Phase I
(1975–1986): Heroic goals

TDR took on eight of the world’s most neglected diseases, affecting millions of people in poor countries. Critically needed new drugs and drug combination therapies were developed for leprosy, malaria and sleeping sickness, and new diagnostics for other diseases. An innovative compound screening network identified the potential of ivermectin for onchocerciasis. TDR’s early support for Chinese research into artemisinin derivatives for malaria helped introduce an ancient remedy onto global research agendas. Pioneering field research and socio-economic research guided effective treatment of diseases, including those socially stigmatized (such as leprosy). At the same time, TDR supported long-term development of research institutions in disease-endemic countries, and high-level training of hundreds of scientists.
In the world

The Cold War was still the dominant issue in international politics. At the same time, in this era immediately following the Viet Nam war, global shuttle diplomacy between the big ‘blocs’ of east and west would accelerate. The People’s Republic of China was gradually expanding not only its diplomatic exchanges, but also its social and scientific contacts with other regions of the world. New interactions between Chinese researchers and scientists would facilitate research into the use of artemisinin, a compound extracted from *Artemisia annua* (sweet wormwood), for the treatment of malaria.

In public health

For public health, it was an optimistic time. The global eradication of smallpox had been certified by an eminent commission of scientists, and was endorsed in 1980 by the World Health Assembly. Malaria was still a serious public health problem, particularly in Africa, although there was optimism about the prospects for a vaccine.

Advances in basic research, such as the development of monoclonal antibodies in 1975, opened up the possibility of developing more sophisticated diagnostic tools, as well as progressing in vaccine and drug research. An improved understanding of the fundamentals in immunology, cell biology and molecular biology, including the development of techniques for the genetic manipulation of organisms, paved the way for gene sequencing and an increased understanding of the biology of many of the major pathogens responsible for tropical diseases, their vectors and their hosts.

At the same time, it was becoming increasingly clear that the great strides in public health that had been made in developed countries since the beginning of the century were not occurring in poorer nations at the same pace. Many, if not most, major disease-control initiatives in the least developed countries were driven vertically by donors, and once these campaigns ended, any public health improvements were at risk. The capacity to conduct research to support and sustain public health initiatives was similarly weak. Private sector pharmaceutical firms based in developed countries had little incentive to invest in research into drugs and tools needed by poor countries that could ill-afford to pay for them.

It was against this background that then WHO Director-General Dr Halfdan Mahler articulated a vision of WHO as a global ‘health conscience’, acting as a countervailing influence to the narrower commercial interests of the marketplace (WHO, 1979). This followed the 1978 ‘Health for All’ Declaration, which was adopted at the International Conference on Primary Health Care in Alma Ata, organized by WHO. This conference emphasized that improving primary health care was key to public health advances in poor countries, as well as being key to social and economic development. Although primary health care, as such, was anchored in the health care system, home-directed and community-based treatment would emerge as innovations of the late 1980s with the same philosophical basis, emphasizing good local use of technology and knowledge.
In TDR — the needs were great

TDR's initial focus was on eight of the most serious and most neglected tropical diseases: malaria, leprosy, schistosomiasis, visceral and cutaneous leishmaniasis, onchocerciasis, lymphatic filariasis and the two diseases caused by parasitic trypanosomatid protozoans — Chagas disease in the Americas and human African trypanosomiasis (HAT), popularly known as sleeping sickness, in Africa. These particular diseases were targeted both because new drugs, vaccines and vector-control methods were desperately needed, and at the same time, basic research advances had opened up new possibilities for finding solutions. Scientists had just managed to culture Plasmodium falciparum in the laboratory, the most deadly of the four Plasmodium species to cause malaria in humans. The bacteria responsible for leprosy, Mycobacterium leprae, which would not grow in artificial cell-culture medium, had just been cultured in armadillos, paving the way for research into new drugs and diagnostics for this ancient malady.

Strikingly, in this pre-AIDS period, TB was not included in TDR's targeted diseases. The scourge associated with the crowded housing and work places of the early industrial era was not regarded as a major public health challenge in the 1970s. This would change by the turn of the millennium, when both TB and dengue would be added to the programme's portfolio, reflecting the re-emergence of TB as a serious problem in HIV-infected populations and the epidemic growth of dengue in fast-developing urban areas of Asia and Latin America.

