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Review: **The delivery of ivermectin (Mectizan®)**

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Summary Over a comparatively short period of time, the development and distribution of ivermectin (Mectizan®) has radically altered the consequences of infection with *Onchocerca volvulus*. To achieve this required the fostering of many partnerships and the development of new tools and methods. The long-term commitment of Merck, the World Bank and other sponsors, as well as governments and non-governmental organizations, has been crucial. Yet the enthusiasm with which communities have taken up the delivery of ivermectin among themselves is perhaps the greatest reason for the success of this programme. The present challenge is sustaining the methods that have brought success so far, and making them part of health services and disease control programmes in some of the world's most impoverished and unstable areas. A major part of this challenge is continuing the commitment to controlling onchocerciasis as memory of the disease is fading, and while the hope of elimination or eradication for most endemic countries remains distant.

keywords onchocerciasis, ivermectin, Mectizan, *Loa loa*, mass treatment, public–private partnership, health systems

Introduction

Since the 1940s, the piperazine derivative diethylcarbamazine (DEC) was the principal treatment for onchocerciasis. But severe reactions to this drug, especially among the heavily infected, made DEC unsuitable for mass distribution. The development of ivermectin (Mectizan®) from *Streptomyces avermitilis* by Merck in the 1970s started a train of events for the control of onchocerciasis that is almost unparalleled in the history of tropical disease control. In 1981, ivermectin entered the veterinary drug market, and 6 years later was licenced in France for the treatment of onchocerciasis in humans. At the beginning, it was not clear how this drug was to reach those who needed it most. Merck originally saw the drug as prescribed for individual patients in the clinic or hospital setting (Frost *et al.* 2002). Mass distribution became the primary approach after community trials by the World Health Organization (WHO) and the distribution experience from the Onchocerciasis Control Programme (OCP) showed the effectiveness and safety of ivermectin. Merck has continued to supply ivermectin directly to health facilities for individual treatment and passive distribution through its humanitarian programme.

After considering various donation options, Merck decided in 1987 to create the Mectizan Donation Program (MDP) to oversee the transfer of ivermectin to organizations and agencies who would provide delivery to affected populations (Fettig 1998; Foege 1998). The development and achievements of this public–private partnership are discussed by Peters and Phillips (2004).

Mass treatment with ivermectin began in 1988. By 1991, several non-governmental organizations (NGOs) had started ivermectin mass distribution programmes. Delivery of ivermectin very much followed a learning-while-doing approach. There was also an early realization that the resources needed would require development of regional partnerships and large-scale external support to make control with ivermectin effective. The success of these methods and partnerships can be seen in the number of treatments set out in the Table 1. The cost-benefit and cost-effectiveness analyses of ivermectin distribution are considered by Waters and Rehwinkel (2004).

In this paper, we trace the creation of the methods and tools needed to deliver ivermectin and the evolution and development of distribution programmes. We examine the formation of regional partnerships for ivermectin distribution in the six countries of the Americas, the 11 West African countries of the OCP, and the 19 countries of the African Programme for Onchocerciasis Control Programme (APOC). We then review how these distribution programmes are functioning through the various levels of the health system. Key issues which have emerged in development of community distribution are approached. Finally, we consider the future of ivermectin distribution from the aspect of sustainability and integration of

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Table 1 Numbers of ivermectin treatments approved through community-based, mass treatment and humanitarian donation programmes worldwide

Year	Community-based	Humanitarian programme	Total
1988	255 000	26 000	281 000
1989	239 200	112 200	351 400
1990	1 321 500	342 500	1 664 000
1991	2 779 800	448 300	3 228 100
1992	4 879 500	509 800	5 389 300
1993	9 050 300	324 600	9 374 900
1994	11 801 800	282 200	12 084 000
1995	15 607 700	269 900	15 877 600
1996	19 141 400	159 700	19 301 100
1997	33 725 000	169 500	33 894 500
1998	30 668 500	73 200	30 741 700
1999	29 740 700	36 800	29 777 500
2000	35 533 300	47 500	35 580 800
2001	44 825 400	58 000	44 883 400
2002	49 960 200	37 600	49 997 800
Total	289 529 300	2 897 800	292 427 100

programmes, using indicators that the APOC and others have identified as central to the success of delivery approaches. Materials for this paper come from the journals, reports and publications by onchocerciasis control organizations, from NGOs and personal interviews.

Creating the tools for ivermectin treatment

For effective onchocerciasis control, ivermectin programmes must give priority to population groups who are at risk of eye or skin disease over those whose light infections pose no major peril. While hypoendemic communities could be treated through passive distribution from health facilities, communities heavily affected would require an active treatment approach using community interventions. This required an easy way to measure community prevalence of infection. As a further goal, programmes must achieve efficient treatment coverage with the resources available. This second goal has required empowering communities to take responsibilities for distribution at the household level, and to commit their own resources to support distributors.

It has been known from pre-colonial times in Africa that the prevalence of onchocerciasis in a community depended on the distance from potential vector breeding sites (Patterson 1978). The OCP developed methods to predict risk for communities by dividing areas into bioclimatic or biogeographic zones based on the distance from breeding sites. Further, sampling within villages verified the endemicity of onchocerciasis in that community. Ngoumou and colleagues applied this Rapid Epidemiological Mapping of Onchocerciasis (REMO) approach to setting priorities for onchocerciasis treatment (Ngoumou & Walsh 1993; Ngoumou *et al.* 1994). This approach worked well in much of West Africa and the Sahel, although not as well in East and Central Africa where fly breeding patterns differed. The integration of this information into a geographical information system (GIS) further increased its usefulness (Noma *et al.* 2002).

There remained a need for a quick method to measure prevalence at village level which did not require the taking of two or more skin snips from each person. These 1–5 mg skin snips were not popular with the community, were tedious and time-consuming to obtain and examine, and further risked transmitting HIV through inadequately sterilized instruments. The OCP and others found that the prevalence of nodules in a cohort of adult males correlated well with the community microfilarial load as measured by skin snips. This approach became the Rapid Epidemiological Assessment (REA) method which allowed programmes to establish treatment priorities by counting nodules (Taylor *et al.* 1992). The nodule prevalence in adult males multiplied by 1.5 is a reasonable estimate of the community prevalence of onchocerciasis. Communities where more than 20% of males had nodules were classified as treatment priorities. Where <20% of males had nodules, clinic-based passive treatment from health facilities was the strategy recommended. Recently there has been increased interest in extending mass distribution to these hypoendemic areas. In some areas such as Sudan and Yemen, the prevalence of Souda skin disease serves as an alternative marker to nodule measurement.

In Latin America, many foci of infection have been known for over a century, although data on some is still incomplete (Blanks *et al.* 1998). In Africa, REMO/REA mapping has been completed for many countries, but Angola, much of the Democratic Republic of the Congo, and parts of southern Sudan remain to be mapped.

The methods of ivermectin treatment evolved from the original vertical programme model of mobile clinics visiting communities to distribute tablets. From the beginning of the MDP, a small group of NGOs led in developing effective distribution methods. These organizations had experience in more horizontal programmes in communities where formal health services were weak or non-existent. Early in their work with ivermectin distribution they began to understand that communities must take the major responsibility for distribution if good coverage was to be achieved (WHO 1991). It emerged that the highest coverage was achieved when communities were empowered to design and implement their own distribution programmes. NGOs began to change their focus from

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being distributors themselves to providing training and logistical support to communities. At a meeting in Bamako in 1994, the concept of community self-treatment was formalized (later renamed community-directed treatment). A WHO 1995 study at eight sites in five African countries compared community-directed treatment with ivermectin (CDTI) to a standard 'programmatic' approach (WHO 1996). In this study, one half of the communities selected distributors and designed their own programmes. In the other half, health workers were sent to communities to dispense treatment. Coverage rates were better in programmes designed by communities, although some communities had difficulties with the reporting requirements. The study found CDTI to be feasible and effective in a wide range of geographic and cultural settings in Africa. Results from this study established CDTI as the preferred distribution approach.

