TDR Annual Report
2014
Celebrating 40 years of research
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I am an extremely lucky man. I have the opportunity to lead and learn from a Programme that has made an incredible impact. We spent 2014 celebrating 40 years of commitment by honouring the many people who were given TDR support at a crucial time in their career and who used that support to make a difference.

Did you know that the reason why insecticide-treated bednets are now the mainstay of malaria prevention is because of research that provided definitive evidence that lives were saved by this simple technology?

Did you know that the reason why so few Africans now fear onchocerciasis (also called river blindness) is because of research that helped develop a drug to kill the parasitic worms, and a strategy where communities lead the distribution and implementation of this annual treatment?

Did you know that the reason leprosy is no longer a disease that ravages countries is because of research that developed a multi-drug treatment?

Did you know that visceral leishmaniasis is on its way to being eliminated in Bangladesh, India and Nepal because of multiple research efforts on diagnosis, new drugs and treatment strategies?

Behind each one of these examples, there were people who used TDR support to make these breakthroughs. And they have continued to build research capacity in their countries, with some becoming international leaders in their own right.

During 2014, we started profiling the people behind this work, which you can find on our website www.who.int/tdr/capacity/alumni

This annual report gives you a condensed version of this history – we will also show you our current key work, but the message I want to reinforce is that these achievements are built upon a 40 year commitment – a commitment to help people help themselves by supporting their education, their training and their research.
This has been a most exciting year for TDR. It included a celebration at the World Health Assembly, where 40 years earlier the establishment of this Programme was agreed. A standing-room only crowd came to hear the panel of alumni and a health minister who spoke movingly of the impact that TDR has had nationally, regionally and internationally.

TDR is an important member of the organizational cluster I lead, that also includes the departments of HIV/AIDS, TB, malaria and the neglected tropical diseases. WHO sees research as a critical component of this global fight against such diseases and TDR has an impressive record of achievement in this area.

It is satisfying to see TDR interacting directly with the other programmes, in areas such as investigating the impact of both human and vector behaviours on disease spread and control. Work is also being done to build national research capacity to deploy seasonal malaria chemoprevention, and train staff in country malaria control programmes and WHO country offices on operational research. TDR’s Structured Operational Research and Training Initiative (SORT IT) is already supporting four South African countries on the way to malaria elimination – Botswana, Namibia, South Africa and Swaziland, as part of WHO’s Global Technical Strategy for Malaria, and the SORT IT approach is expanding to other groups of countries.

TDR is also working closely with the WHO regions to develop flexible research training that responds to the priorities of scientists on the ground. Regional training centres are providing hubs for courses such as ethics, project management and implementation research, and the new small grant scheme provides applicants with support for focused training outside of a university or degree programme.

It is also very pleasing to see TDR lending their expertise to support WHO in its creation of an innovative new approach to funding R&D through a pooled fund. This gives TDR an important role in coordinating the development of affordable new treatments for neglected diseases.

TDR’s budget is well managed and stable, with strong support from our core donors. During this past year, we have been happy to welcome Dr Hannah Akuffo from the Swedish Development Cooperation Agency (SIDA) as the new Chair of the Joint Coordinating Board. She is a passionate advocate of research capacity building in low-income countries with extensive experience in Euro-African research cooperation and funding.

I am feeling proud of these achievements and happy to be able to leave the organization at such a point of strength. I retire at the end of May after having served this organization for 8 years. I have seen many changes during this time but what has never changed is the commitment of so many experienced and passionate people. It has been a privilege to be a part of this, and I know that TDR will continue to thrive with its strong leadership and close ties to WHO.
It has been a rewarding year for me to start my term as Chair of TDR’s Joint Coordinating Board (JCB). I have witnessed the outpouring of respect and good wishes for TDR as it celebrated its 40th anniversary, with a focus on its alumni. What a wonderful way to examine impact – what did that early support do for so many budding scientists in low- and middle-income countries? It is clear there has been extensive impact, from building individual and institutional capacity to developing new products and strategies that have been endorsed and used by countries to improve health. I encourage you to read the special 7-part series in PLOS NTD that was published in January, 2015. It provides lessons learnt and case studies of critical points in TDR’s history. For anyone interested in global health research, this is a must-read.

During the past year the board has been privileged to oversee the completion of one biennium (2014-15) and plans for a new biennium (2016-17). TDR has built a workplan for today’s needs – eliminating the scourges of malaria and visceral leishmaniasis; investigating better ways to implement current products and strategies where they are needed; and customizing training for today’s scientists with personalized support and mentorship that is also developed hand-in-hand with research infrastructure support. The goal is long-term sustainability of scientific capacity and output from the countries where the diseases occur.

As the former Chair of the General Assembly of the European & Developing Countries Clinical Trials Partnership (EDCTP), I am particularly pleased about TDR joining forces with EDCTP this past year to offer a joint clinical R&D fellowship and Ebola research grants, which harmonizes efforts and broadens the scope of activity.

TDR also joined a broad group of national, regional and international groups calling for sustained attention to the needs of maternal and child health issues. A communiqué calling for attention to the issues of healthy women and children was published by The Partnership for Maternal, Newborn and Child Health and commits to collaboration to meet the current Millennium Development Goals (MDGs) of 2015, particularly MDG 4 on reducing child mortality and MDG 5 to reduce maternal mortality, as well as to continue and increase work in the next Post 2015 Sustainable Development Framework.

Similarly, with the Ebola outbreak in West Africa, TDR has been involved in the identification and testing of potential candidate treatments in Médecins Sans Frontières (MSF) centres in these countries. TDR staff have volunteered time to coordinate contact tracing, surveillance and social support in Sierra Leone, provided support to the ethical review of the clinical drug and vaccine trials, is involved in one of the drug clinical trials, and is helping raise awareness of the need for more research on Ebola survivors.

TDR is managing to not only develop and implement plans for long-term research capacity and impact, but is also flexible enough to address emerging issues and crises. This is truly a feature of a value-for-money institution.
CELEBRATING 40 YEARS OF HISTORY

This timeline is the final result of the 2014 celebration of 40 years of achievements and impact.

In this publication, you will find examples of visionary, long-term commitments aimed at creating global, public health goods.

Some of these highlight the new tools that have been created – such as treatments for malaria, diagnostic tests for visceral leishmaniasis, and healthcare delivery strategies for remote, rural communities.

In other instances, the output takes the form of a body of scientific knowledge, such as the genome sequencing of parasites.

Since its inception, TDR has shown a remarkable ability to stimulate pioneering partnerships and collaborations, often between public and private sectors, leading to major advances.

Most importantly, there are numerous examples that show the value and impact of building sustainable research capacity in low-income countries. To be sure, the end goal is for these countries to be able to prioritize and conduct their own research.

Over its 40 years, TDR has provided training and mentorship in basic research, product development for new tools, vector research to understand and cut patterns of transmission, social research to root out causes of stigma and discrimination and implementation research to improve delivery systems.

It is this long-term, multi-disciplinary approach, developed in partnership with communities and many types of organizations, that distinguishes TDR.

