Annals of Tropical Medicine & Parasitology, Vol. 96, Supplement No. 2, S61–S69 (2002)

Progress towards, and challenges for, the elimination of filariasis from Pacific-island communities*

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Received and accepted 15 July 2002

The Pacific Programme for the Elimination of Lymphatic Filariasis (PacELF) — the first regional campaign to attempt to eliminate filariasis as a public-health problem — is using five, annual, mass drug administrations (MDA) of diethylcarbamazine (DEC) plus albendazole to stop transmission. In 2001, nine countries and territories covered by the programme had begun annual MDA campaigns, with population treatment coverages ranging from 52% to 95%. By the end of 2002, it is anticipated that 11 countries/territories will have begun such MDA campaigns. Even with high MDA coverage, the efficiency of *Aedes polynesiensis* as a vector of *Wuchereria bancrofti* may limit the effectiveness of the elimination campaigns in some countries. In areas of limited MDA coverage, additional strategies, such as vector control (as a adjunct to the MDA), or alternative approaches, such as the use of DEC-fortified salt, may be necessary to stop transmission.

THE PACELF CAMPAIGN

In the South Pacific sub-region, 22 countries and territories are participating in the Pacific Programme for the Elimination of Lymphatic Filariasis (PacELF; Burkot and Ichimori, 2002). The goal of PacELF is the elimination of lymphatic filariasis as a public-health problem in its member countries and territories. The programme hopes to achieve this goal by using five, annual rounds of mass drug administration (MDA) to stop transmission, together with clinical management of the existing infections, to minimize pathology. Each MDA is based on diethylcarbamazine (DEC; at a dosage of 6 mg/kg body weight) and albendazole (400 mg/subject). Although treatment with this combination eliminates up to 99% of microfilariae (mff) for a year (Ottesen *et al.*, 1999), its impact on the adult worms is less clear. Despite the evidence for vector control eliminating filariasis from the Solomon Islands (where *Anopheles* mosquitoes were the vectors; Webber, 1979) and Australia (where *Culex* mosquitoes transmitted the pathogen; Boreham and Marks, 1986), vector control has been relegated to a secondary role in the elimination of filariasis from the Pacific.

The limited area of most Pacific islands, the vast distances between islands and the small populations on each island should all help in making an MDA-based elimination programme a success. However, the small populations and vast distances also present unique challenges not found in other regions of the world. The public-health departments

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*This is a revised working paper originally prepared for the WHO (2002) informal consultation on the vectors of lymphatic filariasis.

DOI: 10.1179/000349802125002419

and ministries of the small countries involved have a limited number of staff. The individuals responsible for PacELF's MDA programme are, by necessity, also responsible for maintaining surveillance and undertaking control efforts for the other major vector-borne diseases of the Pacific (i.e. malaria and dengue).

Although PacELF's member countries and territories have a combined population of only 7.6 million, almost 2.9 million (38%) of these people are estimated to be infected with *W. bancrofti* (Table 1). Only four PacELF countries — American Samoa, Fiji, French Polynesia and Papua New Guinea (PNG) — have >10,000 cases of filariasis each and 93% of all cases in the South Pacific are found in PNG. The epidemiology of filariasis in the Pacific is unique. While filariasis in the South Pacific is caused only by *Wuchereria bancrofti*, both periodic and sub-periodic forms of the disease are present. Filariasis can also be a highly focal disease in the sub-region. In the Malampa province of Vanuatu, for example, although the overall prevalence of microfilaraemia reported in 1997–1998 was 3.6%, the village prevalences recorded varied from 28% in Unmet (28 positives of 100 tested) to 2% in Orap (two positives of 100 tested) and 0% in Rensari, Lamap and Tisman (no positives of 394 tested; G. Taleo, unpubl. obs.). The focality of the disease makes it very difficult to treat only microfilaraemics, as the logistics of identifying and tracking the movements of these individuals would be beyond the

TABLE 1. *Prevalences of filarial (*Wuchereria bancrofti*) antigenaemia in Pacific-island countries*[*]

