Phase IV (2007–future): Research that makes a difference

When TDR was established, it was on the cutting edge of innovation, not only in science but institutionally — creating global partnerships between rich and poor and empowering those affected by some of the world’s most deadly and debilitating diseases. Three decades later, TDR’s commitment to research that makes a difference in disease-endemic countries remains unwavering. The core values that shaped the programme’s first thirty years are robust and enduring. TDR’s new strategy, endorsed by its Joint Coordinating Board, offers renewed vigour. As the UN system’s lead agency for research in neglected diseases of poverty, TDR is planning dynamic collaborations and innovations in the new environment of private and public partnerships.
Our global ‘spaceship earth’ — to use the term coined in the 1970s — is hurtling into the future at an ever-quickening pace. New scientific knowledge is constantly unfolding. Geographical and cultural distances between far-flung reaches of the planet are shrinking, giving rise to the global village concept of interdependency. And yet the gaps between rich and poor remain enormous, including large disparities in disease burden and access to health care.

To address new and emergent problems in disease control while remaining innovative, TDR’s strategic focus is undergoing a metamorphosis. From a programme of tropical disease research, TDR’s new strategic vision has been defined as ‘fostering an effective research effort on infectious diseases of poverty in which disease-endemic countries play a pivotal role’.

Emphasis will be placed on fostering leadership among researchers and public health experts in disease-endemic countries, and addressing the most neglected aspects of infectious disease control. This new strategy responds to changing patterns of disease epidemiology, socio-political environments and institutional alignments.

The changing landscape of health and research

The epidemiology of infectious diseases, including those most associated with poverty, has changed. Some diseases, including leprosy, Chagas disease, onchocerciasis, lymphatic filariasis and visceral leishmaniasis, are now moving towards regional or global elimination, while other diseases have emerged or re-emerged, including TB, HIV/AIDS and dengue. These diseases pose risks first of all to those living in poverty, who comprise TDR’s core constituency, and also to the broader global community.

The factors affecting health are highly dynamic and include urbanization, agriculture, deforestation and climate change. Increased mobility and globalized economies accelerate cross-border transmission of communicable diseases.

The potential severity of new and unforeseen disease threats underlines the importance of rapid and accurate responses from both disease control officials and researchers. Yet many of the poorest countries still lack good health care and research capacity. Laboratories, hospitals and other facilities do not have essential hardware for research, education and treatment, and doctors, laboratory technicians, nurses and scientists often feel compelled to seek better economic opportunities elsewhere.

There are reasons for optimism, nonetheless. Our basic scientific knowledge about the agents of disease and the disease vectors has progressed by light-years in just the past 30 years. Advances in genomics, molecular biology, biotechnology, vector entomology and multiple other fields have created vast new possibilities for innovation in research for new drugs, diagnostics and vector-control tools. IT and communication technologies have made it easier to map and track disease trends geographically and share knowledge more equitably around our global village.

Many disease-endemic countries are strengthening their research institutions and investing in researchers, scientists and health care
policy makers, often with support from TDR. In developed countries, a broad new array of public–private partnerships (PPPs) have emerged, harnessing private-sector resources and a public-minded sense of accountability to these new endeavours.

TDR’s new approach

The multiplicity of new participants provides new momentum but also leads to a more complex research environment. The views of researchers and policy makers in disease-endemic countries themselves are still under-represented in global priority setting. Research needs are unequally covered and certain critical research areas remain neglected.

More than ever, stewardship is needed to bring diverse organizations and interests together in coherent, operational research programmes that are supported by — and inform the decisions of — both disease-endemic countries and global health agencies.

More than ever, the global public health sector needs to provide leadership for a coherent approach to priority setting, so that the most serious infectious disease threats are addressed and the needs of the most vulnerable populations are not overlooked. A public sector ‘convener’ of disparate groups and interests is essential to ensure independent analysis, evidence-based guidance and meaningful involvement of disease-endemic countries in research that can make a difference to health policy as well as to actual practice in homes and communities.

As the main UN agency for research in tropical diseases, TDR has played this kind of role for over three decades. In the coming decade, TDR will scale up its activities significantly in these areas, in respond to the changing health and research environment.

Needed: smart investments in health research

In 1975, the estimated global annual research budget on tropical infectious diseases was only about US$ 30 million (WHO, 1975), with TDR's US$ 20 million annual budget representing two thirds of the total global expenditure. Then as today, investment in research on neglected tropical diseases was woefully disproportionate to the need.

Over the past 30 years, global spending on health research has increased sharply and drug development costs have risen, on average, four-fold, from roughly US$ 230 million per drug in the 1970s–1980s to as much as US$ 800 million or more today (Rawlins, 2004).

TDR’s budget growth has been far more modest, increasing from US$ 20 million at the time of its establishment to about US$ 50 million in 2007. Yet in this environment of rising costs, and operating with only a modest budget, TDR has played a pivotal role in tropical disease research achievements, as documented in this historical account.