Much debate has gone into what is community treatment and what constitutes community-*directed* treatment. The fundamental of community 'directedness' is a community ownership of the planning and distribution process. This has sometimes been called a *Community-Directed System of Distribution* to emphasize the extent to which a community has control of distribution. Communities decide how the programme should function, when treatment should occur, and choose the distributors and the distribution methods. Programme personnel have roles as facilitators, but must avoid being directive. Including health workers from the nearest health facility in community training and supervision strengthens the programme. A standardized approach, shown in Figure 1, was developed for mobilizing communities, selecting distributors, conducting a village census and conducting distribution (APOC 1998).

A second methodological study in 1999, replicated the 1995 results, emphasizing the effectiveness of community-directed treatment (WHO/TDR 2000). A single model, however, is unlikely to be satisfactory in all situations.

In the early years of the MDP there was worry that unsupervised community ivermectin distribution might result in serious adverse events being missed or treatment of these delayed. Results from early animal studies gave concern about the inadvertent treatment of young children, persons with epilepsy, pregnant women and nursing mothers. With experience and further research, these concerns proved unfounded, allowing Merck to relax restrictions and clear the way for wide scale use in community programmes (Brown 1998).

Creating the partnerships

With the demand for ivermectin distribution growing, NGOs were finding it difficult to finance additional programmes. Traditional funding sources in Europe and North America could not support expansion of programmes to more of the many areas of need. Governments of endemic countries often did not appreciate the burden which onchocerciasis placed on communities. Even where onchocerciasis control was a priority, governments did not have the resources for large treatment programmes. By 1994, annual treatment with ivermectin in Africa outside the OCP countries had levelled off at around 8 million persons. New approaches to onchocerciasis control based on regional partnerships with increased support were now needed.

The Onchocerciasis Control Programme

The OCP was formed in 1974, as a partnership to control onchocerciasis in the Volta basin of West Africa through vector control measures. This partnership included the Food and Agriculture Organization (FAO), the United Nations Development Programme (UNDP), WHO, the World Bank, and eventually 11 countries of West Africa. Many of the early trials of ivermectin for mass treatment were carried out by the OCP (Remme *et al.* 1990; Dadzie *et al.* 1991). By 1990, ivermectin had become an important complement to larviciding in OCP activities. Because of its well-established infrastructure, the OCP was able to distribute large amounts of ivermectin efficiently through

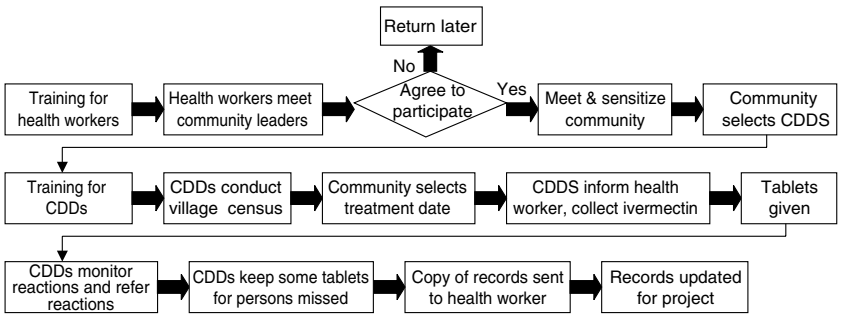

Figure 1 Community-directed treatment with ivermectin.

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its field teams, and later its partner NGOs. During the 15 years of ivermectin treatment by the OCP, distribution methods evolved from community distribution by project teams to being largely community-driven. The results of ivermectin distribution have meant that onchocerciasis is now no longer a public health problem in endemic areas of the OCP (WHO 2001).

When the OCP ended in 2002, ivermectin distribution devolved to the 11 member states. States were encouraged to develop or strengthen their own National Onchocerciasis Group [similar to the National Onchocerciasis Task Force (NOTF) in APOC countries]. These national teams work together with a recently created inter-country Special Intervention Team (SIT) to coordinate onchocerciasis control (WHO/OCP 2002a). This team is based on Ouagadougou to work closely with APOC and the new WHO/AFRO Multidisease Surveillance Centre (MDSC).

At the close of the OCP, microfilariae could be found in skin snips only in areas of Ghana, Togo, Benin and Guinea. In addition to these four areas, there is an extensive onchocerciasis in Sierra Leone where control activities had been suspended because of conflict. These five areas were designated Special Intervention Zones (SIZ). Ivermectin treatment will be needed in the four areas through 2012, and longer in Sierra Leone. A sum of $12.1 million was set aside from OCP trust funds to manage vector control and ivermectin distribution for 5 years (WHO/OCP 2002b). The 2002 OCP final evaluation encouraged NGOs working in former OCP countries to expand ivermectin distribution activities, realizing that additional resources would be required. Surveillance for recrudescence of onchocerciasis is a responsibility of the MDSC.

During 2001, nine countries of the OCP-treated 6.9 million persons with ivermectin, which is shown in Figure 2 (WHO/OCP 2001). The vast majority of these

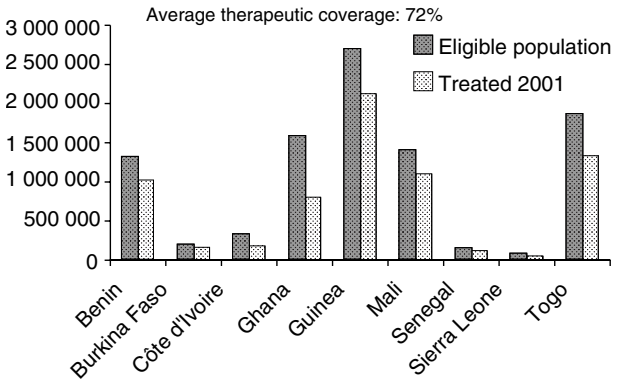

Figure 2 Ivermectin distribution in former Onchocerciasis Control Programme (OCP) countries.

treatments were provided through NGOs. While some health teams were still being used to provide treatment in communities, between 51 (Ghana) and 82% (Burkina Faso) of communities were receiving ivermectin through community-directed methods (APOC 2002a).

The non-governmental development organization coalition

Non-governmental development organizations (NGDO) distributing ivermectin began informally working together in 1990, to produce training materials and pool experiences. Most were blindness prevention organizations, but others were focused on primary health care (PHC). In 1992, these organizations came together as the NGDO Coordinating Group for Ivermectin Distribution (Drameh *et al.* 2002). At that time they joined with the WHO's Prevention of Blindness and Deafness unit to mobilize resources and develop training materials. Later this group was to become the key implementing partner for the APOC. The methods they developed among themselves were to become the standard treatment approach for APOC. Twelve organizations presently belong to this group. Within both APOC and the OCP, they play an important role in mobilizing resources and training communities and health personnel. In many countries they are the engines behind ivermectin distribution. By 2002, NGOs had supported delivery of 173.9 million treatments, over two-thirds of all ivermectin provided since the beginning of the MDP.

The Onchocerciasis Elimination Program for the Americas

Ivermectin distribution began in the Americas in 1990, with both ministries of health and NGOs involved. The Onchocerciasis Elimination Program for the Americas (OEPA) was formally organized in 1991. In the wake of successful polio control in the Americas, there was interest among ministries of health in eliminating other diseases (Blanks *et al.* 1998). OEPA's founders set as their goal the elimination of onchocerciasis from affected countries in the Americas by 2007, through ivermectin treatment. OEPA includes six countries: Brazil, Columbia, Ecuador, Guatemala, Mexico and Venezuela, with 93% of cases in the last three countries. The Pan American Health Organization (PAHO), the Centers for Disease Control (CDC), and other organizations are also members. Organizers of the programme believed a regional initiative would help focus attention on a disease which was seen as insignificant by some governments. A regional initiative also made sense because of the cross-border location of several foci.
The River Blindness Foundation provided $1 million in start-up funds, which was followed by $4 million from the

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Inter-American Development Bank, with subsequent assistance from the Carter Centers Global 2000 River Blindness Program.