Country or territory	Population[†]	No. tested	% of population tested	% antigenaemic	No. of filariasis cases
American Samoa	64,100	3018	4.7	16.5	10,577
Cook Islands	18,700	1884	10.1	8.6	1608
Federated States of Micronesia	118,100	2392	2.0	0.21	248
Fiji	824,700	5983	0.7	16.6	136,900
French Polynesia	233,000	1859	0.8	13.8	32,154
Guam	148,200	980	0.7	0	0
Kiribati	90,700	2824	3.1	1.7	1541
Marshall Islands	51,800	2004	3.8	0.1	5
Nauru	11,500	388	3.4	0.3	30
New Caledonia	212,700	145	0.1	51.7[‡]	?
Niue	1900	1794	94.4	3.1	59
Northern Mariana Islands	76,700	1037	1.4	0	0
Palau	19,100	2031	10.6	0.4	76
Papua New Guinea	4,790,000	4291[§]	0.1[§]	56.2[§]	2,692,430[§]
Pitcairn Island	47	33	70.2	0	0
Samoa	169,200	7006	4.1	4.5	7656
Solomon Islands	447,900	4035	0.9	0	0
Tonga	100,200	4002	4.0	2.7	2704
Tokelau Islands	1500	1311	87.4	0.1[¶]	1[¶]
Tuvalu	9900	574	5.8	22.3	2208
Vanuatu	199,800	4362	2.2	4.8	9573
Wallis and Futuna	14,400	803	5.5	0.7	101
All countries and territories	7,604,900	52,756	0.7	38.1	2,897,871

[*]An atlas for the Pacific Programme for the Elimination of Lymphatic Filariasis (PacELF) is in preparation.
[†]The Secretariat of the Pacific Community's mid-year estimates for 2000.
[‡]Not a random sample (sampling of schoolchildren on Ouvea Island only).
[§]Not based on random population sampling (Melrose *et al.*, 2000); the baseline survey is ongoing.
[¶]Not a resident of Tokelau.

capabilities of the small number of staff involved in the PacELF campaigns. Hence, the only practical strategy is to administer antifilarial drugs to entire populations (excluding those aged <2 years, the aged and the pregnant).

In 1999, Samoa became the first country to implement the PacELF strategy and one of only three countries (the others being Egypt and Nigeria) to begin MDA for filariasis elimination world-wide. Prior to the initiation of the PacELF campaign, Samoa had undertaken 10 MDA campaigns between 1966 and 1997. In 1964, the prevalence and mean intensity (among the microfilaraemics) of microfilaraemia in Samoa were estimated to be 21% and 950 mff/ml, respectively (intensities being estimated by the examination of 20-μl samples of blood). In 1997, however, after 10 MDA, the corresponding values had fallen to 1.7% and 148 mff/ml (intensities then being estimated using 60-μl samples of blood). Individuals found to have filarial antigenaemia in rapid immunochromatographic tests (ICT; Weil *et al.*, 1997) prior to the PacELF MDA in 1999 were followed-up after the drug administration, using both ICT and bloodsmear examination. Of the 192 individuals who were followed in this way, 75% were found to be antigen-negative and amicrofilaraemic, 8% were antigenaemic and microfilaraemic, and the other 17% were antigenaemic but amicrofilaraemic (V. Toeaso, unpubl. obs.). [The filarial antigen may persist even after clearance of mff following MDA (Weil *et al.*, 1997).] These frequencies of antigen clearance after a single round of MDA are substantially higher than those reported in other studies (Schuetz *et al.*, 2000) and may reflect relatively low infection loads.

MONITORING MDA

The long history of MDA-based campaigns in parts of the Pacific, most notably in Samoa and French Polynesia, also presents a special challenge. The challenge comes from the success of the previous campaigns in minimizing filariasis as a public-health problem (e.g. reducing the pathology) while transmission of the parasite persists. As pathology is related to the worm burden in the population, reductions in worm burdens eventually translate into reductions in pathology. In any at-risk population, a reduction in the pathology attributable to lymphatic filariasis may diminish the motivation of the members of the population to participate in MDA campaigns. Thus, as seen in Vanuatu, MDA coverage and the prevalence of microfilaraemia may be directly correlated (Fig.).

So far, more than 10.9 million DEC tablets and 1.7 million albendazole tablets have been distributed to Pacific-island countries and territories as part of PacELF (Table 2). In the MDA campaigns in 2000, which covered six countries and territories, treatment coverages ranged from 24% in American Samoa to 94% in Niue (Table 3). A year later, the MDA campaigns had been extended to cover another three countries and treatment coverages, at 52%–95%, were similar or better than those achieved in 2000. How MDA coverage is reported is important. In Vanuatu, treatment coverage is based on the number of subjects seen to ingest the DEC and albendazole tablets whereas some other countries simply base coverage on the numbers of tablets distributed to individuals. It is important that a standard definition of treatment coverage be used and that, where treatment is not observed, standard criteria for verifying compliance are employed. When treatment coverage was calculated using the number of people in the national census as the estimate of the total population, treatment coverage in Samoa was recorded as 90%, 57% and 68% for 1999, 2000 and 2001, respectively.

