



Eliminating River Blindness

HIGHLIGHTS FROM TDR'S

Making a Difference

30 Years of Research and Capacity Building in Tropical Diseases



**World Health
Organization**

Special Programme for Research & Training
in Tropical Diseases (TDR) sponsored by
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Summary

The global effort to eliminate onchocerciasis (river blindness) is driven by close collaboration between research and public health agencies. Researchers seek answers to real-life problems faced by health workers in the field. Health strategies are refined by research findings. Such synergy is a major reason behind achievements attained so far in reaching over 55 million Africans with treatment – and elimination of onchocerciasis as a public health problem. Since its foundation, the Special Programme for Research and Training in Tropical Diseases (TDR) has been a driving force behind this special research/control partnership, initially in collaborations with the Onchocerciasis Control Programme (OCP) in West Africa and now with the African Programme for Onchocerciasis Control (APOC). Evidence from TDR-sponsored research has guided control strategies — from choice of drugs (ivermectin) to rapid epidemiological assessment (RAPLOA, REMO), and community-directed treatment. TDR also has supported the training of a critical corps of African researchers, now leaders in their field. Featured here are highlights of this history from TDR's recent publication *Making a Difference, 30 Years of Research and Capacity Building in Tropical Diseases*.

“The progress that has been made in combating the disease (river blindness) represents one of the most triumphant public health campaigns ever waged in the developing world.”

(UNESCO Science Report, 2005).

On left: A man blinded by onchocerciasis (Haute-Volta • 1975 • donation from the Private collection of the late Dr Uwe Brinkmann, Harvard School of Public Health).

Above: Rukungiri: A local health worker (seated with cap) arrives in a remote pygmy village. He delivers ivermectin tablets to the community-directed distributors and supervises their activities during central point distribution (UGANDA • 1992 • WHO/TDR/EDWARDS).

Phase I (1975–1986): Heroic goals

The development of ivermectin

As recently as the late 1970s, the drug treatments available for the millions of Africans stricken with onchocerciasis were woefully inadequate, and many could only look forward to a life of progressively more serious symptoms – visual impairments leading to blindness or debilitating itching and skin lesions.

“The two drugs we had for onchocerciasis at the time were notorious poisons,” recalls TDR Director at the time, Dr Adetokunbo Lucas. “We were really desperately looking for a new drug. When we visited the major drug companies, it was clear they 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. So the strategy put forward was to open a compound-screening network.”

The network established by TDR involved researchers in laboratories 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. The most ambitious part of the effort, however, was the establishment of a TDR-supported drug-screening facility at James Cook University of North Queensland, Australia. Here potential compounds were tested in cattle harbouring a zoonotic strain of the *Onchocerca* parasite, regarded as the best predictor of how a compound would act against human onchocerciasis.

“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. It was much more expensive, but also potentially more accurate.”

In July 1978, scientists at the US-based laboratories of Merck, who had been researching a little-known agent called ivermectin, derived from a micro-organism that had initially been found in the soil near a Japanese golf course, sent the compound to the TDR-supported drug-screening facility at James Cook University. 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.

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



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.

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 he 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 Award Foundation for his “bold and unprecedented” decision. Lucas and his successor, Dr Tore Godal, received the same medal jointly for their contributions to TDR.

Top picture: A house-to-house community-based distributor of ivermectin treating members of a household, explaining the difference between the old 6 mg tablets and the new 3 mg ones (NIGERIA • 1998 • WHO/TDR/CRUMP).



Following Merck's announcement, TDR moved 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 over 55 million people in endemic areas of sub-Saharan Africa, with 80 million people targeted for treatment by 2015. 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.

Pioneering field research

At the same time that laboratory research was investigating a new drug for treatment, TDR-sponsored field research was supporting a new global partnership for the control and elimination of onchocerciasis in West Africa, where infection-related blindness and vision

impairment were most widespread. Here, in broad savanna regions, vector control was an immediately available tool for curbing disease transmission. Field operations were conducted by the Onchocerciasis Control Programme of West Africa (OCP), sponsored by the World Bank and WHO – supported by TDR research. However, by the early 1980s synthetic larvicides used were losing their impact. At the same time, scientific interest was growing in biological vector-control, using the natural predators of a vector or parasite. Such tools could supplement chemicals to which resistance had developed, or chemicals of risk to health and environment. TDR thus supported field research into the bacterium *Bacillus thuringiensis* serovar *israelensis* H-14 (*Bti*) to control insect larvae, including that of the blackfly. *Bti* was incorporated into onchocerciasis control by 1982. Other synthetic formulations later superseded *Bti* for blackfly control, but the innovation filled a need at a critical moment in onchocerciasis control history.

