

**COLLABORATIVE GLOBAL PROGRAMME
TO ELIMINATE LYMPHATIC FILARIASIS**

***Programme Background and Overview
Towards Initiating a National Programme
to Eliminate Lymphatic Filariasis***



Lymphatic Filariasis Elimination (CEE/FIL)
Control, Prevention and Eradication
World Health Organization
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WHO's Collaborative Global Programme to Eliminate Lymphatic Filariasis:

Programme Background and Overview

1. INTRODUCTION

1.1 The Problem of Lymphatic Filariasis (LF) and the Outlook for its Elimination

World-wide, 120 million people are infected with the filarial parasitic worms (*Wuchereria bancrofti*, *Brugia malayi* and *B. timori*) that cause lymphatic filariasis, and around a billion people live in areas where they are at risk of being infected. Damage to the lymphatic system leads to lymphoedema, genital pathology (especially hydrocoeles) and elephantiasis in some 44 million men, women and children. A further 76 million have hidden infection, most often with microfilariae in their blood and hidden internal damage to their lymphatic and renal systems.

Lymphatic filariasis is widespread in the South-East Asian, African and Western Pacific Regions of WHO, as well as in some countries of the Eastern Mediterranean Region and the Region of the Americas. Globally, the disease is the second leading cause of permanent and long-term disability, with the deforming, mutilating disease of the limbs and genitals resulting not only in physical crippling but also in serious psycho-social consequences. Furthermore, added to the direct economic costs of managing the acute and chronic manifestations of lymphatic filariasis, are the enormous indirect losses that follow from diminished productivity and incapacitation and which constitute a severe drain on local and national economies. US \$1 billion is lost annually in India alone due to lymphatic filariasis.

For too long there has been little hope of controlling lymphatic filariasis throughout the world, despite the very notable earlier successes in some countries, particularly China and Japan.

Dramatic recent advances, however, in treatment methods both for controlling transmission and for simple, successful approaches to morbidity (disease) control, along with remarkable improvement in techniques for diagnosing the infection, have completely altered this erstwhile gloomy outlook. So much so that following the conclusion by an independent International Task Force for Disease Eradication that lymphatic filariasis was one of only six infectious diseases considered to be "eradicable" or "potentially eradicable", the World Health Assembly in 1997 adopted Resolution WHA50.29 calling for the elimination of lymphatic filariasis as a public health problem globally. Then, providing tremendous practical impetus to this initiative was the recent (1998) decision by the global healthcare company SmithKline Beecham to collaborate with WHO in this elimination effort through the donation of a number of important resources, but, most especially, all of the albendazole (one of the drugs used against LF) free-of-charge for as long as necessary to ensure success of the elimination programme. The subsequent pledge by Merck & Co., Inc. to expand its ongoing Mectizan® (ivermectin) Donation Program to include treatment of lymphatic filariasis where appropriate, and the creation of additional partnerships with other private, public and international organizations, have further strengthened the prospects for success of these LF elimination efforts.

1.2 The Recent Medical Advances

The recent medical advances that have so dramatically changed the outlook for filariasis today encompass four distinct areas.

1.2.1. *New Treatments for Interrupting Transmission*

With the development of new, effective, safe and long-lasting microfilaricidal regimens based on once-yearly, single-dose, 2-drug treatments, the revised approach to controlling filariasis transmission, and even interrupting it, now focuses on community-wide treatment of entire 'at risk' populations with either:

- (a) **albendazole** (400 mg [same dose for all ages]) plus **diethylcarbamazine (DEC)** (6 mg/kg), a regimen suitable for use only in countries that are free from co-endemic infections with *Onchocerca volvulus* or *Loa loa* (see Annex 1) OR
- (b) **albendazole** (400 mg) plus **ivermectin** (200 µg/kg), a regimen recommended for use in countries, or parts of countries, where *O. volvulus* and/or *L. loa* infections are co-endemic with bancroftian filariasis (and thus, where DEC is contra-indicated because of the potentially severe side-reactions it can induce in patients with onchocerciasis or loiasis)¹.

Whichever of these annual treatment regimens is used, it will need to be continued for a minimum of 4-6 years, *i.e.* until the adult worms in the body have come to the end of their normal life-span. In programmes where poor coverage is achieved, and hence where some residual transmission may persist, annual treatments may need to continue for a longer period to ensure complete interruption of transmission.