In Vanuatu during the 2000 MDA campaign, a respectable 78% coverage of the entire population was achieved when using the registered population at the time of the MDA (year 2000) as the denominator

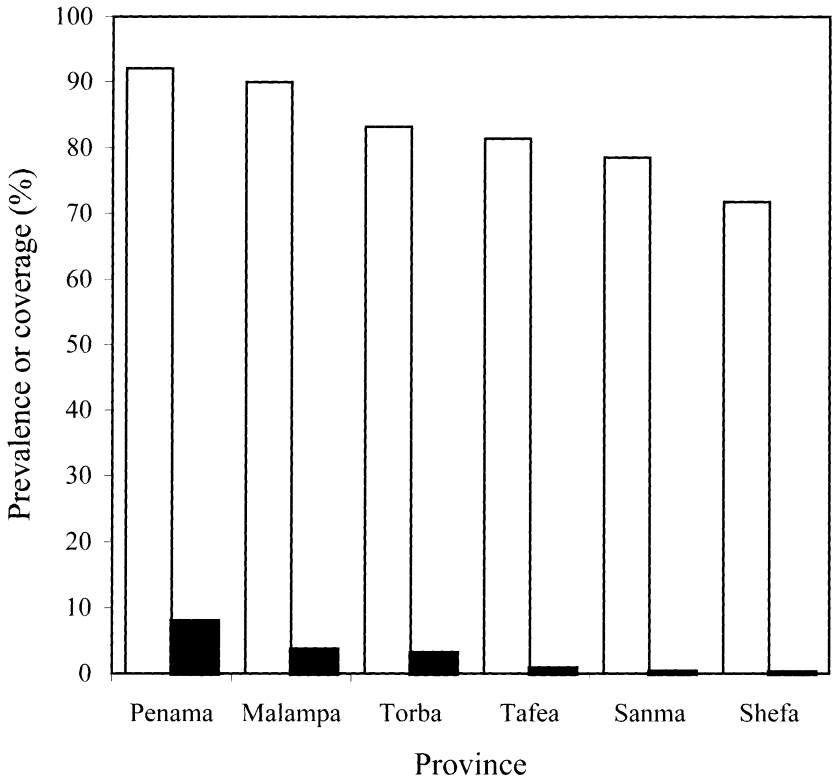

FIG. Relationship between the treatment coverages achieved in mass drug administrations in the provinces of Vanuatu (□) and the local prevalences of microfilaraemia (■) (G. Taleo, unpubl. obs.).

for calculating coverage (F. Taleo, unpubl. obs.). However, when the denominator was changed to the population size from the most recent census (year 1999), coverage was inflated to 83%. When analysed by province, MDA coverage ranged from 75% to 83%. When analysed by individual islands, a wider range in MDA coverage was seen, from a high of 93% to a low of 67%. Analysis by village revealed an even greater variation. Hence, pockets of low coverage may be hidden when results are reported on a country or provincial level. MDA campaigns need to analyse coverage data rapidly, to identify areas with poor treatment coverage. Interviews to ascertain the reasons for low compliance in communities need to be conducted yearly, in order to modify health-communication campaigns to try to maintain a high treatment coverage in the following year's MDA campaign.

At the time of writing, 41,000 ICT kits have been distributed by PacELF to 16 member countries and territories, to monitor the effectiveness of MDA (Table 2). Some concerns have arisen about the programme's reliance on ICT for monitoring campaign success. Filarial antigenaemia may persist for several years following MDA with DEC alone (Schuetz *et al.*, 2000) and there may be a similar effect in MDA campaigns using DEC–albendazole. Preliminary observations from Samoa (detailed above) indicate that antigen persistence may be related to intensity of infection. There is a need for an alternative test (to monitor changes in the prevalence of filarial infection in human communities) that more accurately reflects the amount of ongoing transmission.