*As part of the OCP, helicopters and fixed-wing aircraft are used to spray insecticides (chemical and biological) on rivers and fast-flowing water where larvae of the blackfly, *Simulium damnosum*, breed. The fly transmits the parasites which cause onchocerciasis, or river blindness (WEST AFRICA • 1990 • WHO/TDR/OCP/WARD).*

Research for action — community-directed treatment of onchocerciasis

A highlight of TDR's second decade of operations would be the commencement of the full-scale mass administration of ivermectin for the treatment of onchocerciasis. Yet following Merck's announcement of ivermectin's donation 'for as long as is needed', questions still remained regarding how and where this drug could be used most effectively.

As of the late 1980s, an estimated 37 million people remained infected with the disease, transmitted by *Simulium* blackflies and endemic to more than 30 countries in Africa. However, different parasite strains are prevalent in different regions. In West Africa, gradual progression to blindness often occurs in infected individuals, whereas in forested central, eastern and southern African regions, debilitating itching and disfiguring skin lesions are the primary symptoms.

The trials leading to registration had shown that ivermectin treatment of patients diagnosed with the infection prevented ocular lesions leading to blindness. However, some leading experts argued that in order to significantly reduce the broader range of symptoms and burden of disease, ivermectin should be distributed preventively to almost everyone in communities where infection was widespread. To do so, however, urgent information was required on how safe the drug

was for large-scale administration, and how effective mass drug administration could actually be in reducing onchocerciasis transmission. New TDR Director Dr Tore Godal would move quickly to answer those questions — and translate Merck's donation offer into meaningful action. Together with the OCP, that covered 11 countries in the region, TDR collaborated in 13 large-scale Phase IV community trials examining safety and efficacy of ivermectin in a programme of annual mass drug administration, and, in some cases, ivermectin distribution alongside ongoing vector control programmes (TDR, 1995).

Trial data was integrated into a new and sophisticated computer simulation model, OCHOSIM (developed by Erasmus University, Rotterdam, together with OCP). The model predicted trends in infection prevalence, morbidity and disease transmission. Results indicated that a combined strategy of vector control plus drug treatment would reduce the projected timeline for bringing onchocerciasis under control, and for the elimination of onchocerciasis as a public health problem in the OCP region. However, actual interruption of disease transmission might not be feasible in many hyper-endemic areas. Effectively, in such areas, annual ivermectin treatment would have to be sustained almost indefinitely (Remme, 2004). This posed a significant challenge to disease control.

By the mid 1990s, as field trials had well established the safety and efficacy of annual ivermectin treatment, OCP moved to incorporate mass drug distribution more broadly into its operations alongside ongoing programmes of vector control. But it soon became apparent that field distribution of the drug remained limited. Getting the drug to the people who

needed it in remote areas year after year remained a significant challenge.

At the same time, pressure was mounting to address the disease in areas of Africa beyond the OCP mandate of West Africa. In fact, some 80% of the population at risk of onchocerciasis lives in central, southern and eastern Africa. In these regions, the disease presents different features, mainly debilitating skin lesions instead of the visual impairment and blindness common in West Africa. Disease control also presents different challenges insofar as vectors breed in forests along small streams and rivers. Vector-control programmes like those along the exposed waterways of West Africa's savanna, would thus be impractical. Conversely, any disease control effort would be all the more reliant upon drug treatment.

Clearly a new and highly effective method of drug distribution was required both to optimize ivermectin's distribution in OCP regions, and expand the effort beyond the savanna to other regions of Africa. Yet critical questions had to be answered, including: where to target disease control efforts and how to organize a practical system of annual drug distribution and treatment? Just as important, health officials had to justify to policy-makers a programme of massive disease control in regions where the major symptom of onchocerciasis, i.e. skin lesions, was less pathogenic to the eye.