The OEPA serves as a coordinating body, providing technical assistance to the member states in education and training, epidemiology, information collection and management and medical supervision. One of its first tasks was to help member countries draw up national onchocerciasis plans. OEPA sets basic standards and procedures, and convenes the annual regional onchocerciasis conference. The Guatemala-based organization has encouraged member states to establish distribution methods most suitable to individual country needs. At the same time, it has encouraged development of community-directed distribution methods and integration of services with local health systems. In all countries these are ministry of health programmes, although in some, NGOs play important roles. Mexico has the largest and longest-established onchocerciasis programme, which has been run as a disease-specific activity with *brigadistas* distributing ivermectin. In the past several years it has begun a shift to using community-based distributors. A similar shift has occurred in Guatemala. Ivermectin distribution in Guatemala was interrupted for 18 months from 1994, during a period of uncertainty after health system restructuring. OEPA provided considerable assistance to Guatemala to restart effective distribution.

A unique feature of OEPA is the use of sentinel villages. In each country, six or more villages are selected representing the most severely involved communities. These are followed annually with parasitological, ophthalmological, entomological and serological examination to monitor the impact of ivermectin distribution. Although these assessments are paid for by the individual states, OEPA provides short-term technical assistance for annual surveys. Unlike APOC, no funding for ivermectin distribution projects is provided by OEPA.

There have been various estimates of the population at risk of onchocerciasis in the Americas (WHO 1995, 1996). OEPA now calculates that as a result of ivermectin treatment the population at risk has been reduced from 4.7 to 440 861 million (Sauerbrey 2002). Work by Cupp and others in Guatemala suggested that twice yearly treatment covering all eligible persons could interrupt transmission of the onchocerciasis without vector control measures (Collins *et al.* 1992; Cupp *et al.* 1992). Mathematical modelling by Davies (2002) suggests interruption of transmission can be achieved with an 85% coverage rate. In most places twice yearly treatment is the standard approach, although getting communities to take the second dose in a year has been difficult (Richards 2002). In the last 2001, biannual treatment round, 369 093 persons were treated against an ultimate treatment goal (eligible population numbers) of 439 887. Distribution by country is shown in Figure 3.

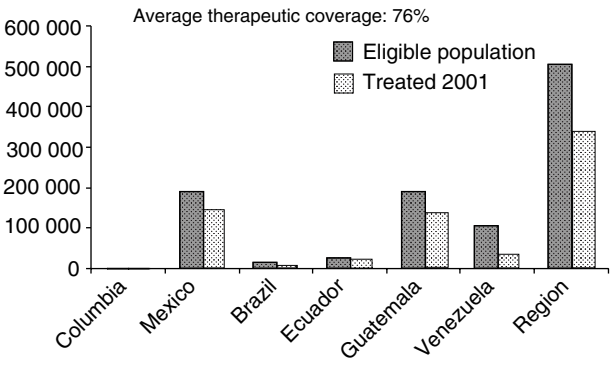

Figure 3 Ivermectin distribution in Onchocerciasis Elimination Program for the Americas (OEPA) countries.

The African Programme for Onchocerciasis Control

The APOC was formed in December 1995, with funding from the World Bank and other donors (Benton *et al.* 2002). The goal of APOC is to establish, within a period of 12–15 years, effective and self-sustainable community-directed ivermectin treatment in the endemic areas of the 19 member countries. Within these 19 countries, 85% of the world's onchocerciasis is present. The APOC objective is to establish country programmes that provide yearly treatment to areas meso- and hyperendemic for onchocerciasis (>20% nodule prevalence). It was estimated through a simulation model that by achieving an overall treatment for 65% of the population, the public health consequences of onchocerciasis will be eliminated with 20 years of treatment (Remme *et al.* 1990). Further modelling suggests this time frame to be optimistic. Individual projects plan for 85% population coverage. The remaining 15% are composed of pregnant women, children under 5, and the seriously ill who are ineligible for ivermectin treatment. The first phase of APOC ran from 1996 to 2001, the second phase runs from 2002 to 2007, and the phase-out period will be from 2008 to 2010. The total 15-year cost is $182.5 million with $45.5 million coming from governments and NGOs, and $137 million from the World Bank and other donors. The bulk of funding is allocated for ivermectin distribution projects, although four small vector control projects are included.

The APOC was conceived as a partnership between donors, NGOs, the UN agencies, and member countries, with the WHO as the executive agency. The MDP, as provider of ivermectin, is integrally involved. Programmes are designed to be part of the public sector health system,

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with NGOs playing the key role of providing training and assisting communities with distribution. At the beginning of a 5-year country project, governments and partner NGOs are expected to provide 25% of funds with 75% provided by APOC. Over the ensuing 5 years, support from APOC is to be progressively phased out, leaving the country projects self-sustaining. Recently, APOC decided that if sustainability is not achieved at the end of 5 years, an additional 3 years of funding at a reduced level may be approved if there is satisfactory progress towards sustainability. The organizational structure of APOC is diagrammed in the paper by Peters and Phillips (2004).

In each member country, APOC facilitated the development of a NOTF, representing government, NGOs and other parties in onchocerciasis control. A National Onchocerciasis Coordinator and his or her staff serve as secretariat to the NOTF, based at the ministry of health. This Ministry of Health-NGO partnership develops national onchocerciasis policy, undertakes REMO assessments of foci, and develops project proposals for submission to APOC for funding. If approved by APOC, a country project makes application directly to MDP for the supply of ivermectin. The MDP apply its own approval criteria to these applications, which are set out in the box. In general, the MDP respects the decisions and plans of the implementing countries and APOC. The presence of *Loa loa* increases the risk of serious adverse events following ivermectin. Where co-infection with onchocerciasis is thought to be present, the MDP requires that a risk assessment be carried out. The RAPLOA method is a promising assessment method that is being validated in several sites (Takougang *et al.* 2002; WHO/TDR 2002). If risks of serious adverse reactions are present, the NOTF must ensure procedures recommended by the MDP are followed (MDP 1999).

The APOC encourages individual communities to be involved in development of country plans. Plans should be integrated into health team activities at the district, health zone, local government area or health facility level. Project funds from APOC are usually channelled through the WHO country offices. Shipping charges and clearing charges for ivermectin are pre-paid by Merck. APOC member countries have agreed to waive customs charges for ivermectin, although reluctantly at times.

During the first phase of APOC (1996–2001), basic planning and management capacity needed strengthening at several levels in participating countries as well as in APOC headquarters. At the end of 2002, 69 distribution projects had been established in 16 of 19 APOC countries. Over 30 additional projects will need to be established in 2003 and 2004, to cover remaining areas within the lifespan of APOC. In 2001, these projects treated more than 30 million people living in over 49 000 communities

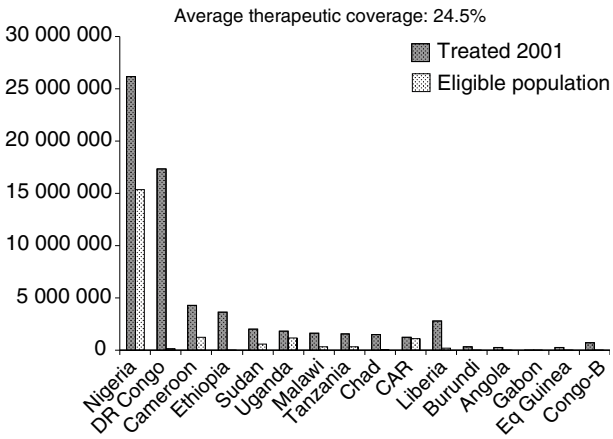

Figure 4 Ivermectin distribution by African Programme for Onchocerciasis Control Programme (APOC) countries (logarithmic scale).

(Figure 4). By 2010, when APOC is due to be phased out, 50 million persons are expected to be receiving annual treatment, 65% of the total project area population (APOC 2001). The policy is for all treatment to be given using community-directed distribution methods. Only three countries, Uganda, Gabon and Central African Republic, achieved the 65% minimum coverage level in 2001. For all countries, coverage averaged 24.5%, with five eligible countries not yet distributing ivermectin.