Early successes in drug development — leprosy, river blindness, malaria and HAT

One of the first achievements of note was the leadership role taken by TDR in the search for a new leprosy treatment. Early in its first decade, TDR helped demonstrate that drug resistance to dapsone, the prevalent treatment for leprosy at the time, was a real and growing problem, as was the lifelong course of treatment required.

“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.”


TDR's experts and advisers pointed out that several compounds had shown potential activity against M. leprae in laboratory tests, but they had not yet been properly evaluated for use in humans. More generally, scientists were beginning to investigate how multidrug therapy (MDT), when two or more drugs act in unison against different chemical targets in a given parasite or pathogen, might be more effective than monotherapy.
TDR thus initiated clinical trials of new drug combinations (dapsone, rifampicin, clofazimine and acedapsone) for leprosy treatment in Mali and India. The early success of these trials contributed to a landmark recommendation by a WHO Study Group in 1982 that MDT be used in leprosy treatment. Other partners would now carry forward a vigorous programme of control and elimination, led by the WHO Leprosy Unit and Programme for the Elimination of Leprosy; the Nippon Foundation through its sister organization, the Sasakawa Memorial Health Foundation; various non-governmental organizations; and the pharmaceutical firm Ciba-Geigy (now Novartis).

“The argument was that before trying to develop an entirely new drug, we should look at the compounds we knew something about that might be used better, in combination,” recalls then TDR Director Dr Adetokunbo Lucas. Lucas was department chairman at the University of Ibadan and head of the committee that designed Nigeria’s national health policy. He joined TDR in 1976, and would guide the organization throughout its critical first decade. “Leprosy is an example of how we did not use the same strategy for every disease, but sat down and tried to find the most appropriate approach.”

The development of ivermectin

In July, 1978, scientists at the US-based laboratories of Merck, who had been researching ivermectin for several years, sent the compound to the TDR-supported drug-screening facility at James Cook University of North Queensland, Australia. Such screening, which tested ivermectin’s effectiveness in cattle harbouring a zoonotic strain of the filarial *Onchocerca* parasite responsible for river blindness, was regarded by scientists as the best predictor of how a compound would act against human onchocerciasis. Results showed the drug was ‘highly effective’ against the microfilariae, or infant larvae of the parasite, although it did not, in fact, seem to kill the adult worm. This screening test was part of a broader TDR effort to intensify the search for a new onchocerciasis drug, which had been established at considerable expense.

“The two drugs we had for onchocerciasis at the time were notorious poisons,” recalls Lucas. “We were really desperately looking for a new drug. When we visited the major drug companies, it was clear they

**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. Then .... WHO took the daring decision to advise a simple regimen of therapy with three drugs to combat resistance — multidrug therapy or MDT. By then, TDR had mapped and quantified the main areas of dapsone resistance, developed clinical protocols for MDT in different parts of the world, and established widescale ‘post-marketing’ surveillance of MDT. By the end of 1994, the global number of registered patients was 1.3 million — a fourfold decrease — with 560 000 new cases being detected annually.”

_Dr Torle Godal, TDR Director, 1986–1998 (TDR, 1995)._  

“The MDT for leprosy must be one of the top five achievements of TDR for the first decade. Although it should be emphasized that it was leprosy clinicians who were doing the work, with TDR support. But the development of MDT was, in fact, one of the reasons TDR’s work on leprosy vaccines ceased. We realized that MDT was going to solve the leprosy problem and we did not need a vaccine.”

_Dr Howard Engers, Director of the Armauer Hansen Research Institute, Addis Ababa, Ethiopia (TDR manager of vaccine research, 1987–2004)._
were not interested in this disease. No one was screening any compounds. We thought that perhaps there was a compound on the shelf that had not been discovered. The strategy put forward was to open a compound-screening network.

Along with James Cook University, the network involved researchers at the University of Georgia (USA); the University of Giessen (Germany); the Wellcome Trust (UK); the London School of Hygiene and Tropical Medicine; and the University of Tokyo.

“We asked industry to give us compounds to test,” continues Lucas, “and we would give them the results. We offered this free of charge and confidentially. We had thousands of compounds sent through small animal screens in the broader network. But since these often yielded false positives, the most promising compounds were sent to the cattle screen, which had been set up by TDR in order to expedite the search for a new drug for onchocerciasis. It was much more expensive, but also potentially more accurate. Among the first compounds to go through the cattle screen was ivermectin.”