In a series of discussions between the World Bank, other donors, WHO, and African governments, a 'wish list' of research needs was generated and TDR was asked to help come up with the answers (Remme, 2004).

The World Bank offered US\$ 1.2 million to accelerate operational research. The research effort would guide and support a new regional programme to control

“Health systems are evolving to leave even more responsibility at the ‘end of the track’. It is thus crucial to develop means of two-way communications with these communities, to learn more directly of the real problems people face and how they can be solved or ameliorated with the minimum of external resources. This was how Uche Amazigo discovered the importance of onchocercal skin disease (onchodermatitis) in communities in northern Nigeria in 1991. And in subsequent multi-country studies social scientists, dermatologists and epidemiologists worked hand in hand to confirm and quantify the impact of the disease from individual, clinical and epidemiological perspectives.”

DR TORE GODAL, TDR Director, 1986–1998 (TDR, 1995).



Larva of the onchocerciasis (river blindness) vector, the blackfly (Simulium damnosum) (GHANA • 2002 • WHO/TDR/STAMMERS).



onchocerciasis. In December 1995, a new umbrella organization, known as the African Programme for Onchocerciasis Control (APOC), was created in 19 central, southern and eastern African countries. Concurrent with this, TDR launched its special initiative for Onchocerciasis Operational Research.

In the 1970s, evidence of the far-reaching socio-economic impacts of river blindness in West Africa, including migration away from fertile river valleys, had helped stimulate the initial wave of investment in onchocerciasis control.

Now, research into the health, social and economic impacts of skin disease was intensified. TDR sponsored research quantifying the burden of disease from oncho-related dermatitis was already underway (AFR Reports/TDR, 1995). This effort was expanded to describe the broader psycho-social and economic impacts of the skin disease. Findings indeed confirmed the need for expanded control efforts in forested areas where the pathology of the disease had not previously been appreciated.

TDR also supported work providing timely new answers about where to target treatment. A method for the rapid epidemiological mapping of onchocerciasis (REMO) was developed. This was based on a simple examination for palpable onchocerciasis nodules in sample communities, which was then extrapolated to an epidemiological map of a broader region.

Inside a village school classroom. Many of the children show signs of onchocercal skin disease on their legs. Infected children cannot pay proper attention due to constant scratching of their itching skin (NIGERIA • 1998 • WHO/TDR/CRUMP).

This facilitated the rapid identification of areas where mass treatment with ivermectin would be needed (Ngoumou *et al.*, 1993).

Finally, in 1994 TDR-supported researchers launched a multi-country, multi-disciplinary study to answer the key question in disease control — how to distribute the drug most effectively. Early in the study, the researchers discovered that the so-called ‘community-based’ approaches being used by NGOs, with very mixed results, were not really anchored in community decision-making.

The teams developed a new framework for ‘community-directed treatment’ (ComDT) that put communities directly in charge of ivermectin administration. The rationale was simple. Communities empowered to organize their own system would do so in a manner best suited to them, with health services providing necessary training. A second phase demonstrated that ComDT was feasible and effective, and led to greater treatment coverage. ComDT was adopted by OCP as its ivermectin delivery strategy and became the backbone of APOC operations in 1996.

By 2007, ComDT had succeeded in extending the annual ivermectin coverage to more than 55 million people in Africa out of an ultimate target population for treatment of approximately 80 million. In collaboration with APOC and local research institutions, TDR has continued to play a supportive research role, including research to fine-tune ComDT methods. TDR also has supported the development of yet another rapid mapping method (RAPLOA) to identify areas of co-infection by *Loa loa* parasites, the causative agent of another filarial infection of humans. In these locales, ivermectin treatment requires closer supervision due to the higher risk of adverse reactions.

Continuous collaboration between research and control officers has proven to be the secret of success in onchocerciasis control. This and the ComDT strategy have helped to make ivermectin distribution one of the most successful programmes of mass drug administration in history, and one of the biggest public health successes in Africa.

The picture has never been all rosy. Serious problems were encountered in sustaining drug distribution when wars and instability struck various endemic countries. In October 2001, a detailed review of the APOC and OCP experiences with onchocerciasis control concluded that while onchocerciasis was well under control as a public health problem in the 11 original OCP countries, it could not be eradicated using the currently available tools. The development of a drug that can kill or sterilize the adult onchocercal worm living inside infected individuals remains a top priority.