Ivermectin distribution and the health system

Ivermectin distribution has generally been viewed enthusiastically both by implementers in the health system and by communities. Support and commitment within the health system has varied considerably at the different levels of the system and among countries. Programme experience has been particularly well-documented in APOC countries, where over 80% of ivermectin for onchocerciasis is now being delivered. The following sections look at experiences with ivermectin distribution at levels within the health system, including the NGO sector, and at the community level.

National level

In Latin America, several ministries of health changed their longstanding nodulectomy programmes to the distribution of ivermectin. There has been a strong central programme for onchocerciasis control in several countries. NGOs have played an important role in some countries such as Brazil, but have played little part of other programmes such as in Mexico. Community-directed treatment is being

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encouraged for economic reasons, as an alternative to the more expensive full-time cadre of *brigadistas*. For the former OCP countries, ivermectin distribution is now vested in the ministries of health. The framework has been established for regional cooperation to support ivermectin distribution, and medium-term financial support is in place.

As an early step, APOC countries concentrated on the establishment of the NOTF, which involved building leadership, planning, and management capacity. This start up phase was not without problems. Some staff were unhappy over the number of meetings and amount of travel involved. Not all countries have been forthcoming in their support for the NOTF, leaving NGOs to carry most of the programme in these locations. In other countries, weak NGOs have pulled down overall performance (APOC 2000b). Where countries had strong leadership at national level this led to good implementation at all levels. Uganda has been such a programme. Weak leadership in Malawi resulted in poor coverage rates, which has caused APOC to threaten withdrawal of support. Many of the 27 on-going CDTI programmes in Nigeria potentially have the leadership and the resources for strong programmes. Although there are national, zonal and state onchocerciasis programmes in Nigeria, in many areas these do not work smoothly, particularly at the state level where there are problems in providing leadership and disbursing money. It is the Local Government Areas (LGAs) and their partner NGOs that play the most important role in implementation of distribution programmes.

Prozesky *et al.* (2001) carried out a detailed evaluation of the administrative functions of onchocerciasis programmes in Nigeria, Cameroon and Uganda. This evaluation produced an exceptionally thorough analysis of issues at all levels of ivermectin distribution. The study found that while management tasks at the NOTF level were not in themselves seen as demanding, there was felt to be duplication in efforts and a lack of priorities in prescribed activities. Planning cycles used by APOC matched neither MoH nor NGO cycles, increasing workloads. Some of the staff seconded by the MoH to assist with data management and analysis lacked the skills and motivation needed. Some managers felt that the administrative resources required would not be sustained in the long run by the ministry of health. There was also a perception that the project was being used by some for financial gain, particularly in the allocation of *per diem* allowances. Transportation was generally not a problem, as APOC has supplied vehicles for the NOTF as well as many field sites.

Money for APOC projects is channelled through the WHO offices in a number of countries. Some country offices added extra staff to handle demands, but in others the WHO offices caused major delays. This was seen as affecting the smooth running of CDTI projects. In both OEPA and APOC countries there have been problems with duty-exempt customs clearance of ivermectin. The ordering and distribution of ivermectin through some element of a country's national drug supply system is seen by APOC as an indicator of integration and sustainability. Others see the ability to move ivermectin outside unreliable government channels as a programme strength (Amazigo *et al.* 1998).

A goal of both OEPA and APOC has been to build advocacy and commitment at the ministry level. Mexico is an example of a programme with strong resources and a committed staff from ministry level to the field teams (Martin-Tellaeche *et al.* 1998). In some APOC countries, strong commitment at national level has been achieved, especially where onchocerciasis is recognized as a major health problem. In other countries, advocacy by the NOTF has been weak. Even where awareness among key health decision-makers is present, this may not be translated into political or financial commitment (APOC 2002a). It is widely acknowledged that the weakest link in development of the APOC programme has been the failure of ministries of health to make serious commitments to support onchocerciasis control.

National level managers have generally deemed as excellent the support from APOC to the national programmes. This support has focused heavily on capacity building, particularly in early stages. Some managers felt the APOC used too strong a top-down approach (Prozesky *et al.* 2001). In the Americas, OEPA is not so directly involved at the national level, as many ministries already have the needed capacities. An important strength of the APOC commitment is the detailed external monitoring of CDTI projects (APOC 2000c). Although these monitoring visits are very resource-intensive, their depth and the wide dissemination of findings help national programmes as well as APOC management. Following the APOC mid-term review in 2000, these monitoring visits include a stronger emphasis on monitoring sustainability indicators.

Conflict situations, unstable governments, migration and incomplete health reform present special challenges to effective ivermectin treatment. In Columbia, the treatment of what is in fact a very small focus has managed to continue 6-monthly treatment in spite of conflict (WHO 2002a). In southern Sudan, effective treatment has been possible in some areas in the midst of conflict (Homeida *et al.* 1999). Sudan has one NOTF but two separate distribution projects. Health personnel from the two sides in the conflict have been able to meet outside Sudan, working together to plan ivermectin distribution. Community responsibility for distribution helps sustain

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programmes when health system support is intermittent. Relief organizations, part of Operation Lifeline Sudan, have played an important support role in the South. Fighting in Côte d'Ivoire stopped ivermectin treatment in 2003, as has fighting in Liberia. In Angola, the absence of infrastructure may slow completion of REMO assessments. Large areas of the Democratic Republic of Congo are inaccessible as a result of an internal conflict. In Sierra Leone, ivermectin distribution was suspended for 8 years.

NGO project level

The project role for NGOs is principally in planning, training and supporting the communities in ivermectin delivery. In some sites they manage ivermectin logistics from central level to community level. NGOs often collect and tabulate treatment data, and frequently pick up slack in other parts of programmes. These organizations bring variable amounts of independent financial resources. Support has mostly come from the vision NGOs such as Christofel-Blindenmission, Organization pour la Prévention de la Cécité, the Carter Center, Sight Savers, Helen Keller and the International Eye Foundation. Other organizations which support PHC have also been involved such as HealthNet, Africare and Interchurch Medical Assistance. UNICEF is a partner in several locations. In spite of much discussion, it is only in phase II of APOC that local NGOs have started to initiate distribution projects. Recently a Ba'hai organization in Cameroon, the MITHOSATH organization in Taraba State, Nigeria and the Christian Hospital Association of Liberia have begun ivermectin programmes (Cross 2000). In Yemen, the Charitable Society for Social Welfare distributes ivermectin. Some 30 local NGOs are active as distribution partners of international organizations in Africa and the Americas (Drameh *et al.* 2002). In Latin America, local NGOs play an important role in Ecuador, Brazil and Guatemala. Where NGOs have a long-term presence in an onchocerciasis area they can bring sustainability to programmes. Examples are the Vosandes Hospital in Ecuador and various mission hospitals in Africa. While local NGOs often make very effective delivery partners, few have the capacity to raise funds internationally, as is needed to build sustainable ivermectin programmes.

While NGOs bring their capacity to work effectively with community, which many ministries of health lack, NGO heterogeneity in methods, organizational structure and approaches has at times created difficulties. Nevertheless, the interest of NGOs in novel methods has created a number of innovative approaches. As communities differ, implementers need to be alert to potential alternative approaches (Onwujekwe *et al.* 2000a). Some of the new approaches have included school health clubs and clan-based distribution systems (Katabarwa *et al.* 2000a; Shu *et al.* 2000).

On the administrative evaluation of APOC, the positive perceptions of the programme achievements were stronger at the project level than at the national level (Prozesky *et al.* 2001). Project managers reported delays in receiving money which held up activities, and duplications in reporting. At the project level there was a perception that the information collected was not used by upper levels in the programme. While projects appreciated the visits by external monitoring teams, it was felt that the approach was not always systematic and needed to be better managed.