“TDR’s major contribution is to have brought much of the absolute best, cutting-edge science to tropical diseases, to a field that could not have been further behind most areas of other biomedical research in 1975.”

Dr Barry Bloom, former Dean, Harvard School of Public Health (TDR, 1995)
1975 – 1984
A NEW KIND OF ORGANIZATION
TDR, like other programmes in UN agencies, had to contend with political realities, especially at a time when the world was sharply divided into two major power blocks. TDR adopted a policy of providing a neutral platform on which scientists from all over the world could work together against diseases that were the common enemies of all human beings. Scientists responded admirably to this approach.

Dr Adetokunbo Lucas, TDR Director, 1976–1986

Since its very inception, TDR’s active and ever evolving engagement ... has been a model for accelerated capacity building. TDR has not only served to transfer state-of-the-art technologies and knowledge to scientists in these countries, but it has also helped create an environment that has instilled respect for scientific rigor and merit.

Dr Javid Hashmi, Chief of Research Capability Strengthening, TDR, 1986–1995

TDR Directors
Dr Howard C. Goodman (1975–1976)
Dr Adetokunbo O. Lucas (1976–1986)

Scientific highlights
- Leprosy multidrug therapy
- Onchocerciasis drug (ivermectin) and free distribution
- New anti-malarials (mefloquine and artemisinin derivatives)
- Development of a new drug, DFMO (eflornithine®), new vector control tools, and new diagnostics (CATT — card agglutination test) for sleeping sickness
- Diagnostics for schistosomiasis, malaria and lymphatic filariasis
- Multi-country studies on Chagas disease prevalence, protocols for Chagas diagnosis and field research on new vector-control tools
- Vector biocontrol (for example, use of Bacillus thuringiensis serovar israelensis [H-14] for onchocerciasis)
- Creation of public registries and repositories for reagents and other materials (such as monoclonal antibodies to parasite antigens)
- Innovative social and economic research of diseases and interventions.
The beginning of TDR – a new kind of organization

In the early 1970s, there was no international research framework for infectious disease control in the developing world – that is, until TDR.

In May 1974 the World Health Assembly called for a programme to define the research priorities of these developing regions and help build the human and capital infrastructure to bring new solutions that met their health needs.

The United Nations Development Programme (UNDP) and the World Bank formally joined WHO as co-sponsors, and UNICEF came on board in 2003.

Innovative from the outset – and standing up for the interests of the disadvantaged in disease-endemic countries – the Joint Coordinating Board is TDR’s strategic driver. It ensures initiatives retain balance and harmony, and fosters close, beneficial partnerships with public, academic and private institutions worldwide.

TDR has had throughout its history two intertwined missions – to build research capacity in the countries where these diseases burden so many, and to help prioritize and fund the research needed. Today the first generation who got their start at TDR are now leading research institutions and ministries of health.

What was put in place 40 years ago now provides the foundation for several elimination campaigns and for a growing body of researchers and institutions capable of identifying research priorities and carrying out a range of studies, from clinical trials to implementation research to policy development.

“[TDR is] a global programme of international technical cooperation ... with the two interdependent objectives of developing improved tools for the control of tropical diseases and strengthening the research capability of affected countries themselves.

Memorandum of Understanding on the administrative and technical structures of TDR, February 1978
Building individual and institutional research capacity

One of TDR’s first steps was to put in place a research capacity-strengthening programme to increase institutional capacity and train individuals to tackle immediate and serious health issues.

To ensure a prolonged (up to ten-year) period of funding, the programme involved capital grants for initial investigation, research and follow-up. Initially, TDR focused on non-competitive long-term grants to help construct or upgrade research facilities, and grew into increasingly competitive grants.

At Brazil’s Oswaldo Cruz Institute FIOCRUZ, grants helped build a new biochemistry and molecular biology department, and supported the work of Dr Bernardo Galvão Castro, who would become the first scientist in Latin America to isolate the HIV virus. At Thailand’s Mahidol University, Dr Yongyuth Yuthavong was supported to put together a course on molecular biology.

By the mid-1980s, 98 institutions had benefitted from TDR support. It had issued over 700 training grants and launched more than 10 MSc courses in entomology and epidemiology in Asia, Africa and Latin America.

Eliminating leprosy

Until the mid-1970s, leprosy was a disease more or less beyond hope. The bacterium was developing resistance to dapsone monotherapy — which was a lifelong treatment. Some 10 to 12 million people were estimated to have the disease.

TDR began by highlighting this resistance and supporting research to identify several potential new compounds. Clinical trials followed to test new combinations, of dapsone, rifampicin, clofazimine and acedapsone, called multidrug therapy (MDT), in Mali and India.

The success of these trials is one of TDR’s top achievements in its first decade, leading to a landmark WHO recommendation in 1982 for MDT treatment of leprosy.

At the same time, social science research began to uncover the social stigma that prevented many women from being diagnosed and treated for leprosy, owing to the fear that they would be unable to marry. These findings would later become important for the implementation of MDTs for leprosy and their broad public acceptance.

By the mid-1990s, the global number of registered patients had decreased fourfold, with TDR’s work on MDT effectively eradicating the need to continue searching for a leprosy vaccine.
1985 – 1994
MORE MEDICINES, DIAGNOSTICS AND VECTOR CONTROL
TDR took up some of the most neglected and difficult diseases. Because of its connection to WHO, it could interact with these countries, which others could not.

Dr Nirmal K. Ganguly, former representative to the JCB, Government of India

TDR’s outstanding legacy goes beyond the many drugs it helped develop, to the formation of the first independent PPP dedicated to a particular product for a specific disease. Its leading role in the formation of the new MMV not only established a portfolio of malaria R&D projects necessary to secure the required supply of new antimalarial drugs, but also pointed the way for other similar partnerships.

Dr Winston E. Gutteridge, Coordinator, TDR Product Research and Development, 1996–2001

TDR Director
Dr Tore Godal (1986–1998)

Scientific highlights
- Insecticide-treated bednets for malaria prevention
- Unit-dose packaging for home and community administration of antimalarials
- Rapid epidemiological mapping of onchocerciasis (REMO)
- DNA probes for lymphatic filariasis and onchocerciasis detection
- Improved blood-bank screening and diagnostics for Chagas disease
- Community-directed treatment for onchocerciasis
- Development of liposomal amphotericin B for visceral leishmaniasis and artemether for malaria
- Tsetse fly traps and screens in sleeping sickness control
- Initiatives for Tritryps genome-sequencing and genetic modification of the malaria vector Anopheles gambiae.
1985 - 1994

Helping millions of Africans avoid the scourge of onchocerciasis

Since its foundation, TDR has been at the forefront of a global fight to combat and eradicate onchocerciasis (river blindness).

TDR effectively became the research arm of the Onchocerciasis Control Programme (OCP) in West Africa, and then the African Programme for Onchocerciasis Control (APOC).

Research on how to curb disease transmission in broad savanna regions of West Africa led to the breakthrough innovation of incorporating the Bti bacterium to control insect larvae, including that of the blackfly, in 1982.