Both treatment regimens are safe for use in community-wide mass distribution programmes (see Section 3.1.4 below). The effect of each dose on microfilarial production lasts for at least a year; and, over that period, treated persons no longer contribute to the transmission pool. Both regimens permit annual mass treatment to be organised in all communities where lymphatic filariasis exists; they avoid the need for "selective treatment" of people with microfilaraemia who must be diagnosed individually; and they do not demand any concomitant vector control, although, if feasible, they may be supplemented by such measures.

1.2.2 *New Treatment to Control Morbidity (disease)*

Even when all microfilariae have been eliminated from the blood and successful interruption of transmission has been achieved, the residual lymphatic damage from earlier infection will persist and facilitate invasion of the damaged skin and lymphatics by secondary external microbial pathogens (bacteria and fungus). These microbial infections cause local

¹ Both of the above regimens contain albendazole, which is donated free-of-charge to the elimination programme by SmithKline Beecham PLC. The albendazole enhances the effects of the microfilaricidal drugs DEC and ivermectin by prolonging the suppressive actions of these drugs on microfilarial production. Albendazole is also one of the most effective gastro-intestinal anthelmintics currently available, and the single 400 mg dose, which can safely be given to all persons over two years of age, is highly effective in eliminating infections with *Ascaris*, *Strongyloides*, *Enterobius*, *Trichuris* and, especially importantly, hookworms.

Regimen (a) above, which contains DEC, also has the added advantage that the 6 mg/kg dose of DEC will kill up to 50% of the adult *W. bancrofti* worms that are present in the human host (*i.e.* the proportion of the total adult worm load that happens, for reasons as yet unknown, to be in a phase of their life cycle that is susceptible to the drug).

inflammation that can induce or exacerbate lymphoedema, elephantiasis and genital damage in those already infected or suffering from the manifestations of lymphatic filariasis. These sufferers constitute the highly visible tip of the iceberg of filarial infection and disease, and

though the incidence of such pathology will decline as transmission control is achieved, such already-affected individuals require and deserve some form of palliative treatment. Fortunately, new research advances have made such treatment feasible.

Indeed, for the success of national LF elimination programmes it is essential that excellent community health education and treatment measures for lymphatic filariasis be established and that community self-help groups be set up to stimulate and maintain personal commitment to the hygiene-focussed activities needed for "morbidity control". These activities can not only halt progression of elephantiasis but can actually reverse the damage already present in many affected individuals; they include:

- regular twice-daily washing of the affected parts with soap and water;
- raising the affected limb at night;
- regular exercising of the limb to promote lymph flow;
- keeping the nails clean;
- wearing shoes;
- using antiseptic or antibiotic creams locally (or, in severe cases, systemic antibiotics) to treat small wounds or abrasions ('entry lesions').

1.2.3 *New diagnostic and rapid epidemiological assessment tools for surveillance and monitoring*

Community-wide mass treatment programmes to eliminate lymphatic filariasis demand the availability of simple rapid epidemiological methods to identify those communities with, or 'at risk' of, lymphatic filariasis. The simple new methods now being used in place of the older, slow, insensitive and tiresome night-blood examinations to detect lymphatic filariasis include two indirect-approximation techniques and three direct-determination methods.

The two indirect approaches are:

- (a) An approximation of infection endemicity from reviews of existing health reports, hospital and clinic records, or from informal surveys of knowledgeable community leaders;
- (b) The clinical examination of adult males for hydrocoeles, with extrapolation to gauge the overall prevalence of infection.

The three direct measures, each highly sensitive and specific, are the following:

- (a) Evaluation of antigenaemia rates in day-time finger-prick blood specimens from children or other sentinel cohorts in the population;
- (b) Examination of human blood for infection by detecting parasite DNA by PCR;
- (c) Examination of mosquito vectors for infection using either traditional entomological methods or PCR techniques to detect parasite DNA.