District/LGA level

Effective ivermectin distribution at the district level (or its equivalent) represents the key to controlling onchocerciasis, yet management capacity at this level is often overloaded with many programmes and activities. Sometimes projects have bypassed the district, going directly to communities in order to show as many results as soon as possible. This approach is common to many health programmes and is a frequent source of difficulties. Districts need to be involved from the beginning before this bypassing becomes entrenched. The goal of APOC ivermectin distribution programmes is full integration with health services at the operational level. An indicator for this integration is inclusion of onchocerciasis in annual district work plans, supervision plans and the creation of budget lines. While good integration into the health system has occurred in some places such as the Cross River and Taraba areas of Nigeria and the Uganda districts, it was noted to be lacking in Tanzania and Malawi (APOC 2002a). Achieving a sense of responsibility for distribution at the district level on a large-scale is a major challenge. Given existing district obligations, priorities and limited discretionary resources, allocation of district funds for onchocerciasis control may not always be easy to achieve. Integration indicators other than financial ones are harder to define (Amazigo *et al.* 2002).

Some district health teams feel they do not have the time or resources to provide adequate supervision or to fully support community programmes (Prozesky *et al.* 2001). Without APOC funding, a number of district health managers think that it will be hard to continue community treatment. Increasingly, ministries of health are decentralizing services to district level, giving health teams considerable latitude in drawing up work plans. In most African countries there are many programmes competing for a

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limited district capacity (Okwero 1998). For sustainability, creating a sense of programme ownership at the district health level is as important as creating the community ownership. Only a serious commitment from district health management can give communities the supervision and support needed to sustain ivermectin delivery. Whether most district health managers have the capacity to make and to sustain this commitment is not certain. Particularly where there are risks of adverse reaction from co-infection with *L. loa*, an orderly integration of services is very important to identify and refer serious adverse events for hospital care (MDP 2001).

First-line health facility

The first-line health facility is seen by APOC as a critical component in support of the community distributors (APOC 1998). In addition to other duties, PHC workers serve as the main contact with the community for ivermectin distribution. These health workers are participants in community training programmes, supervisors for ivermectin distribution, managers of records from the community distributors, and someone to treat adverse events following treatment. Serious commitment from this level to planning, supervising and maintaining community programmes is seen by APOC as a key sustainability indicator (APOC 2002c). From the APOC monitoring reports of 16 projects, supervision of community distributors occurred in 43–75% of projects (APOC 2000a). Because of the remote location of ivermectin programmes, many areas lack functioning first level health facilities. Where present, they may be under-equipped, under-staffed, and the health workers under-motivated. Many health workers at this level are in reality part-time workers, needing additional jobs to compensate for low or irregular pay.

In the assessment by Prozesky *et al.* (2001), first level health workers were very supportive of ivermectin delivery. They saw the programme benefits, and generally understood their role. A major complaint was that community distribution sometimes disrupted routine health facility activities. At both the health facility and the district there were concerns about poor standards and low performance among others in the distribution programme. Much of the concern about poor quality revolved around reporting, financial management and ordering ivermectin supplies. Health workers at the facility level worried that ivermectin distribution could not be sustained without APOC funding. Tarimo (2000) felt that CDTI programmes had fostered a closer link between PHC services and communities. Sékétéli *et al.* (2002) noted that ivermectin projects had built capacity at the health facility level.

Community

At the heart of the ivermectin distribution programmes of OEPA, OCP, and particularly APOC is the community-directed distribution approach. Community ownership of distribution programmes has been a major innovation for mass treatment, and has been fundamental to the success of ivermectin programmes. This approach has been well-received by communities, and has gained their confidence. Where there is extensive disease present, the demand for treatment by the community is great. A well-run community distribution programme will eliminate microfilariae from a hyperendemic community (Guderian *et al.* 1997). The major challenge will be sustaining high coverage through community distribution methods for 20 or more years, well after the itching and skin changes of onchocerciasis have cleared. By this time, most of those blinded by onchocerciasis may have died. Creating or building on a sense of need is the first step in introducing a new programme such as ivermectin. Remarkably little research has been reported on community perceptions about treatment. Yet understanding perceived benefits from treatment is critical to sustaining programmes for the long treatment time needed. In a small Nigerian study, the principal perceived benefits cited from ivermectin in a hyperendemic community were worm expulsion (80%), blindness prevention (68%), increased vitality (68%), reduced itching (64%) and increased sexual performance (29%) (Akogun *et al.* 2000). In Guatemala, communities understood that the purpose of treatment was to improve general well-being and to cure nodules or to rid the body of *microfilaria*, a term introduced by health educators (Richards *et al.* 1995). Negative attitudes to ivermectin noted by Brieger *et al.* (2001) in Nigeria included the inability to work in gardens because of adverse reactions to treatment, and a general avoidance of 'white man's medicines'.

Many studies have looked for factors which would predict success of programmes. In Uganda, communities that selected their own distributors and chose the treatment strategy as a whole community were more successfully in meeting treatment goals (Katabarwa *et al.* 2000b). Successful villages also used the community distributor's compound as the distribution centre, had household heads attend health education sessions, and rewarded community distributors in kind. Where community distributors were truly chosen by the community at large, rather than being appointed by a traditional leader or volunteering for the work, the coverage was better. Using kinship or clan groups in distribution and adapting traditional self-help community arrangements also resulted in better coverage (Katabarwa & Richards 2001; Katabarwa *et al.* 2002).

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In Nigeria, previous treatment with ivermectin was the strongest predictor of compliance (Brieger *et al.* 2001). This study found that distribution from a central location produced higher coverage than house-to-house distribution. Anticipation of adverse reactions was an important deterrent, but fully understanding reactions improved the willingness to take treatment. Fear of adverse events appeared greatest in Cameroon, a country with relatively low-ivermectin treatment coverage. This may be due to potentially serious reactions that have occurred after treatment in persons co-infected with *L. loa* (Boussinesq *et al.* 2001). The importance of a strong health education component plus the endorsement and support of traditional authorities is well-established (Gardon *et al.* 1996; Oyibo & Fagbenro-Beyiku 1998). Absenteeism is a common reason why treatment is not taken, not surprising in rural agricultural and pastoral societies. Treatment during agricultural seasons is associated with low coverage, but at times this is when ivermectin shipments arrive. Following up those who have missed treatment in the initial round is part of prescribed training for community distributors (APOC 1998). Another important factor in non-treatment is a shortage of ivermectin. One reason for this is an underestimate of eligible persons by a poorly conducted community census. Among 14 projects monitored by APOC in 1999, 20% of communities were short of ivermectin tablets at the time of distribution, attributed largely to poor record keeping and requisitioning (APOC 2001). Accurate calculation of anticipated needs is important, as it requires 4 month or more to dispatch drugs after requests are received.

Among the villages surveyed in Cameroon, Uganda and Nigeria by Prozesky *et al.* (2001), community distributors were generally satisfied with progress of the programmes. Some expressed concern about low standards of work and the potential financial irregularities in the programme. At the community, there were doubts expressed about the sustainability of distribution. At several levels in the health system there was worry about the paucity and quality of feedback provided by the distribution programmes to the communities who participated in distribution.

Turnover among community distributors has been a concern to many programmes. In Uganda, building on traditional clans and kinship groups reduced distributor turnover. As with most community programmes, periodic retraining of community distributors is needed. If infrequent the quality of distribution suffers; but if too frequent, costs are increased and people are taken away from their other activities.

Are there some programme designs that would make community distribution more sustainable by strengthening partnerships and increasing integration with the formal health services? A three country, six-site study looked at a variety of approaches that might enhance sustainability (WHO 2000). The research reaffirmed the results of the 1995 WHO study, showing that indeed communities could implement and sustain this community-directed treatment, and that health workers were able and willing to support communities in this. However, the study was not able to identify specific factors which would enhance sustainability.

Key issues in ivermectin distribution

Several issues have been seen as central to the philosophy and methods of ivermectin distribution. These have received intense discussion among planners and managers, and have been the focus of several operational research studies, and have tapped the rich APOC database. Four of these are considered here.