The level of transmission can be estimated by measuring the prevalence of infection in mosquitoes or by detecting new infections

TABLE 2. *The numbers of immunochromatographic test (ICT) kits and diethylcarbamazine (DEC) and albendazole tablets distributed to Pacific-island countries and territories by the Pacific Programme for the Elimination of Lymphatic Filariasis (PacELF)*

	No. of:		
Country or territory	ICT kits	DEC tablets	Albendazole tablets
American Samoa	0	1,000,000	140,000
Cook Islands	3000	150,000	19,000
Federated States of Micronesia	5000	0	0
Fiji	5000	4,700,000	868,000
French Polynesia	0	740,000*	220,000
Guam	1000	0	0
Kiribati	500	900,000	85,000
Marshall Islands	2500	0	0
Nauru	500	0	0
New Caledonia	0	0	0
Niue	2000	25,000	2500
Northern Mariana Islands	2000	0	0
Palau	2500	0	0
Papua New Guinea	5000	80,000	8000
Pitcairn Island	0	0	0
Samoa	3000	1,260,000	170,000
Solomon Islands	3000	0	0
Tonga	2000	840,000	12,600
Tokelau Islands	0	0	0
Tuvalu	2000	84,000	13,000
Vanuatu	2000	1,200,000	180,000
Wallis and Futuna	0	0	0
All countries and territories	41,000	10,979,000	1,718,100

*Purchased directly by French Polynesia.

TABLE 3. *The countries or territories in which mass drug administrations (MDA) were supported by the Pacific Programme for the Elimination of Lymphatic Filariasis (PacELF) in 1999, 2000 and 2001, and the treatment coverages achieved**

Countries or territories and (% coverage) in:		
1999	2000	2001
Samoa (90)	Samoa (57)	Samoa (68)
	American Samoa (24)	American Samoa (52)
	Niue (94)	Niue (89)
	French Polynesia (93)	French Polynesia (95)
	Vanuatu (83)	Vanuatu (83)
	Cook Islands (59)	Cook Islands (64)
		Tonga (82)
		Kiribati (?)
		Tuvalu (81)

*Fiji and Wallis and Futuna are scheduled to begin MDA in 2002 and Papua New Guinea in 2003.

in humans. The incidence of new human infections can be estimated from the results of longitudinal ICT, by observing how many antigen-negative individuals become antigen-positive at follow-up. A complete failure to find antigen-positives by the ICT in the

sample population would verify that transmission had been stopped. Because of antigen persistence, the ICT provides a conservative estimate of the efficacy of the MDA campaigns, since some individuals will be antigen-positive shortly after a campaign even though they are amicrofilaraemic.

Measuring the prevalence of filarial infection in mosquitoes may be an appropriate alternative to ICT for evaluating levels of transmission and thus the success of MDA campaigns. Infections in mosquitoes reflect the prevalence of microfilaraemia more directly than ICT results. However, as microfilaraemias should become ever rarer with each round of MDA, ever increasing numbers of mosquitoes will need to be analysed to detect significant changes in the prevalence of mosquito infection.

At the present time, there is a discrepancy between the stated goal of PacELF and how the programme's MDA campaigns are monitored. The stated goal of the programme is the elimination of filariasis as a **public-health** problem (i.e. the elimination of filaria-attributable pathology). The tool for monitoring progress in the PacELF campaigns, however, is the ICT, a rapid test for the detection of *W. bancrofti* or, more precisely, the detection of circulating parasite antigen, which is only indirectly related to pathology. The argument can be made that the goal of PacELF was achieved in many Pacific-island countries before initiation of the PacELF campaign. Pathology can be eliminated without elimination of parasite transmission. There is, for example, virtually no filaria-attributable pathology in French Polynesia, although transmission of *W. bancrofti* persists and could lead to a resurgence of infections and, consequently pathology, if MDA is discontinued. Given the tenuous relationship between antigenaemia (as an indicator of parasite presence) and pathology, together with the general absence of data on the prevalence of pathology caused by *W. bancrofti*, the goal of PacELF should be re-defined as the elimination of transmission.