All three of these direct diagnostic tests are now available for practical use both in initial surveillance for filarial infection and in monitoring the effects of treatment. The first

uses specific monoclonal antibodies to detect circulating *W. bancrofti* antigens [it is not available for *B. malayi* or *B. timori*] and is a test requiring only day-blood specimens (regardless of any 'nocturnal' or 'diurnal' periodicity of the microfilariae in the blood). It detects all microfilaraemic persons and a proportion of those with amicrofilaraemic 'cryptic' infections. Antigen levels gradually fall to zero when all adult worms have been killed. The test is field-proven and available commercially in either card-test or ELISA format at a cost of approximately US \$ 1.00 per test.

The DNA-based tests, also with outstanding sensitivity and specificity, detect parasite DNA (of *B. malayi* and *B. timori* as well as of *W. bancrofti*) in the human and mosquito hosts, using the polymerase chain reaction (PCR) techniques. These tests are rapid, convenient (as samples can be dried for months on filter paper) and no more expensive than antigen detection, but they do need access to a central laboratory with good quality control. .

1.2.4 *Recognition of lymphatic filariasis as a childhood infection*

Only with development of more sensitive diagnostic tools could the true incidence of lymphatic filarial infection in childhood be determined. Recent studies of *W. bancrofti* infection in populations from 3 different parts of the world have shown that acquisition of infection generally occurs as early 2-3 years of age. Though clinical manifestations of disease often remain hidden for years, internal pathology can develop even in young children. Thus, early treatment and prevention of lymphatic filariasis during childhood is necessary.

1.2.5 *Recognition of the 'added benefits' of community programmes to eliminate lymphatic filariasis*

Since two of the three drugs used in LF elimination programmes (i.e., albendazole and ivermectin) have very broad spectrums of activity against both intestinal and ecto-parasites (Table, Annex 2), intervention to interrupt transmission of LF will additionally bring with it all of the public health benefits resulting from yearly 'de-worming programmes' as well as from treatment of lice and scabies. These de-worming benefits include relief from hookworm-related anaemia along with enhancement of both growth and cognitive development in children. Important, too, is the recent finding that the two-drug treatment with albendazole and ivermectin yields significantly greater efficacy against *Trichuris* infections than either drug alone as well as greater benefits in terms of child growth.

In addition to these ancillary direct health benefits, the establishment of national LF elimination programmes based on once-yearly community intervention throughout large sectors of the population creates opportunities to integrate or coordinate a number of technically similar public health activities, with the result of much greater cost-effectiveness; for example, opportunities for linkages with single-treatment intervention programmes for schistosomiasis, onchocerciasis, intestinal parasites or nutritional supplementation, as well as with once-yearly immunization programmes.

2. THE COLLABORATIVE AGREEMENT BETWEEN SMITHKLINE BEECHAM AND THE WORLD HEALTH ORGANIZATION TARGETING THE GLOBAL ELIMINATION OF LYMPHATIC FILARIASIS

Following, first, the development of the remarkably effective new tools and strategies to eliminate lymphatic filariasis; then, the recognition of this disease as "potentially eradicable"; and finally the resolution by the World Health Assembly calling for the elimination of lymphatic filariasis as a public health problem globally, SmithKline Beecham,

PLC made an extraordinary commitment to collaborate with WHO to effect a rapid acceleration of the effort to eliminate lymphatic filariasis.

The 10 essential points of the Memorandum of Understanding between SmithKline Beecham (SB) and WHO that was announced in January 1998 are summarized below.