Merck’s scientists were enthusiastic but TDR less so because the ultimate TDR goal was to identify a ‘macrofilaricide’, a drug that would sterilize or kill the adult parasite and not just the larvae, and thus cure an infected person rather than just control the disease. Merck proceeded independently to Phase I clinical trials. Serious TDR–Merck collaboration, however, resumed in the later stages of clinical trials, as ivermectin’s efficacy as a treatment and control measure became more evident. TDR contributed to the design of study protocols and definition of dosage and facilitated Merck’s links to collaborative networks in the Onchocerciasis Control Programme (OCP) of 11 West African countries (TDR, 1998).

In February 1986, as the drug was about to be registered, Lucas and Dr Brian Duke, head of WHO’s Filariasis Unit, held a decisive meeting with then Chief Executive Officer of Merck, Dr Roy Vagelos. Merck had been negotiating with development and donor agencies over the purchase of ivermectin, but had received little response. The TDR and WHO officials came ready to drive a hard bargain over pricing for developing countries: “Vagelos made us cups of coffee in his office,” recalls Lucas. “Then, as we sat down to talk, he told us that he had not gotten any response from the donors. He said wanted to see the drug widely used, so he had decided to donate it. But at the time, this remained confidential. In June 1986, as Lucas was about to conclude his ten-year term with TDR, he contacted Vagelos and Merck once more. “I asked them if I could make public Merck’s offer to donate ivermectin at the upcoming JCB meeting — the last one that I would attend as Director.” The result was the 20 June telex to TDR. Vagelos was later awarded a medal by the Prince Mahidol Foundation for his “bold and unprecedented” decision. Lucas and his successor, Dr Tore Godal, received the same medal jointly for their contributions to TDR.

Following Merck’s announcement, TDR helped move rapidly with partners in OCP, WHO and elsewhere to translate the donation offer into policy action. Large scale trials were launched to determine safety and effectiveness of mass drug administration. Subsequent research helped define a public health rationale, epidemiological evidence and strategies for an unprecedented programme of community-directed treatment with ivermectin. Over the next two decades ivermectin (mectizan®) would reach some 60 million of the 100 million people at risk in endemic areas in sub-Saharan Africa. Although not a perfect solution, annual treatment gradually brought onchocerciasis under control in most areas reached, and contributed to the elimination of onchocerciasis as a public health problem in savanna areas of West Africa.

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**Ivermectin comes free**

“Merck and the WHO have collaborated extensively on the development of ivermectin for onchocerciasis ... The special circumstances associated with this disease and the interest of several organizations and governments have caused Merck from the outset to consider ways of accommodating a variety of objectives. First and foremost is ensuring that the drug will be put to optimum use for the benefit of onchocerciasis patients and others who may be at risk. Consequently, Merck is undertaking to make appropriate arrangements, if necessary, with other interested parties, to make needed quantities of the drug available to these governments and patients at no cost to them for the treatment of onchocerciasis.”

Excerpt of Telex from Robert D. Fluss, Merck, to TDR Director Adetokunbo Lucas, 20 June 1986.
**Mefloquine — a counterattack on parasite resistance**

Mefloquine is another significant anti-malarial that TDR was involved in developing. Mefloquine became available at a critical time when other drugs were encountering parasite resistance and artemisinin was not yet widely available. The compound was originally discovered by the US-based Walter Reed Army Institute of Research (WRAIR). But as mefloquine was not covered by a patent and was expensive to produce, there was little initial interest in development. TDR, however, worked with the pharmaceutical firm Hoffman-La Roche to find a more inexpensive way to synthesize the drug, and sponsored more than 12 clinical research studies in Latin America, Zambia and Thailand, leading eventually to registration. Although mefloquine-based therapies were later superseded by lower-toxicity artemisinin-derived compounds, mefloquine is still used widely as a prophylactic by tourists and travellers to malaria-endemic regions. The development of mefloquine was also an example of the intensive and fruitful collaboration that occurred in this first phase between TDR and WRAIR, which yielded a variety of innovations.