Gender

Gender issues affect perception of disease and programme participation in a number of ways. From the beginning, APOC tried actively to encourage participation of women in the design and implementation of community distribution. Despite this intention, the majority of community-selected distributors tend to be male. In a three-country study of 10 APOC projects, women and young people were routinely excluded from decision-making for ivermectin distribution (Clemmons *et al.* 2002). The study found that community meetings to plan distribution and select distributors were composed predominantly or entirely of men. Women expressed different perceptions of the disease as well as the importance of treatment. The social consequences of onchocerciasis, such as skin appearance and marriage prospects, were of more concern to women. As community distributors, women were less likely than men to receive community support, either monetary or in kind. In Uganda, more than 70% of women in treatment areas indicated they had taken part in the selection process for community distributors, and the same percentage would be willing to serve as distributors if asked (Katabarwa *et al.* 2001).

Has the low number of women distributors made a difference in reaching women with treatment? In data from the 10 projects in Cameroon, Tanzania and Nigeria, where men constituted 75% of distributors, treatment levels among women were the same as among men. A study of 9330 persons by Brieger *et al.* (2001) in Oyo State found 81.1% of residents in villages with women distributors received ivermectin compared with 78.4% in villages with male distributors. However, the 1995 WHO study of

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community-directed treatment found that villages with female distributors showed a significantly lower treatment coverage than villages with male distributors (WHO 1996). The importance of gender in the effective planning and distribution of ivermectin appears to vary with the social and power structures of communities.

Treatment costs

At its inception, Merck saw ivermectin as being provided free of charge. This was possible where delivery programmes were largely publicly funded, as in Latin America or was part of a multinational programme as with the OCP. At country level, difficulties appeared where cost-recovery systems were national policy. In such situations, the MDP decided to allow charges to be made for the *delivery* of ivermectin, through the drug itself was to remain free. Supporting distribution through cost-recovery schemes has been proposed as a sustainability approach, although this idea has received little support (Amazigo *et al.* 1998). Allowing communities to set their own fees may be a better alternative than setting fees at the national level. This local approach has been used in some states in Nigeria.

In a Nigerian study of endemic villages where ivermectin had been provided free of charge, communities indicated a willingness to pay for ivermectin. The median cost suggested by the communities ranged from US$0.25 to US$0.38 per treatment (Onwujekwe *et al.* 1998). This cost was above APOC's target distribution cost of $US0.20 per treatment. However, the communities suggested a number of payment methods, some of which would be difficult to implement (Onwujekwe *et al.* 2000b). In Cameroon and Chad, there have been charges for ivermectin distribution at both health facility and community distribution programmes (Godin 1998). Funds collected through cost-recovery are intended to be managed by health management committees, which are elected from within the local health committee. On the negative side, cost-recovery schemes reduced coverage in the Cameroon site substantially, and to a lesser extent in other countries in a 1995 WHO study (WHO/TDR 1996). Recently, charges for ivermectin were abolished in Cameroon. Preliminary reports suggest that coverage with ivermectin is increasing.

How to use funds generated in this manner, and indeed how to manage remunerations or incentives for community distributors has been a problem. In Cameroon, community distributors were paid 32% of funds recovered as incentives. The potential for misuse of funds generated in this way is substantial. Cost-recovery adds considerably more to training requirements, both for community distributors as well as health facility staff.

The APOC has taken a position against paying incentives for distribution, and the Uganda data suggest that distributors paid incentives achieve lower coverage than those who do not (Katabarwa *et al.* 1999). APOC programmes encourage communities to support distributors directly. Yet in an analysis of 1999 monitoring reports, only 38% of communities supported distributors (APOC 2000a). The *per diem* paid to community distributors during their training does represent an incentive, and may be a reason for participation. Much harder to measure, but certainly an important factor, is the motivation which comes by gains in recognition, self-esteem and knowledge (WHO/TDR 2002). The issue of payments to distributors is a concern which pervades many if not most ivermectin community distribution programmes. If not addressed sympathetically, this may discourage community participation in the long run. There are many requests for the time of community members including support for education, community development projects, and commitments for religious and family responsibilities. A distributor who must conduct a census, walk 10–20 km to collect ivermectin from a health facility, distribute tablets, complete forms and return them to the facility, is taking time away from family and community obligations.

Records

A major difficulty experienced in APOC areas has been the inability to obtain accurate community census data to provide the denominator in the calculation of ivermectin coverage rates (APOC 2000a). The community distributor is charged with conducting an initial census of the treatment area, and with keeping records of people treated during the subsequent ivermectin campaign. These records are then provided to staff at the supervising health facility or to project personnel. Although literacy is not a requirement for community distributors, numeracy greatly facilitates record keeping. In some sites, printed community registers have been used, but the costs of printing these were not thought to be sustainable (Prozesky *et al.* 2001). Some community distributors felt they were capable of taking a larger role in data collection and tabulation than they were allowed. When supervisors were able to provide support for community distributors, the quality of the distributors' work and record keeping improved. However, many district health personnel complain they have little time to conduct the level of supervision required. In Uganda, retired civil servants and teachers living in the affected areas have served as supervisors, a strategy which improved treatment coverage (Katabarwa *et al.* 2002). The need for better population figures at the community level is an urgent need in many ivermectin programmes. One

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suggestion was to use treatment information from school children as a proxy for population coverage, an approach which showed promise in Uganda (Ndyomugyenyi & Remme 2002). Another suggestion was to use the standard Extended Programme on Immunization (EPI) cluster survey approach to validate community treatment records (Schwartz *et al.* 1998). In some projects the data collected from these community records has been under-utilized at national level. An indicator of sustainability set out by APOC is the movement of information from community distribution entirely within the government system (APOC 2002d).

Monitoring

In OCP countries a strong monitoring programme was in place from the beginning. Over time this has devolved to the individual states, where there was a good data management capacity built by the WHO/OCP (2002a). There is a hope that the MDSC and APOC will help former OCP countries maintain effective monitoring (WHO/OCP 2002b).

Within APOC, monitoring of distribution in countries has been conducted by APOC and the NOTF. At the country level, project activities and finances are routinely monitored by the NOTF. The data flow begins with treatment reports sent by the community distributors to the health facility level where they are summarized. Health workers feel this adds to workloads, although in itself it is not difficult. Forms from distributors are sometimes incomplete, or missing altogether (Prozesky *et al.* 2001). NGOs play a key role in monitoring programmes, particularly where first-line health facilities are weak or absent. When these data move to the national level, in some countries the capacity to aggregate and analyse these programme data has been inadequate. Country data then move to APOC.

At the APOC level, it is planned that monitoring teams visit country projects twice during their 5-year cycle to assess progress towards achieving objectives. Despite being called monitoring, these are more of an evaluation. Conducting these detailed assessments requires over a month and uses multiple standardized instruments developed by APOC. These results have provided APOC with a wealth of information to monitor individual programmes and to carry out analyses among sites.

Because of the expense of using independent personnel, members from the NOTFs of other countries are increasingly being used for monitoring visits. When APOC visits are conducted, field staff are anxious to discuss the success of community-level distribution, whereas national staff are less enthusiastic about these visits. In the past, project staff felt left out of these evaluations, having little opportunity for input, and only reading the conclusions some time later. There is a recognized need to build the capacity of the NOTF to carry out routine evaluations of their own projects, in addition to the on-going project monitoring. The costs of these at the country level have been of concern, and may add to sustainability problems (APOC 2000c). At the national level, this type of assessment has been published by Uganda (Katabarwa *et al.* 1999).

At the same time, there is a recognized need for community-based monitoring. This participatory approach is well-established for evaluating development projects. Helping communities to take the initiative to monitor their own evaluation would help lessen the strong top-down perceptions about APOC programmes. Community monitoring would also improve the feedback of findings to community, which has been a weak point noted in many national programmes. Strong feedback on achievement is a well-known motivator.

A mechanism for the NOTF to monitor administrative and distribution costs of national programmes is needed. The actual price of integration of ivermectin delivery into the health system is not known. Some way to track community support of distributors is also needed. Monitoring changes in community perceptions about ivermectin treatment would help promotion and advocacy remain targeted.