- (1) SmithKline Beecham will provide albendazole free of charge to WHO for use by governments, and those organizations working in association with (or permission of) these governments, for such duration as is reasonably designed to achieve the objective of WHO, expressed in resolution WHA50.29 adopted by the 50th World Health Assembly in 1997 and calling for the global elimination of lymphatic filariasis as a public health problem. (Since the strategy calls for treatment of all 'at risk' populations annually for 4-6 years, and since up to 1.1 billion people may be at risk of infection, this donation could comprise as many as 6 billion doses of albendazole over the lifetime of the elimination effort [estimated at 20-25 years]).
- (2) SmithKline Beecham will, at its own cost, (i) store, or arrange for the storage of, the albendazole until the time of shipment and (ii) ship, or arrange for the shipment of, the albendazole directly to governments, and those organizations working in association with (or permission of) such governments, in accordance with the requests of WHO.
- (3) SmithKline Beecham shall not be responsible for the importation and customs clearance of the albendazole into any country nor its storage there nor for any customs or other duties that may be payable.
- (4) SmithKline Beecham will also:
 - (a) contribute ancillary support (financial or otherwise) towards initiation and implementation of WHO's programme for the elimination of lymphatic filariasis and towards operational research costs to optimize programme activities.
 - (b) encourage its employees to take an active interest in the programme and to offer their expertise and involvement, as may be appropriate for WHO programme activities or the implementation plans of governments concerned with the elimination of lymphatic filariasis.
- (5) WHO will establish a Programme Review Group of independent experts to be responsible for advising on requests from governments, and from organizations working in association with (or permission of) such governments, for donated supplies of albendazole to be used in national Programmes to Eliminate Lymphatic Filariasis.
- (6) WHO will advise the Governments of its Member States where lymphatic filariasis is endemic on the development of implementation plans on a country by country basis. Each plan will cover assessment, implementation, monitoring, evaluation and operational research as necessary. WHO will provide technical advice and assistance to the Governments of Member States on such plans and their implementation, but the government concerned will be responsible for implementation of the Programme to Eliminate Lymphatic Filariasis at the country level.
- (7) SmithKline Beecham and WHO will also establish a Collaboration Coordinating Committee, involving members of their respective staffs, which will meet regularly to review operational issues relating to the collaboration and to facilitate the implementation of the recommendations of the Programme Review Group.

(8) WHO will ensure that all recommendations for the proper administration of albendazole provided by SmithKline Beecham, including necessary arrangements for reporting adverse events and effecting product recalls, will be transmitted to participating governments and to other organizations working in association with (or permission of) these governments.

(9) High-level representatives of WHO and of SmithKline Beecham will meet annually to decide on the future plans and direction of their collaboration and on the means for creating public awareness of the programme.

(10) WHO will also establish a specially designated financial account for the Programme to Eliminate Lymphatic Filariasis, for the receipt of contributions from all donors to the programme.

3. RESOURCES AVAILABLE TO COUNTRY PROGRAMMES TO ELIMINATE LYMPHATIC FILARIASIS

3.1 Drug Supplies

3.1.1 *Albendazole*

As part of its collaboration with WHO to eliminate lymphatic filariasis, SmithKline Beecham, PLC will donate all the albendazole required by country programmes developed along the prescribed guidelines and recommended by the Programme Review Group (see below).

While this donation of albendazole by SmithKline Beecham is for the specific purpose of eliminating lymphatic filariasis, it is recognized that many people in endemic areas will be receiving albendazole solely because they are in populations 'at risk' for infection with filarial parasites; for such individuals the principal immediate health benefit will derive from albendazole's effectiveness in curing other infections, primarily those caused by the almost ubiquitous intestinal parasites.

Since albendazole has already been commercially available to treat intestinal parasite infections for years in many of these countries (through SmithKline Beecham as 'Zentel' and through other companies as well), the donated drug will be distinguished from other products by its being an oval-shaped, off-white tablet embossed with 'ALB 400' on one side and packaged in containers of 100 tablets. For all eligible persons (see Section 3.1.4) the dosage of albendazole is identical, one single tablet (400 mg) that can be swallowed or chewed (see Appendix 2).

3.1.2 *Ivermectin (Mectizan®)*

Mectizan® will be donated by Merck & Co., Inc. for use with albendazole in programmes to eliminate lymphatic filariasis through an expansion of its on-going Mectizan® Donation Program in Yemen and the 28 African countries listed in Appendix 1 where onchocerciasis is also endemic. An additional application to the Mectizan® Donation Program will be required to obtain this drug, but it is anticipated that delivery of the supplies of Mectizan® and albendazole to individual programmes will be coordinated. Though both drugs will be administered to entire 'at risk' populations once-yearly for the purpose of interrupting the transmission of lymphatic filariasis, it is recognized that many treated individuals will also receive direct health benefits from the Mectizan® because of its

effectiveness against certain intestinal parasites and against lice and scabies (see Appendix 2).

The Mectizan® will be supplied in bottles containing 500 tablets of 3 mg each, and it is to be administered at a dosage of approximately 200 mcg/kg to all eligible recipients (see Section 3.1.4).