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**Paving the way for new malaria drugs — artemisinin**

Malaria remained the biggest killer worldwide, and it was here that a new initiative, led by Chinese scientists and supported at an early stage by TDR, helped to pave the way for significant breakthroughs in malaria treatment. This initiative was research into the anti-malarial properties of the indigenous Chinese plant known as qinghao or sweet wormwood (*A. annua*). The plant had been used historically in traditional Chinese medicine, and Chinese researchers had identified its active compound, artemisinin, as potentially effective against parasites. Interest in new anti-malarials was high as parasite resistance was developing against most other available drugs, some of which had substantial side effects.

TDR, whose far-flung networks already included collaborations in China, would be among the first international institutions to dispatch scientists to China’s artemisinin research facilities, appreciate the value of the endeavour, and transmit that to colleagues elsewhere. Research cooperation into the properties of artemisinin, in an era when the Cold War was still a dominant feature of international politics, involved some delicate diplomacy. But overcoming the obstacles was a shared scientific quest — a better treatment for one of the world’s deadliest diseases and a modern use for an ancient Chinese herbal remedy.

“The Chinese scientists who were working on artemisinin contacted the malaria section of WHO,” recalls Lucas. “They were very anxious to have the drug registered and widely distributed. We said it needed more workup, including pre-clinical laboratory testing of toxicity. Part of that was done through the TDR network.”

“TDR helped to get researchers outside of China involved in artemisinin and get it on the research agenda.”

“We came into the artemisinin story at the time when the Chinese had discovered its very great and important activity as an anti-malarial drug. But our analysis of the data from them showed it had not gone through the kind of scrutiny that a new drug would go through in other developed parts of the world. So what we worked to do with them was to try to get standard preparations of artemisinin through toxicology and standard methods of production so we would have a stable reference material. I went to China in 1979 and we talked about not only artemisinin but other ways in which we could cooperate with the Chinese.”

Many other public and private partners across Asia, Europe and North America would soon take the lead in development of the main artemisinin derivatives (artemether, artesunate and arteether) and ACTs. TDR’s role would evolve into more supportive and focused endeavours, such as research into the development of injectable artemisinin derivatives for severe malaria; field trials demonstrating the value of ACTs in general; and field trials that demonstrated the safety of ACTs in young children. TDR-supported research for in vitro testing of anti-malarial drug resistance would help to develop a global map of parasite resistance to other drugs then in common use.

TDR’s early appreciation of, and response to, the innovative Chinese research into artemisinin demonstrated leadership in the initial phase of exploration, bridging barriers of geography and political mistrust to benefit public health.

DFMO — the ‘resurrection’ drug for sleeping sickness

Towards the end of the first decade came the discovery that d,l-α-difluoromethylornithine (DFMO), originally developed as an anti-cancer compound, could be used to treat HAT. HAT is popularly known as sleeping sickness because of the extreme fatigue and disorientation.

Obtaining evidence for treatment of sleeping sickness

“When we first looked at how to improve treatment for sleeping sickness (HAT), one of the first things we did was look at the response to the arsenic-based drugs which were standard at the time. But we could only find 30 documented autopsies of people who had died from HAT in the literature. It was shocking, really, that treatment was determined on such a narrow base of knowledge. We wanted to gather more information, but the problem was that people who die of HAT live in communities where there are no trained pathologists to do autopsies. So we came up with an unusual solution. We recruited a top neuropathologist from Scotland, who produced an illustrated guidance document showing, stage by stage, how an uninitiated person could do an autopsy on the corpse of a HAT victim. We sent the document to a number of places where people were dying from HAT, and persuaded certain health care workers to follow the procedure. The preserved brains were then sent to Scotland for analysis. By this innovative measure, we were able to have specimens from corpses in the most remote part of Africa examined by the top neuropathology centre in Europe. It turned out that many of the victims were not dying from HAT, but from arsenic poisoning. So one of the first things TDR did, even before DFMO became available, was to recommend that the dose of the drugs that had been used for decades be cut by half. Our African collaborators followed the guidelines so carefully that the Scottish doctor working with us said that the brains he received from them were often in better shape than those arriving from Scotland. I don’t know of any other disease condition where this kind of strategy was used to obtain relevant information. But it needed to be done, so we found a way to do it.”