More recently, TDR investigators have begun to appreciate how ComDT strategies could have other, far-reaching applications. TDR has begun to investigate how ComDT might be used for the integrated delivery of a range of critical public health interventions, including, but not limited to, home treatment with anti-malarial drugs and insecticide-treated bednets.



“REMO (rapid epidemiological modelling for onchocerciasis) and RAPLOA for Loa loa co-infection conceptualized rapid, simple epidemiological assessment methodologies now used on a much broader scale in the health sector. This was something that came out of the TDR corner.”

DR BERNHARD LIESE, Chair, International Health Programs, Georgetown University and former World Bank representative to the JCB.

Health workers and Onchocerciasis Task Force members study local maps showing rivers and villages to help identify communities most at risk and which may be approached to participate in community-directed treatment with ivermectin (MALI • 1996 • WHO/TDR/CRUMP).

Phase III (1998–2006):
The partnership decade

New partnerships for drugs, diagnostics and innovation

One of the remarkable aspects of TDR since its early days has been the pioneering collaborations fostered

between the public and private sectors. In the mid 1980s, many scientists from the private sector were participating in TDR scientific advisory committees, something that was perhaps unparalleled in other global public health institutions (TDR, 1986). However, as the volume of research activity increased, along with cost and complexity, more formal partnerships became necessary. TDR also began to shift successful, but relatively expensive, product R&D projects into new or existing public and private partnerships.

DEC diagnostic patch: a product of control & research synergies

The development of the diethylcarbamazine-citrate impregnated patch (DEC patch) applied locally to the skin for the diagnosis of *Onchocerca volvulus* infection is an example of how field innovations, and close cooperation between research and control officers, can yield important public health advances. Clinical tests of the new patch, due soon to begin large-scale trials, indicate that it can provide a simple and non-invasive surveillance tool for early detection of possible recrudescence of onchocerciasis transmission and infection in an area where infection has been virtually eliminated and active control operations have been stopped.

“It was onchocerciasis control people working in Africa with knowledge they had on the ground and an ability to be innovative, who put forward this tool,” observes Dr Janis Lazdins, who coordinates TDR’s programmes for development of new drugs and products. “TDR, with its technical awareness and know how, saw a way to apply modern drug delivery technology to move this forward.”

The patch involves a very small topical application of the drug DEC — a highly potent anti-onchocerciasis agent but not amenable for systemic use — to provoke a local reaction due to the killing of any oncho parasites present in the skin where the drug is applied topically. Control officers in the field in Africa had initially devised a crude form of the tool by taking a small quantity of the drug in powder, mixing it with skin cream, applying it to a filter paper and then onto the skin for 24 hours. The presence of a small local skin reaction was correlated with local killing of worms, indicating infection with *Onchocerca volvulus*.

“When I saw their idea, having worked in industry with nicotine and estrogen patches, I thought it was great,” says Lazdins, who began to push the innovation at TDR. Dr Bernard Liese, former World Bank representative to the JCB and OCP/APOC, contacted a German company that became interested in the device, and made several state-of-the-art prototypes. These were successfully tested on selected patients at the Onchocerciasis Chemotherapy Research Center in Ghana under the direction of Dr Kwablah Awadzi, and now are to be tested in larger scale trials in field conditions. “The story illustrates highlights features key to the success of onchocerciasis control,” concludes Lazdins. “That is the close cooperation between research and control, and the way capacity has been built in the field to take forward innovative ideas.”

Three decades earlier, the TDR network approach had proved itself with ivermectin. It was a TDR screen of the drug's efficacy in cattle — innovative at the time — that confirmed the potential efficacy of ivermectin against human onchocerciasis. Now, the TDR compound-screening network has been revitalized and expanded to include a broader range of academic and research institutes, and also industry partners. Along with this, new research networks for medicinal chemistry, pharmacokinetics, drug target portfolios and helminth drug discovery have been created to cover other stages of the drug discovery process in a more integrated manner.