At around the same time, scientists at the US-based laboratories of Merck sent a little-known agent called ivermectin to a TDR-supported compound screening process, which showed the agent’s efficacy against the infant larvae of the onchocerca parasite.

As clinical trials progressed, ivermectin’s potential became more evident. TDR contributed to the design of study protocols and dosage, and connected Merck with the OCP networks.

In 1986, with the drug about to be registered, CEO of Merck Dr Roy Vagelos made the momentous decision to donate the drug to whoever needed it, as long as it was needed.

TDR and partners set up large-scale community trials under field conditions to move the drug from individual treatment in hospitals to mass drug administration, strengthening the value of ivermectin in the onchocerciasis control strategy.

To support this mass drug administration, a new model was proven that empowered communities to put in place their own system for ivermectin distribution and administration, with health services offering support and training.

Today, 98 million people in 31 sub-Saharan African countries receive annual treatments through this system.

“TDR’s vision that ivermectin could be used on a mass scale, beyond the therapeutic treatment of infected individuals, led to the community-based trials and eventually established convincing evidence for the present role of ivermectin in the mass-treatment strategy for onchocerciasis control.”

TDR, Third External Review, 1998
Controlling human African trypanosomiasis

Human African Trypanosomiasis (HAT) – also known as sleeping sickness due to the extreme fatigue that afflicts sufferers before death – is particularly prevalent in rural regions, where villages are at daily risk from exposure to tsetse flies, the vectors of sleeping sickness parasites.

Easily erected insecticide-impregnated tsetse fly traps that had been tested in TDR’s first decade were by now halting the epidemic in southern Uganda.

Another important step forward was the use of d,l-\(\alpha\)-difluoro-methylornithine (DFMO). Originally developed by Marion Merrell Dow Pharmaceuticals (now Sanofi-Aventis) as a compound to treat cancer, DFMO showed distinct potential in the treatment of HAT. In 1987 TDR supported Phase III clinical trials that proved its efficacy, with patients even in later stages of the disease responding rapidly.

It was the first new treatment for sleeping sickness in four decades, and is now made available by Sanofi-Aventis through a donation programme under a WHO Memorandum of Understanding.

A young boy has blood taken from his finger tip in a field study to detect the presence of trypanosomes, parasites that cause sleeping sickness. (WHO/TDR)
1985 - 1994

Testing new malaria treatments: mefloquine, artemisinin and Coartem®

Mefloquine was a malaria treatment initially overlooked as both unpatented and expensive. However, TDR’s work with pharmaceutical experts and its sponsorship of more than twelve clinical research studies in Latin America, Zambia and Thailand, helped find a more cost-effective way to synthesise the drug.

TDR was one of the first foreign institutions to explore first-hand the work of scientists at China’s artemisinin research facilities. Research into this indigenous plant used in traditional Chinese medicine showed its active compound was potentially highly effective against parasites. So TDR led large-scale, multi-partner clinical research into their oral use, testing various combinations (called ACTs) of artemisinin with other active compounds:

- amodiaquine plus artesunate;
- chloroquine plus artesunate;
- mefloquine plus artesunate; and also
- artemether plus lumefantrine (Coartem®).

Further research into packaging that could be understood with pictures, and doses put into blister packs, provided effective and safe use of Coartem® for infants over 5 kg in weight. This broad research approach would provide key evidence for the World Health Organization promotion of ACTs as a fundamental part of malaria treatment policy and negotiated preferential rates.

Developing countries could then benefit from the fastest-acting anti-malarials available – destroying parasites in approximately 48 hours on average – with high documented cure rates.

Photomicrograph of Anopheline mosquito larvae. The larvae have been genetically modified to incorporate a gene for the Enhanced Green Flourescent Protein which causes the larvae to glow. (WHO/EURO)

1990
- Eflornithine (DFMO) registration by Marion Merrel Dow for treatment of late-stage sleeping sickness

1991
- Initiative launched to control malaria by genetically engineering the Anopheles gambiae mosquito to interrupt transmission
- DNA probes for detection of Onchocerca volvulus in black flies in control use

1992
- Fumigant canisters that release insecticidal smoke when lit; and control the triatome bugs that transmit Chagas disease. (WHO/TDR)
Genetic modification of mosquitoes

At a meeting in Tucson, Arizona in 1991, TDR joined the MacArthur Foundation in calling for the genetic engineering of A. gambiae, the mosquito that transmits the malaria Plasmodium parasite. Thus started a major effort requiring extensive partnerships and collaborations.

The TDR Molecular Entomology Committee was created to develop tools for this genetic modification. A 15-year programme was agreed to identify the modifiable genes that carried the parasite, develop methods for spreading these genes in wild mosquito populations, and field-test control methods.

TDR gathered together a consortium of high-level international organizations, including the National Institutes of Health (USA), the Pasteur Institute (France), the European Molecular Biology Laboratory (Germany), Celera Genomics (USA), the ONSA network (Brazil) and others, to initiate the sequencing of the A. gambiae genome. While TDR’s monetary investment was relatively small, it provides an example of how strategic leadership and leverage at a critical moment can stimulate a much broader effort.

Just one year after the initiative was formally launched, the A. gambiae genome sequencing project was published in Science, and Nature issued a report on the sequencing of the Plasmodium falciparum genome.

By 2001, TDR had supported more than 100 projects in 19 countries on this work, and then started to focus on the ethical, legal and social implications of testing and evaluating. This included training and networks in bioinformatics and genomics applications to increase the capacity of scientists in low- and middle-income countries to conduct this kind of research and surveillance, and in 2014, a guidance framework with proposed standards for safety was published.

Rapid epidemiological mapping of onchocerciasis (REMO) in disease control use

Social surveys in India identify community-level gender differences in stigma related to leprosy

Effectiveness of mass drug administration with ivermectin demonstrated to prevent eye disease and blindness in longitudinal studies in Africa

Parasite genome sequencing project launched in Brazil

Meeting on genomics launched a new era in basic research, starting with the sequencing of the parasites responsible for leishmaniasis, sleeping sickness and Chagas disease

Leishmaniasis direct agglutination diagnostic test (DAT) and standard leishmanin skin test antigen put into control use

Liposomal amphotericin B for visceral leishmaniasis registered by NeXstar

Single-dose treatment with DEC or ivermectin-albendazole for new global lymphatic filariasis control strategy
1995 - 2004
COMMUNITY AND SOCIAL RESEARCH
TDR is a tried and trusted friend of disease-endemic countries. Institutions have been built or strengthened, individuals have been trained and ministries of health have been given the tools to help them organize and manage research for health.

Dr Peter Ndumbe, Former Chair of TDR’s Scientific and Technical Advisory Committee

“TDR is the only public health research institution that is jointly owned by everybody … all of the member states of the UN and the World Health Assembly own TDR and that is why it is unique. The smallest country in the world has a stake in it, the biggest country in the world has a stake in it. That to me is the comparative advantage of TDR: joint ownership.”