3.1.3 *Diethylcarbamazine (DEC)*

DEC is currently produced by at least a dozen manufacturers throughout the world and is available at a cost of approximately U.S. \$0.01-0.02 per dose (6 mg/kg). Until other specific arrangements are made with the manufacturers, this drug must be purchased by individual Ministries of Health undertaking filariasis elimination programmes. Recommendations for sources of DEC supply are available, but further specific guidelines for production standardization must still be established. DEC is generally supplied in 50 mg or 100 mg tablets.

3.1.4 *Drug safety; Exclusions from treatments*

Each of the three drugs recommended for use in national programmes to eliminate lymphatic filariasis is extremely safe, especially when administered as a single dose. Practical field experience with each extends from the tens of millions (ivermectin) to many hundreds of millions (albendazole and DEC) of people treated during the past 15 (ivermectin), 25 (albendazole) or 50 (DEC) years. At the recommended dosages (albendazole: 400 mg; ivermectin: 200 mcg/kg; DEC: 6 mg/kg) essentially no toxic reactions to the drugs have been noted. When side-reactions do occur following treatment (primarily fever, myalgia and lethargy), they are essentially always the result of the individual's immune inflammatory response to dying parasites affected by the treatment; the greater the microfilarial load of the infection, the greater are the frequency and severity of such reactions. Only rarely (in heavily infected individuals) are these post-treatment reactions to the dying microfilariae severe and require supportive management. While experience with the 2-drug, single-dose treatment regimens for LF is much more limited, there is no evidence that the co-administration of the 2 drugs results in any enhanced toxicity or reactogenicity compared with the single drugs given alone.

The endemic populations eligible for community-wide treatment should exclude only those who are sick or infirm, children under the age of 2 years, for DEC, and 5 years, for ivermectin, pregnant women and lactating women who are breastfeeding infants less than 2 weeks of age. It should be noted, however, that even for these exclusions that there is no direct or anecdotal evidence of any complication resulting from treatment with single-doses of any of these drugs during pregnancy or lactation.

3.2 **Technical support**

WHO will provide technical support to national programmes to eliminate lymphatic filariasis primarily through its network of Country and Regional Offices and their associated Collaborating Centres. This support can include, among others, direct consultation; development of training courses; and the provision of reference manuals, guidelines and assistance with issues such as defining initial prevalence and distribution of infection, cost-effectiveness analysis, impact assessment, morbidity control, communication strategies, and others.

3.3 Financial Resources

It is recognized that the largest share of resources for all country programmes to eliminate lymphatic filariasis will come from the countries themselves, some of the resources being in cash funds but most being in personnel and infrastructure contributions. Sources of 'outside' funding support will be country-specific, and the options are varied. Bilateral development assistance programmes, regional development funds, grants from international organizations or non-governmental development organizations, and development loans from the World Bank are all potential sources of funding for filariasis elimination programmes.

Identification of 'partners' or potential partners to assist at all levels of national programme activities towards filariasis elimination will be part of the consultation available through WHO during the development of national programme plans of activity. Indeed, since national programmes will not succeed in the absence of sufficient financial resources, the availability of adequate funding will be an important criterion that the Programme Review Group will focus on before recommending a supply of drug to be donated for a national filariasis elimination programme.

4. DEVELOPING A NATIONAL PLAN OF ACTION TO ELIMINATE LYMPHATIC FILARIASIS

Given the encouraging background of the recent medical advances and the new public and private sector initiatives, the Ministries of Health of the 73 countries afflicted with lymphatic filariasis are now committed to taking action by setting up their own elimination programmes. The first step involves the establishment by each Ministry of Health of a National Task Force (NTF) for the Elimination of Lymphatic Filariasis (ELF), which, with assistance and advice from WHO as necessary, will be responsible for preparing its own National Plan of Action. This Plan will be extremely important because, once it is approved by the Ministry of Health and by WHO, it can be utilized by the country for developing the partnerships necessary for funding its National Programme to Eliminate Lymphatic Filariasis (PELF).

4.1. Developing a National Task Force (NTF) for the Elimination of Lymphatic Filariasis (ELF)

The NTF-ELF is a body to be convened by the Ministry of Health. It is responsible for drawing up a National Plan document, which describes the National Programme for the Elimination of Lymphatic Filariasis (PELF) in detail and which can be presented to donors or other organizations for funding support or cooperation with the elimination programme. The NTF-ELF also meets at regular intervals to provide advice, supervision and assistance on the running of the national PELF.