ALTERNATIVE STRATEGIES

Fortified Salt

To eliminate filariasis in 5 years, it has been estimated that at least 80%–90% of each at-risk population will have to treated annually with DEC–albendazole. Countries in which coverage using annual MDA of DEC–albendazole falls below this target have the option, as part of the global filariasis-elimination strategy, of considering a campaign in which DEC-fortified salt is used instead. This approach was highly effective in reducing the intensities of microfilaraemia in parts of Brazil, China, India, Japan, Tanzania and Taiwan (Houston, 2000) as well as the prevalences of microfilaraemia in parts of China, India and Taiwan (Gelband, 1994). The major advantages of an elimination campaign based on the delivery of DEC as a fortified salt are the low incidence of side-effects and the ease of distribution (provided there are limited sources of salt and salt distribution can be easily controlled). The major disadvantage is limited control of the dosage received by individuals.

Vector Control

Mosquito control could be used not only to help reduce filarial transmission in areas where MDA coverage is poor, but also to prevent a resurgence of filariasis where the disease has been successfully eliminated as a public-health problem. In the past (Hawking and Denham, 1976), filariasis transmission in the Pacific has been divided into four zones according to the primary vectors: *Anopheles* spp. in PNG, the Solomon Islands and Vanuatu; *Culex quinquefasciatus* in Micronesia; *Aedes polynesiensis* in Polynesia; and *Ochlerotatus vigilax* in New Caledonia. This simplification ignored the complexity of transmission. At least 22 species of mosquito transmit *W. bancrofti* in the South Pacific [see Table 1 in article by Zagaria and Savioli (2002)]. In the Samoas, *Ae. samoanus* transmits the parasite at night while *Ae. polynesiensis* transmits it by day (Ichimori, 2001). Fiji alone

has at least five vectors: *Ae. polynesiensis*, *Ae. pseudoscutellaris*, *Ae. rotumae*, *Oc. fujiensis* and *Cx. quinquefasciatus* (G. Prakash, unpubl. obs.). In PNG, perhaps all nine members of the *An. punctulatus* complex found there may transmit *W. bancrofti* (although only three morphologically distinguishable species — *An. farauti*, *An. koliensis* and *An. punctulatus* — have so far been confirmed as vectors of the parasite). *Culex quinquefasciatus*, *Mansonia uniformis* and *Ae. kochi* are also reported to transmit the parasites causing filariasis in PNG (Hawking and Denham, 1976). Where there are multiple vector species in Pacific-island countries and territories, however, there is usually one species that is responsible for most of the transmission. In these areas, vector control targeting the primary vector can reduce transmission significantly, thereby enhancing the effect of MDA on transmission. For countries where *Anopheles* and *Culex* mosquitoes are the most important vectors, there are proven effective interventions against these mosquitoes. Bednets, both insecticide-impregnated and unimpregnated, can reduce the transmission of malarial parasites and filariae by anopheline mosquitoes. Polystyrene beads have proven effective in reducing filarial transmission by *Cx. quinquefasciatus* (Maxwell *et al.*, 1990). Outdoor- and daytime-biting *Aedes* provide a more significant challenge (Burkot and Ichimori, 2002). Where *Ae. polynesiensis* transmits *W. bancrofti*, vector control will be necessary as an adjunct to MDA in order to achieve filariasis elimination. The reason is based on the biology of this vector tempered by the realities of human behaviour (e.g. that high MDA treatment coverage will be difficult to maintain for 5 years in the absence of pathology). *Aedes polynesiensis* exhibits a characteristic, known as 'limitation', in which the efficiency of the vector increases with falling microfilarial densities (e.g. a higher proportion of the mff ingested survive to the human-infective, third-stage larvae when fewer mff are ingested). Even with 85% treatment coverage using DEC in a semi-annual MDA for 35 years in Maupiti, French Polynesia, new cases of filariasis in children appeared and infected mosquitoes were still found (Esterre *et al.*, 2001). Despite the success of the PacELF MDA campaigns in achieving treatment coverages up to 95%, history indicates that elimination of the parasite will, unfortunately, probably not succeed in Polynesia without adjunct vector-control measures. Unfortunately, effective control strategies that significantly impact *Ae. polynesiensis* population dynamics are unproven. More basic and operational research will be needed to develop and evaluate methods of reducing filarial transmission by this mosquito (WHO, 2002).