Dr Kayode Oyegbite, former representative of UNICEF to the JCB

TDR Directors
Dr Robert G. Ridley (2004–2011)

Scientific Highlights
- Incubation and foundation of Medicines for Malaria Venture (MMV) and Foundation for Innovative New Diagnostics (FIND)
- Support for creation of TB Alliance and Neglected Diseases Initiative (DNDi)
- Establishment and transition of several anti-malarial drug development projects to MMV and DNDi
- New drug discovery networks
- Miltefosine for visceral leishmaniasis
- Tools and field research supporting visceral leishmaniasis/lymphatic filariasis elimination campaigns
- Validation of syphilis diagnostics for elimination efforts
- Validity of ACT use in home management of malaria
- Rapid assessment (RAPLOA) of onchocerciasis/Loa loa co-endemicity
- Extension of community directed interventions beyond onchocerciasis
- *Anopheles gambiae* and Tritryps genome collaborations
- Partnering Multilateral Initiative for Malaria (MIM)
- Establishment of Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)
- Thousands of people trained in new Research capacity strengthening (RCS) short courses
- 70% of R&D partners engaged are from developing countries
- WHO recommendation to stop using single-drug treatments for malaria and move to only artemisinin-combination therapy (ACT), supported by TDR studies.
1995 - 2004

Eliminating lymphatic filariasis

Happily, by the end of TDR’s third decade, lymphatic filariasis was one of four original TDR-targeted diseases heading towards regional or global elimination.

At its worst a cause of elephantiasis, hydrocele and lifelong disability, the disease is indigenous to 83 countries, with 119 million people worldwide estimated to be infected.

In 2000, spurred by the recent introductions of diethylcarbamazine (DEC) and DEC plus ivermectin, WHO and its national partners established the Global Programme for Elimination of Lymphatic Filariasis (GPELF).

TDR field research and support not only played a key role in guiding implementation strategies, but also in highlighting to national policy makers the economic cost of the disease against the cost-effectiveness of mass drug administration.

TDR identified the number of annual doses needed to break disease transmission and helped rural communities manage their drug administration and treatment through community health care workers. Together with donations of drugs such as ivermectin by Merck, and albendazole by GlaxoSmithKline, hundreds of millions of people have received the treatment they desperately need.

- Method for rapidly identifying urinary schistosomiasis in highly endemic communities put into control use
- Onchocerciasis control extended to forest areas in Africa to address skin disease
- New community-led approach for onchocerciasis annual mass drug treatment becomes mainstay of the African Programme for Onchocerciasis Control (APOC) delivery strategy
- Drug delivery strategies developed for lymphatic filariasis elimination in Africa
- Improved multidrug therapy (ROM: rifampicin, oflaxacin and minocycline) for leprosy control
- Effectiveness to treat and prevent onchocerdermatitis demonstrated in field trials in Africa

Shertallai: Patients awaiting attention outside the Filariasis Clinic at the Vector Control Research Centre (VCRC), 1993. (WHO/TDR/Chandran)
Multilateral Initiative for Malaria builds research capacity among African scientists

In 1998, TDR helped establish a key platform for African-based researchers to strengthen malaria research and collaboration in Africa.

The Multilateral Initiative for Malaria (MIM) was launched in collaboration with the US Department of Health and Human Services; US. National Institutes of Health; the Wellcome Trust; and the Pasteur Institute in Africa.

African researchers were given access to technology, facilities and expertise; wider networking capability; and TDR grants that, uniquely for the time, went directly to researchers, rather than being distributed through a developed country institution.

Perhaps most significantly, the programme enabled breakthrough research on drug and insecticide resistance through an improved research infrastructure and new molecular genetics capability. Investigators in Ghana, Mali, Nigeria, Tanzania, and Uganda helped pool evidence of resistance to chloroquine and sulfadoxine-pyrimethamine, which eventually led to the introduction of more effective artemisinin-based combination therapies.

Within 10 years, 69 research grants had been awarded to principal investigators in 36 African-based institutions in 17 countries. Many grantees became internationally competitive and attracted large grants, and have gone on to lead major research institutions and programmes.

In a 2007 external review of the programme, one participant said, “The MIM/TDR grant is a life line; it has helped those of us with no big CVs to get grants and start our real research careers.”

Initiating a worldwide genomic sequencing effort

Three of the world’s most neglected tropical diseases are caused by parasitic trypanosomatids – African trypanosomiasis (sleeping sickness), Chagas disease and leishmaniasis.

In the mid-1980s, initial progress on sequencing the Chagas disease Trypanosoma cruzi genome demonstrated that antigens could be produced in the laboratory by recombinant DNA technology, creating improved diagnostic reagents.

A decade later, TDR and Brazil’s Oswaldo Cruz Institute (FIOCRUZ) co-sponsored the ‘Tritryps project’ to sequence the genomes of the three related parasites. This brought together researchers from both developed and developing countries and was supported by the Wellcome Trust, the European Commission, the US National Institutes of Health (NIH), and national research institutes.

The Tritryp genomes were completed 11 years later, providing a first peek into the biology of the trypanosomatids and a blueprint for genome-wide studies that are starting to generate new products to fight these long-neglected diseases.

This work is another example of visionary, long-term commitments aimed at creating global, public health goods. In this case, it is a body of scientific knowledge that many others throughout the world are using to create useful health products.
Supporting a paradigm shift in malaria treatment

It was 1998 and the world was in danger of losing an effective malaria treatment. Parasites were developing resistance to chloroquine, the major drug treatment for half a century, and its replacements, sulfadoxine-pyrimethamine and mefloquine. Evidence on new treatment options was urgently needed.

In the meantime, Chinese researchers had discovered a new class of potent antimalarials, the artemisinins, extracted from the plant Artemisia annua. Studies supported by the Wellcome Trust in the mid-90’s had shown that the combination of an artemisinin derivative, artesunate, with mefloquine was highly effective in Thailand where mefloquine resistance was rampant. TDR coordinated a series of multi-country trials in Africa and Latin America between 1999-2001 comparing single-agent treatments with the medications then recommended (chloroquine, amodiaquine and sulphadoxine-pyrimethamine) to regimens where they were combined with artesunate. Collectively all these studies, together with further studies on their cost effectiveness, helped provide the evidence for a paradigm shift in malaria, from single-agent to combination therapy.

A technical consultation at WHO in 2000 reviewed these data and recommended to malaria endemic countries to stop using single-drug treatments and move to only artemisinin-combination therapy (ACT). A year later, a list of 4 recommended ACTs was distributed. These treatments have since become the cornerstone of malaria control and elimination, helping to reduce thousands of deaths and illnesses every year.

“...it involved an excellent partnership between TDR, the Indian authorities and the private sector. And the initiative involved capacity building with the Indian hospitals involved in the drug trials.”