A tsetse fly trap being sprayed. Rural populations are most at risk of sleeping sickness. Even during daily activities, villagers may be exposed to tsetse flies, the vectors of sleeping sickness parasites. Easily erected insecticide-impregnated traps placed in tsetse habitats or around village perimeters help to reduce disease transmission (Ivory Coast • 1992 • WHO/TDR/EDWARDS).
that incapacitates victims before death. DFMO was initially developed by Marion Merrell Dow Pharmaceuticals (now Sanofi–Aventis). With TDR support, Phase III clinical trials of the drug began in 1987, and the rapid response of patients even in late stages of Trypanosoma brucei gambiense sleeping sickness gained DFMO the nickname the ‘resurrection’ drug. DFMO, or eflornithine® as it was licensed, was the first new drug for sleeping sickness in 40 years. It is noteworthy that Sanofi–Aventis now makes the drug available through a donation programme under a WHO Memorandum of Understanding.

Pioneering field research and social science research

In terms of field research, emphasis was being placed on vector control, particularly for diseases where the promise of new and more effective drugs was still remote. Reducing insect vector populations through environmental management or manipulation has historically been recognized as an important aspect of disease prevention, and knowledge of how certain species act as predators on vector populations was expanding. Interest was also growing in biological vector-control tools that might replace chemicals to which parasites or vectors had developed resistance, as well as chemicals increasingly recognized as posing long-term risks to health and the environment, such as dichloro-diphenyl-trichloroethane (DDT).

TDR thus supported research into ‘larvivorous’ fish species that prey upon the larvae of malarial insects living in both water containers and flooded agricultural fields. It also supported research into the use of the bacterium Bacillus thuringiensis israelensis H-14 (Bti) to control larvae of mosquitoes and other vectors. Bti was incorporated into control programmes by 1982 and was soon followed by another bacterial vector control tool, Bacillus sphaericus (Rowe, 1984). Bti, in particular, would play an important role in controlling the blackfly vector for...
onchocerciasis in the savanna regions of sub-Saharan Africa in the mid-1980s, where vector control was the main means of disease control and the synthetic larvicides available at the time were losing their impact. In the case of onchocerciasis, Bti was later superseded by other synthetic formulations, but it remains an important tool for mosquito control in the USA. Elsewhere in Asia, Africa and the Americas, Bti and B. sphaericus have been used successfully in a range of field trials and pilot control efforts, and larvivorous fish have been deployed against malaria vectors in rice fields and water containers, although such tools are still not widespread in mainstream vector control or vector-borne disease-management programmes (Walker, 2002).

Also in the mid-1980s, TDR-supported field research trials of HAT vector control began to demonstrate the efficacy of pyramidal tsetse fly traps for control of the vector population, in the absence of better drug treatment.

Across nine countries in Latin America, an unprecedented series of epidemiological studies supported by TDR between 1980 and 1985 helped develop a standardized protocol to determine the prevalence of Chagas disease and accurately map the patterns of infestation by the insect vectors of the Trypanosoma cruzi parasite. One aspect of successful prevalence mapping was a TDR capacity-strengthening effort that helped scientists and laboratories in endemic countries to standardize their serological techniques and criteria for diagnosis of the infection.

“It was the first time that disease prevalence information was generated in a way that was truly comparable,” notes Lucas. “That generated a first-ever map of Chagas prevalence in all of the endemic areas of Latin America.”

In this decade and the next, TDR also supported field research on the effectiveness of various vector-control tools, including vector detection sensors, insecticidal paints, fumigant canisters and housing improvements, as well as measures to halt Chagas transmission through blood banks by improving serological screening. Together, the new diagnostic, screening and vector-control tools would help provide the evidence base for the Southern Cone Initiative. Launched in 1991, the initiative was a regional strategy for control of Chagas disease, coordinated by the WHO Regional Office for the Americas. It was followed in 1997 by similar initiatives in Central America and the Andean Pact regions (now the Andean Community). The results have been impressive; large areas of the Southern Cone region are now free of domestic vector infestation, and disease prevalence more generally has been reduced (Remme et al., 2006).

Social research was another area in which TDR would be called to innovate. In 1976, WHO Director-General Dr Halfdan Mahler had emphasized that “TDR was not designed simply to advance medical technology, but rather as a contribution to the promotion of human welfare in the widest sense in the context of a new international order in economic and social affairs.”