Ironically, the country with the highest prevalence of filariasis in the Pacific may be the one most likely to enjoy the most dramatic success in terms of filariasis elimination. PNG, with a filariasis prevalence estimated (from the results of rapid antigen-detection tests) to be 56% (Melrose *et al.*, 2000), should see dramatic declines in both filaria-attributable pathology and prevalence of antigenaemia. Not only are the populations in highly infected areas of PNG likely to be keen to participate in MDA campaigns (because they have high prevalences of symptomatic filariasis) but also the primary vectors, members of the *An. punctulatus* complex, are inefficient. Bednets, whether insecticide-impregnated or not, significantly reduced both malarial and filarial transmission by the members of the *An. punctulatus* complex in PNG (Charlwood and Dagoro, 1987; Graves *et al.*, 1987; Burkot *et al.*, 1990).

The potential strength of vector control as a component in the PacELF campaign can be seen by the success of previous anti-mosquito campaigns on the elimination of lymphatic filariasis from Australia and the Solomon Islands. In Australia, 10.8% of 1200 patients examined at the Brisbane Hospital in 1908–1909 had *W. bancrofti* mff transmitted by *Culex* mosquitoes (Boreham and Marks, 1986). A rigorous sanitation campaign directed against the larval breeding sites succeeded in eradicating lymphatic filariasis from Australia. In the Solomon

Islands, like PNG, members of the *An. punctulatus* complex were the vectors of *W. bancrofti*. A DDT-spraying campaign, designed to control malaria, succeeded in eradicating filariasis from the Solomon Islands because the same mosquitoes, which fed at night and rested indoors, transmitted *W. bancrofti* (Webber, 1979). The eradication of filariasis from the Solomon Islands and parts of PNG succeeded using only anti-mosquito measures to interrupt transmission.

The impact of vector control as an adjunct to MDA for filariasis elimination will depend on the availability of trained staff to implement control measures of proven efficacy. Implementation of vector control in the Pacific will require a revitalization of entomological expertise. Several Pacific-island countries already have Ministry of Health personnel whose job descriptions require them to conduct mosquito surveys and to control mosquitoes. In Fiji, mosquito surveillance and control are two of the 92 defined responsibilities of health inspectors. Although it is not strictly necessary to train many individuals to be able to identify mosquitoes to the species level, it is necessary that vector-control specialists be knowledgeable on the biology of the local mosquitoes, including their breeding and feeding habits, in order to undertake control measures effectively.

Evaluation of the efficacy of interventions against mosquitoes requires some expertise in mosquito identification. Training in vector biology, mosquito identification, mosquito surveillance and control will be necessary prerequisites to implement effective mosquito-control campaigns, not only for filariasis elimination but for dengue and malaria control as well. Research on the effectiveness of anti-vector measures, as well as operational research on the implementation of these measures, will be needed for the daytime- and outdoor-feeding *Ae. polynesiensis*. The goal of such research should be not to delay the implementation of elimination efforts but to enhance the efficacy of MDA in the attempt to stop transmission.

SUMMARY

In the absence of an effective macrofilariacide, it is crucial that treatment coverage of entire populations with microfilaricides remains high for 5 years or more, in order to stop transmission. To achieve a high treatment coverage for a number of years will require an aggressive health-communication campaign, coupled with an efficient reporting system using a standardized and verifiable definition of treatment coverage. Rapid analysis of treatment coverage is needed to identify potential problem areas where treatment coverage is insufficient to interrupt transmission. A backup plan for implementation of alternative strategies, including the use of DEC-fortified salt, should also be in place should treatment coverage of DEC–albendazole drop.

Even so, it may be optimistic to expect to achieve elimination of transmission within all PacELF countries and territories in the absence of vector control, particularly in areas where *Ae. polynesiensis* is the major vector. Past experience has shown that campaigns for the control of vector-borne diseases based on a single strategy are often unsuccessful. Large-scale campaigns to achieve elimination of a disease have a limited number of years in order to achieve success before compliance drops or resistance by the parasite or vector develops. It is important to implement a multifaceted strategy, including MDA and vector control, aggressively and synchronously, to stop filarial transmission using all available tools (Bockarie, 2000). Implementation of an effective vector-control strategy will require technical-level support for Pacific-island countries, in the areas of vector biology, vector identification and vector control. Support at the professional level, in the area of operational research to design and evaluate vector-control strategies, will also be required.

ACKNOWLEDGEMENTS. The authors would like to thank the Ministries and Departments

of Health in the 22 PacELF countries and territories, both for their support of the PacELF attempt to eliminate filariasis from the Pacific and for sharing the results of their MDA campaigns. We are also grateful to P. J. Lammie of the Centers for Disease Control and Prevention (Atlanta, GA) for numerous helpful comments on the manuscript.

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