Moxidectin, which is being investigated as a possible onchocerciasis macrofilaricide (that would kill or sterilize the adult worm) is now in Phase II trials in Ghana, in collaboration with Wyeth, owner of the drug.

The next wave of implementation research — community-directed models for other health interventions

A decade ago, TDR and its research partners helped demonstrate how insecticide-treated bednets could dramatically reduce deaths from malaria. The programme also helped document how new anti-malarial combination treatments and unit-dose blister packs could improve the efficacy and delivery of anti-malarial drugs, particularly by caregivers and trained members of the community.

But implementation of these and other basic health measures remains a great challenge in many parts of the developing world. Only 4–5% of Africa's youths currently sleep under bednets (UNICEF, 2006). Many do not have access to anti-malarials. Immunization campaigns often miss their targets. Health systems in developing countries are frequently stymied over how to deliver treatment at the grassroots level in an efficient and integrated manner.

The community-directed treatment strategies used to control river blindness have, however, indicated one potential response to these challenges. The ComDT programme for onchocerciasis control is perhaps the most successful model of a disease control and drug administration strategy in Africa today. The secret of its success lies in the system of treatment, where communities themselves manage the distribution and administration of the drug ivermectin. ComDT is now well established in thousands of African communities, where some 60 million people reside. By 2010 distribution programmes will cover communities where some 100 million people live — nearly one-sixth of sub-Saharan Africa's population. ComDT therefore represents a powerful model for delivery of other interventions.

Recognizing the potential of this tool, and at the request of the board of APOC that includes 19 African health ministers, TDR in 2004 launched a multi-country study to examine to what extent a community-directed approach could be used for the integrated delivery of other needed drugs and tools. This study into what were termed 'community-directed interventions' (CDI), tested how the distribution of interventions such as bednets and anti-malarials, along with ivermectin, could be controlled and managed by

community members in the regions where ComDT was well established.

Results from the second year of the study from 40 health districts in Nigeria, Cameroon, Uganda and Tanzania indicated that, indeed, the community-directed approach has potential for broader applications. The percentage of people covered by insecticide-impregnated bednets and home-administered anti-malarials doubled or tripled in the CDI-administered locales. This is in comparison to control districts that received the same amount of intervention materials, but where delivery was by conventional means. Preliminary economic data also indicated that the total cost of delivery was similar in the CDI and control districts, suggesting that CDI was more cost-effective.

“This is something that comes out of our long experience in onchocerciasis control,” says TDR research coordinator Dr Hans Remme, “where ComDT is now a proven strategy that is working very well, with good treatment coverage sustained in most areas. In some communities there is 10 years of experience and it is still going strong.

“The theory was that this same approach would be useful for other interventions, and we built upon it. This is not your standard community-based intervention, where you use a few local people to carry out an intervention. It is really a process where you put the community in charge from planning to execution. The community collectively decides if it wants to do the intervention, and if so, how to go about distributing it: where, when and to whom.

“It is an amazing development, and what we have seen is that it has potential for other applications. The study has also shown that the addition of other interventions

was not detrimental to ivermectin treatment; quite the contrary, ivermectin coverage improved even further. Presented with the evidence of the effectiveness of CDI, the board of APOC has now strongly recommended it should be used on a wider scale.”

“In the past several years, TDR has explored how a successful model for addressing one disease — onchocerciasis — can be used effectively to address multiple disease problems, in a single comprehensive strategy of community-directed interventions. The model, which has been tested initially in the APOC countries of Africa, demonstrates how TDR research can support the future scale-up of other critical interventions in a range of settings and locales.”

DR ROBERT RIDLEY, TDR Director, 2004–present.

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

By the close of the programme's third decade, onchocerciasis had made major advances towards global elimination as a public health problem, thanks not only to effective drugs but also effective treatment strategies — particularly community directed treatment (ComDT), which is drug distribution managed and directed by the communities themselves.

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 even more effectively in real-life settings.

The very recent TDR research into community-directed interventions has now etched a model where multiple primary health care treatments, including anti-malarials, can be distributed in an integrated manner through the same system developed for ivermectin treatment.

Following the initial positive results, and in line with recent APOC recommendations, TDR will thus be expanding its operational research on the same CDI approach. Future research will develop and test such community-directed models more widely in various African settings, exploring where such approaches are most suitable, with what kinds of interventions, and how they might be scaled up.