With no social research community and no significant tradition to build upon, it was another three years before the first TDR Steering Committee for Social and Economic Research (SER) became operational. Over time, the output from this effort began to support other aspects of biomedical research and assist in translating new interventions into implementation. In the area of leprosy, for instance, 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. In the 1990s, research into the socio-economic impacts of onchocerciasis, including the economic loss due to human migration away from disease-endemic, but fertile, river valleys, and the social stigma associated with onchocerciasis-related skin and eye conditions, would be critical in convincing policy makers of the importance of mass ivermectin administration.

“Ultimately, tropical diseases must be controlled by endemic countries. Even when an experimental tool fails, there will be trained men and women who are capable of developing a new one.”

DR FARROKH MODABBER, Consultant DNDi; Coordinator RCS and Manager Leishmaniasis Vaccine initiatives, TDR, 1984–2000.
Building research capacity

An early emphasis of research capacity strengthening (RCS) was on long-term grants to support the construction of research institutions in disease-endemic countries, more so than on targeted scientific priorities. The basic instrument was a non-competitive long-term grant that was designed to help an institution acquire or upgrade existing research facilities. Although part of the grant requirement was a programme of scientific research, scientific merit was still secondary to institution building. The programme involved capital grants for initial investigation, research and follow-up, so that funding could continue for a prolonged period of a decade or so. A major RCS review by TDR’s Scientific and Technical Advisory Committee (STAC) in 1992 noted that proposals for RCS institutional grants in

Critical action at a critical moment

“The TDR grants to the molecular biology and immunology departments were critical action at a critical moment, important to the rebuilding of FIOCRUZ in the late 1970s,” says former TDR Director Dr Carlos Morel.

Founded in 1900, the Oswaldo Cruz foundation (FIOCRUZ) underwent a major institutional and financial crisis in the early 1970s. In 1978, Morel, who had done his PhD thesis work at the Swiss Cancer Institute in Lausanne, Switzerland, joined the FIOCRUZ faculty to build a new biochemistry and molecular biology department. At approximately the same time, Dr Bernardo Galvão Castro (who later would become the first scientist in Latin America to isolate the HIV virus) took over as head of the immunology department. Both of them received institution-building grants from the TDR RCS programme. Castro received a long-term grant, while Morel received a US$ 100 000 grant to develop a course on genes and antigens.

“These were a small drop in the budget of FIOCRUZ,” observes Morel. “But they were critical to getting international support in two key areas of science that had been neglected. It was not only a question of money, but of prestige, leadership and international recognition.”

At about the same time, on the other side of the globe, another young scientist, Dr Yongyuth Yuthavong, was building another course on molecular biology at Mahidol University in Thailand, also with support from a TDR grant. Both Morel’s and Yuthavong’s efforts yielded manuals that in the 1980s became standard reference works for students of molecular biology in many developing countries. While Morel would later become president of FIOCRUZ, prior to assuming the Director’s post at TDR, Yuthavong would become Thailand’s Science Minister.

Oswaldo Cruz Foundation (FIOCRUZ) in Rio de Janeiro, which has benefited from TDR research capability strengthening (RCS) support (Brazil • 1992 • WHO/TDR/EDWARDS).
TDR's research capability strengthening (RCS) programme has supported capacity building activities in field research and in the knowledge of disease impact and control at the community level, as in the training course portrayed here in Ndola (Zambia • 1980 • WHO/TDR).
this first phase tended to be “ambitious development plans, often carrying requests for expensive laboratory equipment and proposals for research projects in several diseases or more than one disciplinary area.” (TDR 12th Programme Report, 1995). This approach was judged to be successful in various external reviews both in terms of scientific output and in terms of increasing the capacity of key institutions at a time when such support was needed. But by the late 1980s, RCS grants evolved into increasingly competitive formats reflecting, indeed, the increased capacity of the research institutions in disease-endemic countries. Two examples of institutions that benefited from early TDR support were the Oswaldo Cruz Institute (FIOCRUZ) in Brazil and Mahidol University in Thailand, both now internationally recognized centres for tropical disease research. TDR also played a critical role in fostering a major malaria research centre in Mali, the Malaria Research and Training Centre, which today is doing “some of the most advanced malaria research on the continent,” in the words of Lucas. “There are other institutions in Africa doing comparable work, of course”, he says. “However, the Mali institution is truly an example of an African institution that was developed by TDR.” By 1986, TDR had supported 98 institutions, issued more than 700 training grants and launched more than 10 MSc courses in entomology and epidemiology in Asia, Africa and Latin America. One third of TDR-sponsored publications were authored or co-authored by scientists from disease-endemic countries (TDR, 1987).