As noted in the first chapter, more than half of the new drugs for tropical diseases to have come on the market in the past three decades were supported by TDR. The corner has been turned for five of the

“...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. Of course you need the products. But there is more to it than that. 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 JCB.
eight diseases that were part of the programme's original portfolio, namely lymphatic filariasis, visceral leishmaniasis, onchocerciasis, Chagas and leprosy. Malaria remains one of the world’s most serious killers, but new tools, including bednets and artemisinin-based combination therapies, offer greater hope for bringing the disease under control — particularly if operational research can show us how to use those tools most effectively in homes and communities. Meanwhile, new attention is being focused on sexually transmitted diseases, re-emerging dengue and TB/HIV co-infections, while diseases such as human African trypanosomiasis (sleeping sickness) and schistosomiasis still require much more attention.

TDR cannot and does not claim credit for those accomplishments on its own — only on behalf of the many partners and collaborators who pushed this work forward. Yet it is fair to say that if TDR had not played its role, the burden of disease would have been even higher, the threat even more sinister.

In terms of cost-effectiveness, TDR’s record over the past 30 years remains unmatched. This is true not only in terms of its record in leveraging partnerships to develop new and more efficacious drugs and control tools, but also in terms of capacity building and intervention studies that identified simple and inexpensive measures for putting drugs and tools to better use.

Involving thousands of scientists, control officers and community members, in endeavors ranging from field innovations — such as fixed-dose packaging of anti-malarials and insecticide-treated bednets — to global initiatives in genome sequencing, TDR has repeatedly demonstrated its organizational strengths as a leader of partnerships.

TDR’s new 10-year strategy, endorsed by its Joint Coordinating Board (JCB), will better position TDR to play its role with renewed vigour — as the UN system’s lead agency for research in neglected diseases of poverty — in a dynamic environment of PPPs (TDR, 2006). Strategic goals include:

- Stewardship for research on infectious diseases of poor populations: as facilitator and knowledge manager to support needs assessment, priority setting, progress analysis and advocacy, and to provide a neutral platform for partners to discuss and harmonize their activities.
- Empowerment of researchers and public health professionals from disease-endemic countries, moving beyond traditional research training to build leadership at individual, institutional and national levels so countries can better initiate and lead research activities, develop a stronger presence in international health research and effectively use research results to inform policy and practice.
- Research on neglected priority needs that are not adequately addressed by other partners. In terms of diseases addressed, TDR’s focus will be redefined to include not only the 10 diseases now in its portfolio but infectious diseases of poverty more broadly, including a limited number of well-defined activities within this broader disease scope.

The new strategy thus formalizes TDR’s expanded disease scope to include aspects of research in TB, HIV/AIDS and sexually transmitted diseases, and focuses programme activities on two contrasting areas of the research spectrum:

- Implementation research to evaluate the use of new drugs and tools in real-life settings and enhance access to interventions (TDR, 2005).
- Innovation-driven leadership of discovery research for the next generation of new drugs and products.
WHO is placing a renewed focus on primary health care and on access to health care services in the spirit of the ‘Health for All’ Alma-Ata charter, with a special focus on Africa and vulnerable populations, particularly women. TDR’s new strategy will support this global focus, while reinforcing strategic links with co-sponsoring agencies, including WHO.

**Research in real-life settings — relevant to the broader health agenda**

Inexpensive and effective disease control interventions, such as insecticide-treated bednets and anti-malarial drugs, remain underused in most developing nations (Donaldson & Banatvala, 2007). Implementation research is anchored in the recognition that drugs or control tools function very differently in the field than in controlled trials or laboratory settings, and research on how to improve access, distribution and use of available tools can make a critical difference to health and to health systems. Social and behavioural research is also gaining recognition as another means of identifying and overcoming gender and socio-economic barriers to effective access to, and use of, tools and treatments (Irwin, et al., 2006; Sachs et al., 2001).

In the coming decade, TDR will build upon its track record in implementation research and socio-behavioural research, exploring how vital interventions can be scaled up and fine tuned effectively in real-life settings. For instance, recent TDR research in communities with experience in community-directed treatment for onchocerciasis has now etched a model for integrated delivery of multiple drugs and tools, beyond the annual ivermectin dose.

Such research indicates that community-directed models can potentially increase access to health interventions among poor rural populations. Integrated delivery also has the potential to achieve greater cost-efficiencies (Brady, Hooper & Ottesen, 2006). Future research will develop and test such community-directed models more widely in various African settings, exploring where such approaches are most suitable, how they might be upscaled, and with what kinds of interventions.