Dr Carlos Morel, former TDR Director

- Manuals on good laboratory practice and good clinical practice published
- WHO recommends moving from single-drug treatments for malaria to only artemisinin-combination therapy (ACT)
- Germline transformation of Anopheles mosquitoes
- Milefosine registered by Zentaris for visceral leishmaniasis treatment in India
- Anopheles gambiae malaria parasite genome published
- Series of social research methodologies published

The development of miltefosine was, in my view, one of the major successes of TDR in this period. It was the first oral drug for VL, it involved an excellent partnership between TDR, the Indian authorities and the private sector. And the initiative involved capacity building with the Indian hospitals involved in the drug trials.
Establishing the effectiveness of bednets to control malaria

Today the use of insecticide-treated bednets is a mainstay of malaria control. The evidence of effectiveness for this innovation came from TDR support in the 1990s. Following the success of small-scale trials in The Gambia, TDR funded far larger-scale trials across Africa, in what was to prove one of the programme’s most ambitious investments.

The Ghana trials had shown a highly significant 63% reduction in childhood deaths from malaria due to bednets. This was sufficient for TDR Director Dr Tore Godal to recommend the funding of large-scale trials necessary to prove whether this could work on a broad scale. A unique blend of highly controlled scientific trial and operational research was set up in sites across Ghana, Burkina Faso, Kenya and The Gambia that covered 400 000 children.

The final results that insecticide-treated bednets could reduce overall childhood mortality by an average of around 20% led to the WHO recommendation that they be a standard preventive treatment in malaria-endemic areas, and their extensive distribution across the African continent.
2005 - 2014
ACCESS FOR THE
MOST VULNERABLE
What are the most important lessons from the early history of TDR? To have the courage to experiment.

Dr Adetokunbo Lucas, TDR Director, 1976–1986

The fashion today is ‘output-driven’ projects. But if you only look at the achievements of TDR, if you only make a list of all the products that have been developed, it would truly miss the point. The point is this: TDR developed a culture for research-based decision-making and a functioning network organization. This is a rare thing in an international organization. You have to look at the catalytic function of TDR as one of its main strengths.

Dr Bernhard Liese, Chair, International Health Programs, Georgetown University and former World Bank representative on the JCB

TDR Directors
Dr Robert G. Ridley (2004–2011)
Dr John Reeder (2012–present)

Scientific highlights
- WHO recommendation to stop using single-drug treatments for malaria and move to only artemisinin-combination therapy (ACT), supported by TDR studies
- Visceral leishmaniasis elimination progresses with new diagnostics, treatments and delivery strategies
- WHO calls for stopping TB serological tests and issues new recommendations based on TDR-supported evidence
- Rapid malaria diagnostic test evaluations improve quality of marketed tests
- Effectiveness of rectal artesunate to treat severe malaria established
- Ivermectin shown capable of eliminating onchocerciasis
- Trapping methods for 6 vectors of sleeping sickness standardized across 9 African countries
- Antifilarial drugs shown to reverse lymphatic pathology in children with Brugia malayi infection (lymphatic filariasis)
- Trypanosomatid genome sequences published
- Community-based approaches reduce dengue mosquito breeding.
Eliminating visceral leishmaniasis in Bangladesh, India and Nepal

In 2005, a Memorandum of Understanding signed by the health ministers of Bangladesh, India and Nepal signalled a major joint effort to eradicate the deadly disease of visceral leishmaniasis (VL) over a ten-year period.

TDR research helped adopt diagnostic tools, test drug treatments, and develop measures to control the parasite-carrying sandflies with bednets and insecticide sprays.

TDR has shown that a single dose of liposomal amphotericin B (manufactured as AmBisome®) can be provided at primary health care centres instead of just at hospitals which are often far from where patients live. The single intravenous drip takes about 2 hours instead of the standard dose of miltefosine pills taken over a 28 day course.

Although the best available treatments may be present at the primary health care centres only several kilometres away, this is of limited value if VL cases remain undiagnosed in the villages.

TDR worked with multiple partners to study new ways to reach into the community to find potential cases.

Early diagnosis and treatment are essential for not only individuals, but also for the community because it reduces VL transmission. If a community’s overall level of infection is reduced, fewer cases can be transmitted by the sandflies that carry the parasite.

Together with the national control programmes, WHO, and drug development partnerships like Drugs for Neglected Diseases initiative, visceral leishmaniasis is well on its way out of this region.

Ambitious targets are underpinned by research promoted over the years by TDR and its partners. This work increasingly includes operational and implementation research aimed at improving access.

“We greatly need research and development for innovative new tools, particularly for diseases like African trypanosomiasis, leishmaniasis, and Buruli ulcer.”

Dr Margaret Chan, WHO Director-General; keynote address at the Prince Mahidol Award Ceremony, Bangkok, Thailand, February 2007.
Helping communities manage dengue and Chagas disease

Dengue has long plagued urban regions of Latin America, while Chagas disease presents a persistent threat to the continent’s rural areas.

Working with the Ecosystem and Human Health Program of Canada’s International Development Research Centre (IDRC), TDR’s research combines an environmental and community approach to develop healthy solutions that can reduce the use of insecticides and improve overall housing conditions.

In Uruguay – a dengue-free country but still at risk from its proximity to disease-prevalent Brazil and Argentina – residents have learned the importance of emptying receptacles containing stagnant water and treating water tanks with environmentally safe larvicides.

In Brazil, early studies looked at replacing insecticides to kill the mosquito larvae with covers for outside family water store containers.

On the banks of Colombia’s Magdalene River, a similar approach went hand-in-hand with a new social enterprise to produce window curtains to keep mosquitos out of households.

In Bolivia, this approach is also helping fight Chagas disease in the farming communities. Villagers have been taught the value of checking mattresses for nests of the triatomine bug, and reducing breeding grounds by keeping dirt floors clear of leaves and debris and moving farm animals further away from the house.

The work has been conducted in 13 different countries in Latin America and Southeast Asia, and is now being investigated in some countries for full national scale-up.

RAPLOA (rapid assessment procedure for determining areas of Loa loa endemicity) developed, validated and incorporated into disease control use

Review of gender in tropical disease control published

Strategic review of traps and targets for tsetse and African trypanosomiasis control

Tsetse fly ecology; Tsetse flies in a test tube awaiting dissection after being trapped in a field near the river Comoe. Tsetse flies are the vectors of the parasites which cause sleeping sickness, Burkina Faso, 1990. (WHO/TDR/Baldry)

Evidence-Informed Policy Networks (EVIPNet) launched in 2005, using TDR research evidence for pilot

Effective project planning and evaluation for biomedical and health research publication and training launched
2005 - 2014

A new treatment approach by the community, for the community

Most low- and middle-income countries struggle with not having enough healthcare providers to deliver vital services. One approach to address this has been the use of community health workers, called CHWs, where people are trained to diagnose and treat common ailments in the villages in which they live.

TDR supported critical research into the effectiveness of this model, and showed that CHWs can reduce childhood mortality due to malaria, and effectively and safely distribute annual treatments for onchocerciasis.

In 2000, TDR published a report that pointed to the “absence of capacity and understanding in how to engage with communities and ensure their participation, and of the ability to adapt research methods and health technologies to local contexts.” Support went to both training scientists from low- and middle-income countries on this research methodology, as well as to conduct the research.

A broader strategy has come out of this called community case management that is used to address the symptom of fever, which can be caused by any of the three major childhood killers – malaria, pneumonia or diarrhoea. The CHWs have shown that they can correctly diagnose and provide the appropriate treatment, so that children are getting the treatment they need, when they need it.