The NTF-ELF is usually composed of members who have experience and expertise in the various disciplines which relate to the PELF. Among these may be included persons with special knowledge and practical experience in:

- Epidemiology, especially in relation to filariasis assessment, mapping and control;
- Treatment of lymphatic filariasis for both transmission and morbidity control;
- Biology and control of the vectors of lymphatic filariasis;
- Organizing public health campaigns in the field;
- Health education and training of health workers;
- Primary Health Care and community medicine;
- Finance and Administration of Public Health programmes;
- Private sector health care activities;

Social and behavioural science;
Community/political leadership.

The Secretary of the NTF-ELF is often the National Lymphatic Filariasis Co-ordinator, *i.e.* the person appointed to be in overall charge of the National PELF. The country

representative of WHO and representatives of other organizations working with the Ministry of Health on the national PELF may also be invited to take part in the deliberations of the NTF-ELF

Whereas in most countries where lymphatic filariasis is endemic a single NTF-ELF will suffice, in some very large, populous and heavily infected countries or in countries divided by national strife, it may be more practical to set up a Regional Task Force for each major region of the country and then to coordinate these Regional Plans nationally.

4.2 Guidelines for Preparing a National Plan for the Elimination of Lymphatic Filariasis

The National Plan Document is of vital importance to record the background, objectives, strategy, administration, management and proposed budget for the National Programme to Eliminate Lymphatic Filariasis. It can also serve as a descriptive document for presentation to potential outside donors who may wish to become partners for supporting or assisting the programme.

Since communications between the National PELF and extra-national bodies (*i.e.* UN agencies, the World Bank, other potential donors among the non-governmental development organizations [NGOs] and private sector) are often made through WHO, it is important that the National Plan Document conform to a standard recommended by WHO.

The following are some of the major technical and administrative issues that should be addressed in the National Plan Document. These also form the core of the Application document required for the drug donations to support a National Programme to Eliminate Lymphatic Filariasis.

4.2.1 Background Information about the Country

4.2.1.1 Physical and demographic features, including:

- Location and borders,
- geography, ecology and climate,
- demography and cultural differences.

4.2.1.2 Administrative and Health Structure, including:

- The administrative divisions of the country and how the structure of the health services relates to these (from the Ministry of Health to the local Village Health Committee and the Primary Health Care workers). *It is particularly important to define the "operational unit" - the smallest administrative area that would be considered for treatment or no-treatment in mass-distribution programmes (e.g., District or town).*
- The total health budget,
- Description of any similar, large public health programmes carried out in the past.

4.2.1.3 *The Primary Health Care system, including:*

- Which areas of the country are adequately covered and served by PHC,
- What roles NGOs play in supporting health care,
- What functions the PHC system serves and what health activities or campaigns have been successfully integrated with it,
- How a PELF could be usefully and effectively integrated with other PHC supported programmes,
- The percentage of endemic communities targeted for mass treatment that have an existing and functional PHC structure,
- The human resources available to support a national PELF,
- The route of patient referral from the periphery to central health care facilities,
- Whether the government imposes any cost-recovery system for health services provided.

4.2.1.4 *Knowledge of the distribution and endemicity of lymphatic filariasis, including:*

- A summary, with the aid of maps, of the distribution and extent of the areas where lymphatic filariasis is endemic, indicating the sources of information on which the distribution, prevalence and intensity data are based and the methods used to obtain the endemicity data.
- Details of the species of lymphatic filarial worms found in the area and the principal species of mosquito vectors.
- Description of the most prevalent clinical manifestations of lymphatic filariasis in the area, and the major socio-economic consequences of the disease.
- An outline of previous control campaigns (treatment or vector control) that have been put into effect in the area, whether any of these are still on-going, and what lessons were learned from carrying out these programmes
- The threshold level of endemicity above which mass treatment will be undertaken to reduce or interrupt transmission (in an elimination programme this level will be at, or very close to, zero).
- The numbers of (a) urban and (b) rural areas that will need mass treatment and the size of total populations (> 2 years old) living in these areas.
- The methods that will be used for Rapid Epidemiological Assessment of those areas where the degree and extent of endemicity is not yet known and a time-table for surveying these areas.