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<th>TDR/JCB institutional milestones</th>
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| **1974** | - World Health Assembly calls for an intensification of research on major tropical parasitic diseases (WHA27.52).
| | - World Health Assembly requests WHO’s role in the development and coordination of biomedical research (WHA27.61).
| | - WHO Advisory Committee on Medical Research recommends the institution of an expanded WHO programme for research and training related to tropical communicable diseases and agrees on objectives for the expanded programme.
| | - First TDR Steering Committee Meeting (IMMLEP Project Group).
| **1975** | - TDR commences formal operations.
| **1976** | - UNDP becomes a co-sponsor of the Special Programme.
| | - The World Bank joins UNDP and WHO as co-sponsors of the Special Programme.
| | - World Health Assembly adopts goal of ‘Health for all by the year 2000’.
| **1978** | - Meeting of Cooperating Parties endorses the Memorandum of Understanding on TDR’s Administrative and Technical Structures.
| | - First meeting of the Standing Committee (comprising representatives of the three co-sponsoring agencies).
| | - First session of the Joint Coordinating Board (JCB).
| | - WHO Alma-Ata Declaration on Primary Health Care is identified as best strategy for meeting health for all goal.
| **1979** | - First meeting of the Scientific and Technical Advisory Committee (STAC).
| **1980** | - World Health Assembly endorses certification of smallpox eradication.
| **1982** | - Submission of the First External Review Report to JCB (5).
| **1983** | - TDR resource contributors adopt procedures for the selection of JCB members by the contributors (paragraph 2.2.1 of the Memorandum of Understanding).
| **1984** | - First session of the JCB held outside WHO HQ — JCB (7) held in Bangkok, Thailand.
At a field survey to detect schistosomiasis, an infected child demonstrates that he has swallowed the medicine given to cure his infection. Children are weighed and the correct dosage of drugs (Praziquantel) is also prescribed by weight. (TANZANIA • 1988 • WHO/TDR/MORENA).
A man blinded by onchocerciasis (Haute-Volta • 1975 • donation from the Private collection of the late Dr Uwe Brinkmann, Harvard School of Public Health).
“When I got to my position as director of research in the Ministry of Health, I received information on what TDR was doing in Cameroon. I realized that when I was a young guy, TDR was conducting a study on onchocerciasis in the region where I was going to primary school, and maybe I was part of one of the trials with kids in that primary school.”

DR PIERRE ONGOLO-ZOGO, Chief, Division of Operational Health Research, Ministry of Public Health, Cameroon and representative to the JCB, Government of Cameroon.
Microscopic examination of blood samples and improved serodiagnostic tests such as the Card Agglutination Test for Trypanosomiasis (CATT) allow for a large number of people to be screened for gambiense sleeping sickness infection in a relatively short time (IVORY COAST • 1992 • WHO/TDR/EDWARDS).

“TDR has achieved so much with so little, thanks to partnerships and cooperation with many other players in the field of research and control of tropical diseases.”

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/BALDRE).
Jiangsu province: A couple set fish traps in water close to a ruined building. Areas such as this are regularly flooded when rivers rise following heavy rains. The flooding means that intermediate host snails can re-invade areas previously cleared, parasites can develop, and the waters can become sources of infection for anyone living nearby (China • 1999 • WHO/TDR/Crump).
“TDR supports research on schistosomiasis in many ways using a holistic, long-term strategy, targeting all the facets of the parasite life cycle as well as the behaviour of people living in the endemic areas, an approach which is now starting to pay off in a big way.”

Research capability strengthening: Laboratory practice during a 1978 workshop on enzyme-linked immunosorbent assays (ELISA) at the Institute of Parasitic Diseases, Chinese Academy of Sciences, a WHO/TDR collaborating centre for malaria, schistosomiasis and filariasis (China • 1978 • WHO/TDR).
“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.”