The future of ivermectin delivery

Sustainability and integration of ivermectin distribution are two interrelated issues, which dominate the short- and medium-term thinking about onchocerciasis control, particularly in Africa. The longer term issues of elimination and eradication have attracted considerable attention. In considering the future of ivermectin delivery, two terms have been used, *self-sufficiency*, meaning the ability to continue distribution with only in-country resources, and *self-sustainability*, the continuation of a programme using local as well as external resources. This latter definition is the one generally used.

Sustainability

Sustainability of control programmes has been defined by Tarimo (2000) as the ability of the benefits achieved by the community distribution to be continued by governments, communities, and local institutions after the end of APOC support, through the same activities or other approaches. In 1997, the NGDO coordination group working with APOC began considering elements needed to sustain community-directed treatment from the programming standpoint (WHO 1997). These included:

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- Good treatment coverage.
- A sound infrastructure to support community distribution.
- Adequate ministry of health budget.
- Some method for cost-recovery.
- Results-oriented leadership and management.
- Stable government and
- Affordability at all levels.

When asked to apply these criteria to their own programmes, ivermectin distribution managers polled were pessimistic about programme sustainability.

Tarimo proposed a framework for sustainability containing three main elements: operational indicators, strategy and policy, and global or regional factors. From these, indicators for a sustainability analysis can be developed.

Operational indicators include leadership and involvement of local infrastructure. The community distributors must have adequate training for their tasks, and be appreciated. Linkage from the first-line health facility should be functioning in a supportive manner. *Risks to sustainability* are lack of representative community decision-making, lack of programme feedback on coverage results achieved, excessive workload for distributors, the lack of links with the health system and the sidelining of first level health workers.

Strategic indicators include the presence of a realistic policy and strategy for long-term onchocerciasis control. The presence is needed of a viable system to support community distribution, and links with other non-health programmes, such as farmer's groups and religious organizations. How community distribution is being used to support other health programmes such as tuberculosis and schistosomiasis control is an important indicator. The information indicator is the ability of programmes to monitor and evaluate their own activities, and to provide this information to implementers. A key strategic indicator is financial sustainability. This is both cost of treatment to the community, and provision of adequate support in the health system for programme management. *Risks to sustainability* are lack of clear national policy, no solid infrastructure and insufficient resources to support programmes. Poor capacity to collect, analyse and feedback information to the community and decision-makers impairs sustainability. Also the failure to move beyond vertical programming will compromise sustainability.

Global or regional indicators consist of long-term commitment from bilateral, and multilateral sponsors, and from NGOs. They also include the development of health policies that complement and interrelate to each other, rather than being only specific to a single disease. *The risks* here are of programmes that will consume resources in a poorly coordinated way, yet fail in the objective of eliminating the public health consequences of onchocerciasis.

In considering sustainability of programmes in Nigeria, J. Watson (2002, personal communication) saw the willingness of federal, state and local authorities to budget for training and supervision of onchocerciasis as an important sustainability indicator. Other indicators he suggested included the ability of the public sector to order ivermectin from MDP and to handle the transport and delivery of drugs without the help of NGOs.

The APOC mid-term evaluation pointed out the lack of attention to project sustainability. Since this evaluation, the focus of APOC monitoring has shifted from management issues to sustainability indicators. Guidelines issued by APOC judged projects to be sustainable if they were effective, efficient, uncomplicated, integrated into health services, had adequate resources, and used CDTI as the routine distribution method (APOC 2002e). Sustainability indicators were identified and grouped into nine categories. These included planning, supervision, training, leadership, funding and procurement/distribution. Particular attention is paid in checklists to cost-containment, integration of services and government contributions to control activities. Assessment instruments were created for national or state (Nigeria) level, district (LGA) level, first-line health facility level, and community levels. The use of matrices and weights with thresholds can help evaluators assess if these indicators are being achieved. Assessments now on-going are focused in preparing projects to be fully sustainable.

Several monitoring visits have shown national programmes still heavily dependent on APOC funding. Two in particular, Tanzania and Malawi, were noted to be making very little, if any, progress towards increasing local support for the programme and decreasing their dependency on APOC funds. APOC sustainability indicators may be excessively rigid. Countries with comparatively more discretionary health resources, such as Nigeria should be expected to attain sustainability sooner than poorer countries such as the Democratic Republic of the Congo or Ethiopia. When will countries such as Angola and the Democratic Republic of the Congo with weak or non-existent health infrastructure reach financial sustainability? Certainly not in a 5-year period.

Applying the various sustainability indicators and components, it seems clear that most APOC countries have made rather uneven progress towards sustainability. At one end of the health system, communities have taken enthusiastically to community-directed treatment, and in many places achieved impressive results. First-line health facilities and district management teams have generally been supportive. For the most part, the NGO partners have

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mobilized the resources and established the programmes to support communities. Where the progress towards sustainability has been the most disappointing has been at national levels. Here ministries have failed to fund the NOTFs and to support administrative and management structures to the extent agreed when APOC began. The support which national programmes have received from governments is often 'in kind' in the form of office space and seconded administrative personnel. In many cases this support has been substandard. Even where support has been provided, it is seldom at the levels needed to sustain control activities without APOC support.

This is a critical moment for national programmes. Failure of the political will to support onchocerciasis control at the ministry level can unravel the successes of the community programmes, which cannot survive without health systems support. There is a risk that NGOs may become discouraged if they are expected to carry an increasing share of costs as APOC withdraws support, and if governments fail to deliver support promised.

Although advocacy for onchocerciasis control has been a goal of all three regional onchocerciasis partnerships, results at the national level often have been disappointing. One APOC country evaluation found senior leadership at the ministry level largely unaware of the presence of the programme (APOC 2002a).

From the ministry perspective, there are many competing health priorities and onchocerciasis may not be one of them. The median government expenditure for health in sub-Saharan African countries without onchocerciasis in 2000 was US$11 per person (WHO 2002c). In former OCP countries the median expenditure was US$6.0 per person, and for APOC countries the figure was $4.50. Ministries have seen an influx of resources for onchocerciasis control including vehicles, training, international travel and salary top-ups for staff. This abundance may have lulled them into thinking that demands for more ministry support were premature and alarmist.

By contrast, in OCP countries the immediate concerns about sustainability are somewhat less. Well-established national onchocerciasis data management capacity was inherited from the OCP era. The NGO partnerships have been well-established, and $12.1 million in funding has been set aside for the next 5 years for five geographic areas, although much of this will go to supporting vector control in Togo. However, sustaining technical skills and government political will be a major challenge in the transition period to the SIT coordinating programmes in member countries. Another major challenge is re-establishing onchocerciasis control activities in Sierra Leone.

In OEPA countries, sustainability of onchocerciasis control is threatened by budgetary worries within ministries of health. Community-directed treatment has been embraced in several locations as a cost-cutting approach to improve programme sustainability.

Integration of services

An overarching theme of ivermectin delivery in Africa has been integration of delivery methods. This is more of a concern in Africa than in the Americas where onchocerciasis control has been generally a long-standing responsibility of health services. This integration is seen as making ivermectin delivery an integral part of the health system, in both the public and non-government sectors. A further consideration is the integration of other disease-specific programmes into the community-directed approach developed for ivermectin.

In Africa, the NOTF was seen as the integration of programming at the ministry level. But for operational purposes, sustainability was always viewed as integration of activities at the district, or sometimes health facility level. While this has happened, with integration at the district level arguably stronger than at the national level, there have been difficulties. Perhaps the foremost problem is the weak capacity of many district teams. In the past decade, there has been a steady erosion of management capacity and health resources in much of rural Africa. Expecting district services to support community programmes as well as struggling first-line health facilities may be unrealistic in such places. The poor state of these facilities prompted Tarimo (2000) to suggest that APOC facilitate strengthening of services at the district level.