- Any endemic areas where mass treatment programmes cannot currently be undertaken for security reasons.
- Any endemic areas which extend across country borders (identifying which other countries are involved and what actions should be taken).

4.2.1.5 *Distribution of other infections whose control might be linked with a national PELF, including:*

- Onchocerciasis,
- Intestinal parasites,
- Schistosomiasis.

4.2.2 Targets of the Programme

Whereas the goal of the programme is to eliminate lymphatic filariasis as a public health problem, the objectives of the programme need to be defined in terms of accomplishments in:

- Interruption of transmission through mass treatment of endemic populations;
- morbidity control, for those already suffering from clinical manifestations of the disease, by simple management measures linked with community self-help.

4.2.3 Strategy and Tactics

The organization and specific activities of the programme must be designed to demonstrate the country's commitment to the elimination of lymphatic filariasis, not just its control. This commitment should be reflected in the approach to the epidemiological assessment, the microfilaricidal treatment strategies and the morbidity control efforts.

4.2.3.1 *Epidemiological Assessment to determine the distribution of infection², including*

- Methods and sample sizes to be used in (a) urban and (b) rural communities.
- The number of sentinel communities that will be monitored to assess changes in the prevalence and intensity of infection as the programme advances and how frequently they will be re-examined.
- What measure will determine the threshold level of endemicity above which mass treatment will be undertaken, and how this threshold will be defined.

4.2.3.2 *Microfilaricidal treatment to control transmission, including:*

- Whether different drug distribution methods will be adopted in urban and rural communities,
- The methods that will be used to achieve maximal coverage in mass treatment of (a) urban and (b) rural communities,
- The drug regimen to be used in the mass distribution programme³,

2. A separate handbook and practical guidelines will be issued by WHO.

3. The regimen of albendazole-plus-DEC in single-doses co-administered once-yearly is the regimen of choice for all countries *except those with endemic onchocerciasis and loiasis*. Since it is too dangerous to use DEC for mass treatment in such countries, ivermectin should be substituted for DEC and administered concomitantly with albendazole in these cases. *The countries where the albendazole-plus-ivermectin regimen is recommended for use are found in Section B of Appendix 1.*

- The source of DEC, if it is to be used, and its cost,
- The delivery chain for the drugs to be used, from the port of entry, through central storage, and on to the peripheral distribution points.
- The provision for the Ministry of Finance to allow the drugs concerned to enter the country free of Customs Duty and without undue delay.
- How the drugs will be stored in order to preserve their potency and to avoid theft or misuse.
- The mechanism to be used to ensure the delivery of the mass treatment drugs to the communities (e.g., who will collect the microfilaricidal drugs from the last point in the delivery chain and take them to the communities for distribution to the people; how the people will be mobilised for treatment; whether community-based distributors will be used, and if so, how they will be selected; how they will be trained and re-trained; whether and how they will be rewarded for their services; whether health workers from the local Health Centre will be used and, if so, how and where will they be trained and re-trained for this specific task; what records will be kept of the identity and numbers of people treated; who will be responsible for collecting and keeping these records; what experience-level will be required of the person responsible for supervision and monitoring of drug distribution).
- Any national policy for cost-recovery that may be applied to the distribution costs, and, if one exists, how it will be applied and how it will affect the distribution programme.
- What markers will be used to assess programme effectiveness and who will monitor the programme success.

4.2.3.3 Morbidity control by simple hygienic methods applied in conjunction with community self-help, including:

- How communities will be alerted to, and educated about, the new simple hygiene methods aimed at reducing the suffering caused by the chronic and disabling lesions associated with filarial lymphoedema, elephantiasis and genital lesions.
- What means will be employed to develop self-help organizations within communities in order to put these methods into practice.
- What, if any, simple medicaments, cleansing agents, dressings etc. for use in morbidity control will be provided by the health services.

4.2.4 Health Education and Training

Provision of health education about lymphatic filariasis will be needed for the community, including:

- The purpose and benefits of the PELF,
- the nature and significance of the disease,
- details of the treatment strategies for interruption of transmission (with its ancillary benefit of controlling intestinal parasite infections) and for control of morbidity,

- the need for long-term perseverance,
- the anticipated benefits,
- the means through which this educating will be achieved, along with the resource materials already available or still needed.