Both the World Health Organization and UNICEF have since called for scaling up this approach, and TDR has expanded its support and training in implementation and operational research, working closely with national control programmes and research organizations to help communities help themselves.

2007
- Evaluation methodology on VL diagnostics published
- MIM evaluation finds malaria research capacity strengthened in 17 African countries

2008
- Publications:
  - Implementation and operational research frameworks
  - Ethical guidelines for social science
  - Evaluation of TB diagnostics methodologies and research priorities
  - Social context of schistosomiasis and control
  - Report on moxidectin development
  - Health economics research capacity report
  - Implementation and operational research frameworks published
- Marketed TB serologic diagnostic tests evaluation identifies none that are effective

ESSENCE on health research initiative launched to increase collaboration among international funders to strengthen African research capacity

African Network for Drugs and Diagnostics Innovation launched
Onchocerciasis treatments:
- First evidence that onchocerciasis elimination is feasible with ivermectin treatment published
- Moxidectin begins Phase 3 clinical trial

First rapid malaria diagnostic test evaluation finds uneven quality (starts series of regular evaluations that improves quality and appropriateness of tests)

 Genome sequencing to fight sleeping sickness and build African research capacity

In 2004, with funding from TDR, WHO and the Wellcome Trust Sanger Institute – and overseen by the International Glossina Genome Initiative (IGGI) – a project took shape to map the genetic blueprint of Glossina morsitans, one of 32 species of tsetse fly that transmits the deadly trypanosomiasis parasite and causes sleeping sickness.

With TDR support, IGGI was able to meet annually, growing steadily larger and planning peripheral projects to incorporate African scientists.

Ten years after the project began – a decade of work involving 150 scientists (half from African institutions) – the genetic code of a highly unusual insect, whose capacity as a vector had long puzzled scientists, was sequenced and annotated. This led to improved trapping systems and other control methods.

Importantly for TDR, the project also marked the first time that African countries were closely and collaboratively involved in an initiative from the very start. The sequencing project helped strengthen capacity in African institutions, and the side projects that developed as its momentum grew encouraged more and more interest and involvement from the Sanger Institute, whose financial contribution is estimated to be around $4 million.

The success of the initiative inspired further sequencing work, with US National Institutes of Health awarding funding to IGGI to sequence and annotate four other species in the Glossina genus as well as the common housefly.

Antifilarial drugs, in the doses employed in mass drug administrations by the Global Programme to Eliminate Lymphatic Filariasis, reverse lymphatic pathology in children with Brugia malayi infection. Before this, the only other option was chemotherapy.
Improving policy and practice by evaluating rapid diagnostic tests

An early focus of TDR was on increasing standards for conducting quality drug trials in low- and middle-income countries. But it became quickly apparent that there was an equal need to apply this to diagnostic tests.

Companies were free to manufacture and market tests without the oversight and quality control of an independent and authoritative regulatory body. By 2005, it was unclear how well the growing numbers of rapid diagnostic tests (RDTs) actually worked in harsh field conditions.

TDR played a crucial role in initiating evaluations of RDTs for several diseases – such as dengue, tuberculosis (TB), and sexually transmitted diseases.

Evaluations of rapid malaria tests helped incentivise manufacturers to meet international performance recommendations based on the evaluation programme.

TDR’s extensive scrutiny on a variety of tuberculosis tests underpinned 12 WHO diagnostics policies. This included a WHO recommendation to end the use of serological tests to diagnose TB – the first such negative policy recommendation issued by the organisation against a widely used care measure.

This overall area of work shows how research has provided a critical foundation to ensure quality for new health tools, and has played an important role in how these tools are monitored and their use agreed by national, regional and international authorities.

Visceral leishmaniasis elimination research tools published

Community-based approaches to reducing dengue mosquito breeding through environmental approaches developed

2010

2011

Visceral leishmaniasis (VL) patients receiving treatment at the Kala azar Medical Research Centre, Muzaffarpur, India, 2006. (WHO/TDR/Ghalib)

TDR wins Gates Global Health Award

Ambassador John Lange, the Bill & Melinda Gates Foundation; Dr Robert Ridley, TDR Director; Dr Margaret Chan, Director-General, World Health Organization; and Mr Jeffrey L Sturchio, President, Global Health Council; after the presentation of the 2011 Gates Award for Global Health to TDR in Geneva, Switzerland.
TDR was a gamble in many ways. We made up these rather awkward titles to emphasize that there was no hierarchy in TDR, only team members and the director.

Dr Richard Wilson, TDR Programme Management, 1975–1985

- WHO calls for ending use of TB serological tests based on TDR-supported evidence
- Number of effective rapid malaria diagnostic tests increases due to ongoing evaluations
- WHO issues new recommendations based on TDR research that improve TB diagnostic procedures

Manual on rectal artesunate use to treat malaria published, and treatment transitioned to MMV for manufacturing solution

Conclusive proof established that ivermectin can eliminate onchocerciasis

Standardization and optimization of trapping methods for 6 HAT vectors across 9 African countries

Operational research and training (SORT IT) initiated at TDR

Evidence on single-dose liposomal amphotericin B use in rural public Bangladesh hospitals contributes to VL elimination plan

Dr John Reeder becomes TDR’s 6th Director

Dengue clinical management handbook published
2014 KEY ACHIEVEMENTS

Supporting high quality research that leads to improving health among the most vulnerable

Visceral leishmaniasis (VL) elimination in the Indian Subcontinent is on track with the help of numerous projects conducted with the countries’ researchers and control programmes. One study showed that disease incidence can be reduced by 65% through community-based bednet impregnation; another found that training of more than 1000 community workers (ASHAs) resulted in a 5-fold increase in identifying and referring cases. Liposomal amphotericin was adopted as a first-line treatment in Bangladesh due to the evidence of its efficiency from a TDR and WHO-supported study.

Research to improve dengue and Chagas disease prevention through environmental and community approaches has identified new methods. A special issue of the Transactions of the Royal Society of Tropical Medicine and Hygiene and three video productions have helped transfer the results into policy and change.

Dengue detection and surveillance in 10 countries has been improved due to several projects. This includes dengue contingency plans and alarm signals for dengue outbreaks.

Evidence for policy has been generated from 6 systematic reviews on schistosomiasis treatment, malaria treatment and diagnostics, plus an additional review of how the strength of a recommendation in WHO guidelines (GRADE) affects the uptake of the recommendation in national guidelines.

Moxidectin for onchocerciasis elimination: Modeling from the data from the Phase 2 study data resulted in moxidectin being included in the list of ‘alternative treatment strategies’ to accelerate elimination of onchocerciasis in Africa where feasible. Data available to WHO has been licensed to an Australian not-for profit organisation (Medicines Development Limited, MDL) which intends to register moxidectin for onchocerciasis, lymphatic filariasis and scabies.

Childhood fever management in remote settings is being improved due to research and advocacy. A major symposium on Integrated Community Case Management (iCCM), organized by UNICEF, brought researchers and policy-makers together. The studies were also reviewed and summarized in a special issue of the Journal Global Health on “Current scientific evidence and future directions for Integrated Community Case Management in Africa”.