Mobilizing communities for ivermectin distribution can increase utilization of health services by communities to meet other needs. In this way, the accountability of local health services to the needs of those whom it ostensibly serves may be increased. There are suggestions that a stronger link with health facilities may have occurred in Cameroon as a result of CDTI activities (Nyiama 1998), but documentation for these changes is weak. In Nigeria, J. Watson (2002, personal communication) reported that the collaboration between NGOs, state ministries of health, and the communities raised the low opinion that communities had of the government health services. Access to health services in the Central African Republic was noted to be better as a result of the community-directed treatment programme (Tarimo 2000).

At the district or LGA level, programmes such as ivermectin distribution face increasing competition for limited district resources from other specific programmes such as Stop TB, Roll Back Malaria, Safe Motherhood, Integrated Management of Childhood Illness, and Reproductive Health, to name a few. District teams usually

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consider which programme will be most advantageous to the district and perhaps to them personally, as few districts have the capacity to give the required resources to all programmes.

Another set of integration definitions relate to community distribution. The success of the community-directed treatment for onchocerciasis has prompted thinking about how this community approach could be used for other health programmes. This thinking has followed two lines. The first is that as community-directed treatment for onchocerciasis has been shown to work on a large-scale, it can be used for treatment of a variety of diseases. The second line of thinking sees sharing the same CDTI structure with other programmes as reducing costs and improving sustainability of ivermectin distribution.

There are many potential candidate programmes for a community-directed approach. Immunization programmes have shown the value of 'community guides'. Many NGOs have used community mobilizers to improve antenatal care and child health. Vitamin A, mosquito net and reproductive health projects have used community-based distributors. Where community-based IMCI is being implemented, Community-Based Resource Persons (CORPS) are needed. There has been considerable interest in using similar community approaches and perhaps establishing joint programmes to control lymphatic filariasis (Gyapong *et al.* 2001; WHO 2002b). Ivermectin is already a part of many African lymphatic control programmes in areas where *L. loa* is co-endemic with onchocerciasis. Homeida *et al.* (2002) found that of 441 community ivermectin distributors in four projects, 258 had responsibilities in at least one of 20 other community health activities. Provided there was coordination, the authors did not see major conflicts with multiple programme responsibilities. Ivermectin community distributors in Nigeria have also worked in polio campaigns, community sanitation and health education programmes. A PHC project in Uganda provided community ivermectin distributors with quantities of condoms, which they sold, keeping the proceeds as an incentive (Kipp *et al.* 1998). In Ecuador, training is provided to persons selected by the community not just in ivermectin treatment but for other common health conditions as well.

Such a collaborative approach is not without risks. Many programmes pay community representative incentives, if not actual salaries. In such a bidding war, ivermectin distribution might lose out to better-resourced programmes. With various training sessions, special events, workshops and national days, community distributors could be pulled in many directions, sometimes simultaneously. Katabarwa *et al.* (2002) found that where community distributors had responsibilities for other health activities, ivermectin coverage rates were lower. Then there is a risk that too many uncoordinated programmes may overwhelm communities, as well as the district management team supporting these programmes.

Another potential to sustain distribution programmes is integration with non-health activities. Among those suggested are school programmes, forestry projects, and community development projects. It is important that the community directedness concept be flexible enough to allow further development and collaboration. It has been observed that CDTI is at risk of becoming a new orthodoxy.

Particularly among vision NGOs, integration of onchocerciasis control with other services has already been occurring. Community distributors are seen by some organizations as becoming eye care workers dealing with trachoma, cataract identification and vitamin A distribution. This diversification may lessen the dependence on a single donor for a specific type of programme. Onchocerciasis control is one of the key elements in the Vision 2020 global initiative for the elimination of avoidable blindness, which also includes cataracts, glaucoma, and causes of childhood blindness.

The purpose of ivermectin programmes is to eliminate the effects of onchocerciasis. While the wish to tackle other problems in the community or through the health system using CDTI methods is laudable, it is critical not to lose focus on the central goal of ridding communities of onchocerciasis.

Elimination and eradication of onchocerciasis

The ultimate goal of onchocerciasis control is to eliminate the public health consequences of infection. How long ivermectin must be given to a community is uncertain, although simulations suggest that high treatment coverage must be maintained for perhaps 20 or more years, depending on local factors. In the Americas studies raised the hope of eradication (Collins *et al.* 1992; Cupp *et al.* 1992). A conference in 2002 concluded that for most if not all of the Americas and possibly Yemen, transmission of onchocerciasis can be eliminated using current tools (Carter Center 2002). Winnen *et al.* (2002) suggested that while elimination was possible from most foci in Africa, resource requirements are prohibitive. The inability to cover all African foci and all people in these foci means that the length of treatment with ivermectin is probably indefinite, unless a macrofilaricide is discovered.

The search for a macrofilaricide has been underway for many years. Recent discoveries about the role of *Wolbachia* endobacteria and sensitivity to common antibiotics may in the end hold the ultimate key to eradication (Hoerauf *et al.*

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2001; St André *et al*. 2002). While ivermectin is a more efficient control approach than vector control, for Africa it remains an interim control strategy. Mathematical simulations show a macrofilaricide would have a substantial advantage for eliminating onchocerciasis in Africa (Alley *et al*. 2001). Nevertheless, continuing the present ivermectin strategy will not only greatly lessen morbidity now but will make eventual elimination with a macrofilariacide an easier task. When eventually a macrofilariacidal drug does become available, it is probable that a community-based distribution system will be needed for treatment.

The appearance of ivermectin resistance could change the prospects for elimination and lessen the degree of control that could be achieved. Resistance has been reported increasingly from nematodes, but has not been documented in *Onchocerca volvulus* (Dent *et al*. 2000).

Conclusions

The growth of ivermectin distribution and evolution of distribution methods in the 17 years of the MDP has been remarkable. In the beginning, thinking about drug delivery centred around passive distribution at health centres. Over the lifespan of the MDP, distribution of ivermectin has passed through various stages to now being perhaps the best example in developing countries of a community-directed programme taken to scale.

The achievements of APOC have been impressive in a relatively short period of time. Widespread infection with *O. volvulus* is limited to Africa, where health systems are weak and resources for health are limited. The challenge to establish methods to reach more than 50 million persons at risk of serious disease is great. Sustaining these delivery methods for ivermectin is an even greater challenge. Substantial support from bilateral and multilateral agencies, coupled with a dedication from NGOs and the solid commitment from Merck has largely eliminated the serious consequence of onchocerciasis. Programmes now face the question of how to sustain these achievements until the disease is fully controlled. Once the memory of this terrible scourge fades, will communities commit their own resources indefinitely for a treatment whose most obvious benefit is the passage of *Ascaris* worms and clearance of ectoparasites? Will blindness NGOs consider their work with onchocerciasis carried out and move on to other ocular issues? Is it even feasible to expect many debt-ridden countries to support onchocerciasis control without substantial continuing outside assistance? Are African health systems, already buckling under stress, able to take on yet another disease programme? Who will maintain the enthusiasm and the energy for ivermectin advocacy when APOC is phased out? It seems certain that many endemic countries will not be able to shoulder the full costs of distribution programmes in the time frame envisioned by APOC.

For the former OCP countries, it may be too early to tell how sustainable these programmes will prove to be. There is a real danger that these countries will not feel the ownership that is needed for full integration into national health systems. While ivermectin distribution continues in areas previously part of vector control activities, distribution in other areas such as southern Ghana and Cote d'Ivoire is uncertain. Although there are trust funds to support ivermectin distribution in these countries, there is a danger that the remaining vector control area in Togo will consume much of these resources.

In OEPA countries, ivermectin distribution has always been a country responsibility. Here the greatest dangers would seem to be the loss of priorities for onchocerciasis control within ministries of health. The internal politics of ministries and the devolving of responsibilities from centrally controlled vertical programmes such as in Guatemala and Mexico may pose problems in sustaining good coverage without strong support from the centre.

Great strides have been made towards the goals of controlling and even eliminating this great disease burden. Although APOC and OCP countries have projected exit strategies and timetables for their assistance programmes, it seems almost certain that further external assistance will be required for some time beyond what has been envisioned.

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