDR

Evaluating diagnostics: the CD4 guide
Nature Reviews Supplement: Microbiology
Vol. 6, No.11, November 2008

Accurate CD4 counts are crucial laboratory markers for assessing immunodeficiency and the risk of disease progression in HIV-1 infection. HIV-1 causes a huge burden of morbidity and mortality, particularly in developing countries. This fourth supplement in the series focuses on CD4 immunodiagnostics, which can be used to monitor CD4 counts and to decide when to treat individuals with antivirals and whether treatments are effective.

To download: http://www.nature.com/nrmicro/supplements/index.html

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Print and multimedia publications now available from TDR
Framework for operations and implementation research in health and disease control programmes

Expert group report
37 pp., 2008 (ISBN 92 9224 110 9)

The product of a joint effort by the Global Fund to Fight AIDS, Tuberculosis and Malaria, TDR and an inter-agency technical working group, this IR/OR framework, first published in 2008, is now available in both French and Spanish along with the initial English version. The overall goal of the framework is to standardize the practice of OR across the international health community and to stimulate the integration of OR into health programmes. Limited number of hard copies available in English, French and Spanish.

To download all three versions:
http://www.who.int/tdr/svc/publications/training-guideline-publications/listpubs
http://www.theglobalfund.org/en/me/?lang=en

Joint TDR/EC expert consultation on biomarkers in tuberculosis

Expert group report, TDR and the European Commission
143 pp., 2008

The emergence of multi- and extensively drug resistant tuberculosis has aggravated the impact of TB, especially on HIV-infected individuals, and added urgency to the search for new vaccines, diagnostics and drugs. However the lack of suitable and validated biomarkers to assess areas of clinical management of TB patients remains a major obstacle to these efforts. This report provides an overview of biomarkers currently under study, treatment response and outcomes, technological platform s, and collaborations between researchers and funding agencies.

A human rights-based approach to neglected tropical diseases

WHO information sheet/web version

Neglected tropical diseases (NTDs) affect one billion people around the world, often the most vulnerable populations living in poor rural areas. A source of social stigma and poverty, NTDs can result in lifelong disability and even death. Affected populations often do not have access to treatment and preventive measures, and research and development have been insufficient. This WHO information sheet, developed jointly with TDR and WHO's Department of Health, Ethics and Trade, aims to improve understanding about NTDs among health planners, human rights groups, development partners and civil society organizations. Available in English, French and Spanish.

To download:
http://www.who.int/tdr/svc/publications/tdr-research-publications/human-rights

New laboratory diagnostic tools for tuberculosis control

Stop TB Partnership: Retooling Task Force and New Diagnostic Working Group
January 2009

There is a lack of easily digestible information available to national tuberculosis programmes, as well as to funding and technical agencies, regarding new TB diagnostic tools in the development and implementation pipeline.

With this in mind, this brochure describes 19 new or improved diagnostic tools, among the many such initiatives under way worldwide. Three of the tools described in this document have already been endorsed by WHO and are being implemented by countries, while the others are still under development or in piloting phase, and are expected to be ready for review for scaled-up use in the coming years.

The brochure represents as an interim document until a more complete blueprint of current R&D efforts can be developed. The purpose is not to recommend specific tools, but rather to provide summary information about tools being developed and becoming available, so that all who play a part in TB control, especially in national TB programmes, can make well-informed decisions when retooling.

To download:

Ethics in human and social sciences research in the health field

Iara Coelho Zito Guerriero, Maria Luisa Sandoval Schmidt and Fabio Zicker
Sao Paulo: Editora Hucitec
308 pp., 2008 (ISBN 978 85 60438 63 1)

Ethical guidelines issued by the Council for International Organizations of Medical Sciences (CIOMS) have long established norms for the conduct of biomedical research. However, when it comes to the social sciences, the guidance has never been so clear. Thanks to a TDR-supported initiative by the Health Secretary of Sao Paulo, Brazil, this may soon change in Brazil. A 2007 seminar in Sao Paulo addressed the ethical challenges unique to qualitative social sciences research, particularly in developing countries. More than 150 participants presented on issues ranging from the ethics of ethnographic studies involving vulnerable populations to issues related to specific procedures such as informed consent and confidentiality. Those presentations formed the basis for this book, subsequently distributed to all of Brazil’s 590 institutional ethics review committees as well as the National Commission on Ethics in Research (CONEP).

For copies please contact: Dr Iara Coelho Zito Guerriero at: guerriero@stu.ca
Call for contributions

Call for contributions to a WHO systematic review of information on maternal outcomes and prevalence of birth defects in Asia, Africa and Latin-America.

WHO/TDR are issuing two calls for contributions to this planned systematic review, which is part of a broader WHO effort to establish a Global Pregnancy Register (see page 6).

The call includes requests for contributions of:

- Studies, publications or reports that monitored pregnant women in Africa, Asia or Latin America, and assessed the newborn at birth.
- Individual patient data from research in Africa, Asia or Latin America, where pregnant women were prospectively followed to term, and where the newborn has undergone a systematic physical examination.

Please contact Dr Melba Gomes (gomesm@who.int) with either “Systematic review of pregnancy outcomes - reports” or “Systematic review of pregnancy outcomes – Individual Patient Data” in the subject line of the message if you have information to contribute.

Reprints of relevant publications/reports can be mailed to:
Dr Melba Gomes, scientist,
Special Programme for Research and Training in Tropical Diseases (TDR)
World Health Organization,
20 Avenue Appia, 1211 Geneva, Switzerland

Grant awards

Innovative vector control interventions (BL5)

TDR’s Strategic and Scientific Advisory Committee on Innovative Vector Control Interventions recommended the following projects for funding in 2008 in response to calls for proposals from investigators worldwide.

A80361 Seydou DOUMBIA University of Bamako, Faculty of Medicine, Pharmacy and dentistry, MALI. Evidence-based for the improvement of integrated malaria vector control strategies in East, Central and West Africa. US$ 200 000

A80360 Maria Inés PICOLLO Centro de Investigaciones de Plagas e Insecticidas, Villa Martelli, ARGENTINA. Design and evaluation of complementary or alternative strategies for the control of Chagas disease vectors. US$ 193 000

A80309 Brij Kishore TYAGI Centre for Research in Medical Entomology, ICML, Madurai, INDIA. Asian centre for training in biosecurity assessment for human health and environment using genetically modified vectors. US$ 50 000

A80310 Ivan Dario VELEZ-BERNAL Universidad de Antioquia, PECET, Medellin, COLOMBIA. Latin American biosafety training centre in relation to potential release of genetically modified disease vectors. US$ 50 000

Empowerment Function (BL2)

TDR’s Strategic and Scientific Advisory Committee for Empowerment recommended the following Leadership Training Grants to researchers in 2008, in response to a global call for LTG proposals.


To our readers:
We want to hear from you. Please send us your feedback, as well as letters and ideas on possible stories for TDRNews and on TDR-related tropical disease research issues, events, institutions, publications and personalities. Thank you!

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