A guidance framework was published for testing genetically-modified mosquitoes for malaria and dengue control. Commissioned by TDR and the Foundation for the National Institutes of Health (FNIH), the published framework proposes ethical, legal and efficacy standards for safety testing comparable to trials of other new public health tools.
A commitment to strengthening research capacity where it’s needed most

Expanded training for researchers in low- and middle-income countries

- 22 postgraduate training grants
  (9 MSc and 13 PhD)
- 9 postdoctoral training grants
- 26 grants through the second round of the IMPACT grant scheme with a specific focus on strengthening capacity in implementation research (IR).

The Structured Operational Research and Training Initiative (SORT-IT) is growing

Public health programmes in low- and middle-income countries, working with WHO, identify their challenges or bottlenecks on specific issues and identify staff to be trained to use their country’s own data to conduct research that can lead to local health system improvements. Participants have worked on topics such as multidrug-resistant tuberculosis, malaria, neglected tropical diseases, maternal and child health, HIV and non-communicable diseases. Thirteen courses were held in 2014 in Central Asia and Latin America.

An increasing TDR regional presence

The small grants scheme has been renewed in collaboration with WHO regional offices, and the number of Regional Training Centres (RTCs) supported by TDR to conduct and disseminate training courses relevant to the TDR strategy is growing. The fifth RTC (for the African Region) was selected in Accra, Ghana in 2014, and preparations were made for the selection of the sixth RTC (for the Eastern Mediterranean Region) in 2015.

New training materials and approaches

To help equip researchers to undertake implementation research, including the publication of the Implementation Research toolkit.
CURRENT WORK

Join our efforts to improve the lives of millions and reduce the impact of infectious diseases

Building national research capacity

No research without capacity building, no capacity building without research. This is the TDR approach. Customized mentorship and networks, workshops, PhD and Master’s degrees, fellowships in product development, a growing number of regional training centres, plus research support are some of the elements in place to strengthen capacity throughout low- and middle-income countries. TDR is also working to increase the numbers of women who stay in health research.

Eliminating malaria, visceral leishmaniasis and onchocerciasis

Elimination is now in view for these three diseases. A range of research on diagnosis, new drug treatments and their implementation are providing critical support to finishing this important goal in Bangladesh, India and Nepal for visceral leishmaniasis. Countries are benefitting from improved surveillance and tools to kill the malaria mosquitoes, as well as the development of an alternative drug for onchocerciasis.

Reducing the numbers of children who die

Fever is one of the most frequent symptoms of childhood disease. But what causes it and how best can it be treated? TDR is working with the World Health Organization and UNICEF to build a body of knowledge on how trained community volunteers in remote, low-resource settings can properly diagnose and treat fever-related illnesses like pneumonia, diarrhoea and malaria.

Helping vulnerable populations survive climate change

Tropical countries are more vulnerable to climate change that affects water supplies, the diversity of plants and wildlife, and the number of parasites that attack both people and valuable cattle. This new area of work is looking at how to help communities become more resilient and develop solutions to deal with the changes that are happening.
Joining the fight on Ebola and other emerging diseases

The West African outbreak has required a worldwide response. TDR is contributing in numerous ways – ethical review of new treatments and vaccines, the identification and testing of potential drug treatments, support to contact tracing, surveillance and raising awareness on the issues facing Ebola survivors.

Improving dengue detection and surveillance

Work to improve alarm signals for outbreaks and developing cost-effective responses is bringing together WHO, national governments and many other partners to work in countries fighting this growing epidemic.

Strengthening community approaches to manage multiple diseases

Many people in tropical countries live in remote areas far from health centres. TDR provided early evidence on how community health workers can diagnose and treat diseases and continues to build on this area of research.

Slowing the transmission of dengue and Chagas disease

Research is showing how when communities work together to learn how to reduce dengue mosquito breeding, and keep their homes free from the Chagas bugs, transmission can go down, communities are strengthened and the environment can be improved.

Protecting people’s safety

A pregnancy drugs safety database to look out for the safety of mothers and their unborn children is being developed. Training is underway on safety monitoring systems on pharmaceutical products. A framework that provides the highest level of science for addressing the ethical, legal, social and regulatory issues on genetically modified mosquitoes provides guidance for numerous countries and their citizens.

Strengthening health policies with research evidence

A range of systematic reviews of research on malaria, schistosomiasis and dengue are providing countries with the analysis they need to make critical health policy decisions and revisions.

In Colombia, initial research that showed that community members could develop environmental approaches to reducing dengue transmission is now going into national scale-up. Here women sew window screens and men install the frames. (WHO/TDR)
FINANCIALS

A strong financial base to build a focused portfolio

The year 2014 is the first year of the 2014-2015 biennium. Income in 2014 was in line with the expectations. The US$ 50 million budget scenario was initially implemented and scaled up to US$ 54.6 million as funds became available. In 2014, US$ 19.1 million was spent or committed. This reflects the initiating phase of a new portfolio focusing on research capacity strengthening and implementation research. This benefited from the establishment of new technical advisory committees and the application of new business models to enhance TDR’s efficiency.

Two budget scenario levels for 2016-2017 have been approved by TDR’s Joint Coordinating Board, US$ 45 million and US$ 55 million.

Figure 1: Financial situation at the end of 2014

Figure 2: Financial outlook 2016-2017
TDR Annual Report 2014 – Celebrating 40 years of research

TDR uses its Performance Assessment Framework to measure progress in the implementation of its vision and strategic plan. Key performance indicators have been developed in consultation with TDR stakeholders (see table above). These help assess not only what TDR does (TDR achievements and its contribution to changes in countries) but also how it does it (application of core value and management performance). Measurements are compiled in the annual TDR results reports: www.who.int/tdr/publications/about-tdr

TDR made good progress on a number of indicators including technical outputs and core values. Reflective of an increased reach, the number of peer-reviewed publications supported by TDR in 2014 increased massively compared to the previous year, from 120 to 227. The proportion published in open or free access was 88%, a significant increase from 50% in 2013, and a reflection of recent policies of both TDR and WHO on open-access publications. The percentage of publications with first authors from a disease endemic developing country was 67%. First authors come from 54 such countries in addition to 18 developed countries from all six WHO regions, reflecting TDR’s global scope. At the same time, regarding gender equity, the proportion of women who either received TDR grants, were first authors of publications supported by TDR, or were members of TDR advisory committees increased constantly and is at the highest level ever for TDR.