A growing body of research experience indicates that community-directed models can potentially expand access to primary health interventions among poor rural populations, filling a major gap that now exists between available tools and their delivery. Integrated delivery also has the potential to achieve greater cost-efficiencies (Brady, Hooper & Ottesen, 2006).

From disease elimination to eradication?

The elimination of river blindness as a public health problem has advanced in two major phases. The initial phase of disease control efforts focused on the savanna areas of the 11 West African countries of the Onchocerciasis Control Programme in West Africa (OCP). The OCP was dissolved in 2002 after elimination was achieved, due to the combined use of innovative vector-control tools such as *Bti*, rapid diagnostics supported by TDR, and ivermectin.

In the second stage of efforts focusing on the areas covered by the African Programme for Onchocerciasis Control (APOC), ivermectin administered through community-directed treatment (ComDT) has eliminated onchocerciasis as a public health problem in communities where it has already been administered annually for a number of years. Treatment has prevented debilitating itching, disfiguring skin lesions, visual impairment and blindness — an annual saving of some 1 million disability-adjusted life years (DALYs).

Kita: The whole community gathers in the village to receive their ivermectin tablets, queuing in lines to have their height measured and names recorded so that those absent can be treated later (MALI • 1996 • WHO/TDR/CRUMP).



However, ivermectin is a ‘microfilaricide’, which kills the parasite offspring, but not the adult worm. Therefore, except in locales with favourable entomo-epidemiological conditions (for example, endemic areas of Latin America and foci in Africa still being investigated and defined more precisely), disease transmission cannot be permanently interrupted with ivermectin, and so annual treatment must continue for an indeterminate length of time. This places a considerable burden on health systems. In addition, there always is the risk that parasites may develop resistance to any drug used in treatment.

These factors all have made the search for a ‘macrofilaricide’ — capable of killing or sterilizing adult worms more effectively — a compelling research issue in the third stage of onchocerciasis research and control efforts — aimed at disease eradication.

One potential drug now being tested is moxidectin, owned by Wyeth Pharmaceuticals, and currently the focus of a TDR-sponsored Phase II clinical trial in Ghana involving 192 infected people. Final data from this study will be available in 2008–2009. If successful, further studies will be needed over some years to test safety and efficacy in larger populations. Regardless of the outcome of any one particular trial, however, the future challenge is clear — to find a drug that is sufficiently safe and efficacious to pave the way for onchocerciasis eradication in all areas of Africa.

Kore village, Kita: A father sits with his son on his lap. Community members gather for a meeting in the shade of a large tree, to be addressed by health workers and national onchocerciasis task force members. A meeting with the community to explain about the disease and how they can treat it themselves with ivermectin, is the third step in the process to engage them in community-directed treatment (MALI • 1996 • WHO/TDR/CRUMP).

“The onchocerciasis programmes of OCP, and, later, APOC, have used TDR as their operational research arm for the better part of 20 years. This has provided the conceptual and scientific underpinning for the programme. Where have you ever seen any control programme shift from one mode of operations, like aerial spraying (of vectors), to a mode such as community-directed interventions, so smoothly and seamlessly, without becoming caught up in endless ideological battles? This was due to a research culture which everyone shared — a culture of research-based decision-making.”

DR BERNHARD LIESE, Chair, International Health Programs, Georgetown University and former World Bank representative to the JCB.

Three decades of remarkable change have occurred in our global village, in health, and in scientific research as the joint UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) celebrates the 30th anniversary of the founding of its governing body, the Joint Coordinating Board (JCB). In the case of the onchocerciasis (river blindness), the public health achievements realized have been particularly remarkable. Tens of millions of Africans once at risk of the debilitating skin lesions and itching or progressive loss of vision due to this parasitic disease are now symptom-free. The public health success is due largely to the close and fruitful collaborations between the worlds of health research and control efforts, as well as between the public sector, industry and non-governmental agencies and donors.

This selection of 'highlights' of TDR-sponsored research into onchocerciasis is excerpted and adapted from the TDR anniversary publication: *Making a Difference, 30 Years of Research and Capacity Building in Tropical Diseases* (WHO/TDR 2007).

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