**Innovation in product development and discovery**

Despite the drug innovations seen in recent years, parasitic diseases still affect one in six people worldwide, killing more than 500,000 people every year. There is a continuing need for new drug innovations to improve drug safety and efficacy, and overcome parasite resistance to older compounds. While new PPPs are playing an important role in product innovation, the vital role of the global public health sector in promoting a high-level research agenda based upon objective criteria and needs cannot be ignored. A global public health institution is best positioned to convene relevant stakeholders, help link networks and partnerships, gather the most relevant evidence based on broad expert consensus, gain the broad cooperation of governments and agencies for testing and scale-up, and promote coherent guidelines for use.

The development and expansion of TDR’s discovery networks and diagnostic research frameworks are indicators of the role that TDR has recently had in this arena. Other planned and future TDR activities include research into the treatment and care of patients that are co-infected with TB and HIV/AIDS, innovative vector-control interventions and a new helminth drug development initiative.

The renewed emphasis placed by WHO on these diseases through its Neglected Tropical Disease Department also provides an important point of public health focus. TDR’s new strategy will simultaneously support WHO’s control efforts, stimulate research and foster research leadership for product development in disease-endemic countries.

**People, products and partnerships**

From leprosy treatments to insecticide-treated bednets; evaluation of diagnostics for TB, malaria and syphilis; home management of malaria and other innovations; TDR has seized upon small stories of success and built them into much larger experiences.
TDR’s role as a leader, convenor and innovator in research over the past decades is well documented. As an instrument of the international community, TDR promoted goal-oriented, merit-based research institutions, focusing on capacity strengthening in the least developed nations where the need was greatest but where the research could be shared for the benefit of all.

Its success is unmatched in bringing together experts from poor and rich countries, from top scientists to trainees, from industry to the public sector, and from countries in disparate social, geographical and political settings, in the battle against diseases of the poor. Of necessity, the creation of new knowledge and understanding is a public good, and so requires public involvement and investment. Funds have been provided to TDR by an unflinching core group of governments, public sector agencies and foundations all committed not just to improving health but also to ameliorating poverty, the twin objectives of the Millennium Development Goals.

While this commemorative history has illustrated the high points, every summit of achievement has been carved by as many or more valleys. These included institutional challenges as well as the scientific and technical challenges of the research — dead ends for promising endeavors, efforts that ran into unforeseen complications, initiatives that failed to yield conclusive results — positively or negatively.

Certainly there were also times when powerful interests sought to influence or intervene in the more objective processes of research. Amidst the pressures, TDR strived to remain above the fray as a trusted mediator and honest broker. Yet there were times when the programme’s own positions had to be re-examined. By remaining focused on a goal, identifying the concrete obstacles or issues and creating ‘learning’ solutions and systems that could be adapted or fine-tuned with more experience, many such hurdles were overcome.

“For every success that has been documented, there are numerous non-successes,” notes current TDR director, Dr Robert Ridley. “That is the nature of science and of research. Mistakes are made, and the failures, as much as the achievements, guide the next step that you need to take. But in the end, if the goals are solid, if the commitment of the partners, the governing board, and the individuals or investigators involved in implementation is solid, then that leads to success.”

Adds Liese, “Historically, you cannot ignore the more rocky times. These have included times when challenges were introduced by the donor community, when there were administrative hassles, when issues arose over the separation between research and disease control functions, and the more recent question of TDR’s future role and direction.

“But what makes an organization strong, is its internal capacity to adjust its course and deal with these issues. And if you look at the kinds of changes TDR has made over the years, the things it has taken on and phased out, it has done quite a lot. And responding to these questions is what the new strategy is all about.”

TDR is proud of the role it has played over the past 30 years — guided by the JCB and its scientific steering and technical committees — as a champion of research and training, as a facilitator and catalyst for action, and as a conduit for the voice of the poor and disadvantaged who still suffer the disproportionate burden from devastating diseases.

TDR has always been, and will continue to be, about people, products and partnerships — and how best to bring all three of these elements together in research to achieve the single, unifying common objective of better health and well-being for all.
Institute of Endemic Diseases (University of Khartoum): A laboratory technician carrying out an electrophoresis test (Sudan • 1997 • WHO/TDR/CRUMP).
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.
What are the most important lessons from the early history of TDR? To have the courage to experiment. Many aspects of the organization and management of TDR were untested and therefore experimental. Many of the experiments have proven successful, and less successful aspects were modified. To dare to keep science alive in a large bureaucracy: one constant danger was that the programme would be submerged in a sea of bureaucratic red tape. But despite all that, TDR has kept faith with the ideals and objectivity of science.”


Flags at the high level ministerial meeting in Accra, Ghana, in June, 2006, where 14 ministers of health and heads of delegations from African nations and other developing countries from Asia, the Middle East and South America met to commit to future directions and coordination in health research. TDR and WHO research departments and WHO’s Regional Office for Africa provided technical and financial assistance to this international gathering and to an earlier (March 2006) high level meeting of African ministers and delegations in Abuja, Nigeria (GHANA • 2006 • WHO/TDR/GUTH).