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<tbody>
<tr>
<td><strong>TECHNICAL EXPECTED RESULTS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome:</td>
<td>Number and proportion of innovative knowledge, new/improved solutions or implementation strategies successfully applied in developing countries</td>
<td>0</td>
<td>30 ≥75%</td>
<td>17 (+4) 70%</td>
<td>Measured annually, cumulative over 6 years</td>
</tr>
<tr>
<td></td>
<td>Number of tools and reports that have been used to inform policy and/or practice of global/regional stakeholders or major funding agencies</td>
<td>0</td>
<td>7</td>
<td>3 (0)</td>
<td>Measured annually, cumulative over 6 years</td>
</tr>
<tr>
<td>Main output:</td>
<td>Number and proportion of innovative knowledge, new/improved solutions or implementation strategies developed in response to requests from WHO control programmes and/or diseases endemic countries</td>
<td>0</td>
<td>35 ≥87%</td>
<td>16 (+6) 100%</td>
<td>Measured annually, cumulative over 6 years</td>
</tr>
<tr>
<td></td>
<td>Number of peer-reviewed publications supported by TDR and percentage published in open access journals</td>
<td>233 Not measured</td>
<td>≥150/year 100%</td>
<td>554 (2012-2014) (+227 in 2014) 88% open access (2014)</td>
<td>Measured annually</td>
</tr>
<tr>
<td>Feeder outputs:</td>
<td>Number and evidence of new/improved tools, case-management, control or implementation strategies generated through TDR facilitation with systematic quality review by external committees</td>
<td>0</td>
<td>40</td>
<td>16 (+6)</td>
<td>Measured annually, cumulative over 6 years</td>
</tr>
<tr>
<td></td>
<td>Proportion of peer-reviewed publications supported by TDR with first author from Disease Endemic Country (DEC) institutions</td>
<td>61%</td>
<td>≥70%</td>
<td>67%</td>
<td>Measured annually</td>
</tr>
</tbody>
</table>
### Key stakeholders in disease endemic countries engaged in setting the research agenda and ensuring research reflects their needs

| 9. Number and evidence of research-related agendas, recommendations and practices agreed by stakeholders at global, regional or country level | 0 | 9 | 8 (0) | Measured annually, cumulative over 6 years |

### Expected results

| 10. Proportion of TDR outputs produced with key DEC stakeholder active involvement | Not measured | 100% | 100% | Measured annually |

### APPLICATION OF CORE VALUES

| Equity | 11. Proportion of TDR grants/contracts awarded to institutions or individuals in DECs (total count and total dollar amount) | 59% DEC | 75% DEC | 70% DEC (amount) 62% DEC (count) | Measured annually |
| Gender | 12. Proportion of experts from DECs on TDR advisory committees | 58% | 60% | 71% | Measured annually |
| Gender | 13. Proportion of women among grantees/contract recipients (total count and total amount) | 35% (n) 17% ($) | 50% | 43% (% count) 28% (% amount) | Measured annually |
| Gender | 14. Proportion of women on TDR advisory committees | 32% | 50% | 43% | Measured annually |
| Gender | 15. Proportion of women as first author of peer-reviewed publications supported by TDR (within a calendar year) | Not measured | 50% | 47% | Measured annually |
| Effective partnerships | 16. Resources leveraged as direct contributions (co-funding, services or in-kind) to TDR projects (examples) | Not measured | tbd | 1:3 (provisional data) ($TDR : $ partners) | Measured annually |
| Sustainability of outcomes | 17. Number of effective public health tools and strategies developed which have been in use for at least two years | 51 | 67 | 71 | Measured annually, two years after adoption |
| Quality of work | 18. Proportion of project final reports found satisfactory by peer-review committees | Not measured | Not measured | 100% | Measured annually |

### MANAGEMENT PERFORMANCE

| Effective resource mobilization | 19. Percentage of approved biennial budget successfully funded | 78% | ≥100% | To be measured in 2015 | Measured in the second year of each biennium |
| Effective management | 20. Percentage of income received from multi-year agreements | Not measured | tbd | To be measured in 2015 | Measured in the second year of each biennium |
| Effective management | 21. Percentage of staff workplans and performance reviews (including personal development plan) completed on time | Not measured | ≥90% | 90.4% | Measured annually |
| Effective management | 22. Proportion of expected results on track | 60% | ≥80% | 69% | Measured annually |
| Effective management | 23. Proportion of significant risk management action plans that are on track | Not measured | ≥80% | 100% | Measured annually |
TDR is able to conduct its work thanks to the commitment and support from a variety of funders. These include our long-term core contributors from national governments and international institutions, as well as designated funding for specific projects within our current priorities.

<table>
<thead>
<tr>
<th>Contributor</th>
<th>Total for the biennium 2014-15 (US$) as of 31 Dec, 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Member States</strong></td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>4,076,087</td>
</tr>
<tr>
<td>China</td>
<td>110,000</td>
</tr>
<tr>
<td>Cuba</td>
<td>5,000</td>
</tr>
<tr>
<td>Germany</td>
<td>814,111</td>
</tr>
<tr>
<td>India</td>
<td>55,000</td>
</tr>
<tr>
<td>Japan</td>
<td>270,000</td>
</tr>
<tr>
<td>Luxembourg</td>
<td>1,336,898</td>
</tr>
<tr>
<td>Malaysia</td>
<td>25,000</td>
</tr>
<tr>
<td>Mexico</td>
<td>10,000</td>
</tr>
<tr>
<td>Norway</td>
<td>2,200,381</td>
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<tr>
<td>Panama</td>
<td>7,000</td>
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<tr>
<td>Portugal</td>
<td>63,532</td>
</tr>
<tr>
<td>Spain</td>
<td>61,958</td>
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<td>Sweden</td>
<td>10,401,755</td>
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<td>Switzerland</td>
<td>1,829,268</td>
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<td>Thailand</td>
<td>46,026</td>
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<tr>
<td>Turkey</td>
<td>5,000</td>
</tr>
<tr>
<td>United Kingdom of Great Britain and Northern Ireland</td>
<td>7,633,588</td>
</tr>
<tr>
<td>World Bank</td>
<td>1,250,000</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>900,000</td>
</tr>
<tr>
<td><strong>Total Member States</strong></td>
<td>31,100,605</td>
</tr>
<tr>
<td>Bill &amp; Melinda Gates Foundation</td>
<td>2,905,385</td>
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<tr>
<td>Drugs for Neglected Diseases initiative (DNDi)</td>
<td>829,969</td>
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<tr>
<td>European Commission</td>
<td>1,250,137</td>
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<tr>
<td>Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH, Germany</td>
<td>89,673</td>
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<tr>
<td>International Development Research Centre (IDRC), Canada</td>
<td>4,352,301</td>
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<tr>
<td>Royal Tropical Institute (KIT)</td>
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<tr>
<td>United Nations Development Programme (UNDP)</td>
<td>932,368</td>
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<tr>
<td>U.S. Agency for International Development (USAID)</td>
<td>608,076</td>
</tr>
<tr>
<td><strong>TOTAL REVENUE</strong></td>
<td>42,180,916</td>
</tr>
</tbody>
</table>
The Special Programme for Research and Training in Tropical Diseases (TDR) is an independent global programme of scientific collaboration established in 1975. It has a twin mission to improve existing and develop new approaches for preventing, diagnosing, treating, and controlling neglected infectious diseases, and to strengthen the capacity of developing endemic countries to undertake this research and implement the new and improved approaches. TDR is sponsored by the following organizations:

UNICEF • UNDP • World Bank • WHO