Training will be necessary for all staff members and community-based distributors of albendazole and either DEC or ivermectin, along with re-training on an annual basis, to assure their competence to perform the procedures demanded for their roles in the programme.

4.2.5 Administration and Management

- The names, titles and qualifications of the National Lymphatic Filariasis Co-ordinator and all members of the National Task Force need to be provided.
- The formal links between the NTF-ELF and the Ministry of Health need to be defined, including an organogram to show the relationships between the different bodies (national and otherwise) concerned with the elimination programme.
- The leaders of the elimination programme should be selected to include:

A Programme Director, who is responsible for co-ordinating and overseeing the programme and making decisions that assure its success. [Ideally this person will have successfully managed other public health programmes or operations of comparable scope. The Director need not be a physician but should have experience in managing health projects in the field.]

A Medical Supervisor, who is responsible for making sure that sound medical practices are observed and that treatment requirements are followed. [This person, who must be a licensed physician, ideally with experience both in public health and filariasis control, must be readily available at all times for consultation. The Programme Director and the Medical Supervisor may be the same person.]

A Drug Inventory Controller who is responsible for managing the storage, security, accountability and delivery chain for the programme's albendazole (and other drugs) tablets. [This person should be experienced in pharmaceutical store-keeping and delivery and must also play a similar role in the procurement, storage, and delivery of diethylcarbamazine (DEC) or ivermectin tablets used in the programme.]

- The Ministry of Health staff of different grades of experience who will be working full-time and part-time on the programme needs to be described.

4.2.6 Time Plan

A time plan will be necessary to show how the various control activities will progress year by year towards the programme's objectives and goals.

4.2.7 Budget

A budget summary for the first 5 years of the programme including internal (national) and external sources of funding will be required.

For obtaining financial assistance to the programme, a more detailed budget must be submitted that includes at least the following major categories:

- Personnel,
- Supplies,
- Training,
- Travel,
- Communication,
- Consultants,
- Operating expenses,
- Auditing,
- Supervision,
- Capital equipment.

5. APPLICATION PROCEDURES TO OBTAIN DONATED SUPPLIES OF ALBENDAZOLE (FOR USE WITH IVERMECTIN OR DEC) IN COUNTRY PROGRAMMES TO ELIMINATE LYMPHATIC FILARIASIS (PELF)

5.1 Initiation of Application

Applications for cost-free supplies of albendazole (for use in combination with ivermectin⁴ or DEC) in National Programmes to Eliminate Lymphatic Filariasis (PELF) must originate from the Ministries of Health (MoH) which will be responsible for their own actions in the programme, as well as for those of any organizations working in association with (or permission of) the government. The MoH of each country participating in the programme will be required, as a first step, to draw up a detailed implementation plan and complete a specific Application following the guidelines developed through WHO (whose essentials are described in Section 4 above and detailed in the Application form itself).

The Application should be forwarded with a covering letter from the responsible ministerial authority to WHO for subsequent review by an independent Programme Review Group. *This Group's primary objective is to facilitate the earliest and widest possible initiation of such national programmes, consistent with their safe and rational implementation.*

5.2 Approval Criteria

To be successful the Application for the donation of albendazole submitted by the MoH must meet a set of 'minimum requirements', that are detailed below; where there is concern, however, about whether all of the criteria have been met in the Application, the Programme Review Group will actively support efforts to resolve this concern.

The nine 'minimum requirements' for Application approval are the following:

1. Ministerial commitment to the elimination of lymphatic filariasis
2. Sufficient epidemiological and parasitological data to begin operations, and provision to expand that data progressively as needed to support the requirements of a full national programme (a phased approach generally being anticipated for larger countries)
3. Potential to integrate with other public health services/programmes
4. Existence of a National Coordination Committee or a similar body

⁴ A separate application to the Mectizan® Donation Program will be required to obtain this drug.

5. Clear identification of resource requirements needed to implement the intervention programme; for Applications requiring expansion of initial operations, the provision of evidence that:
 - the targets for the initial operations are being met
 - the epidemiological data are available to justify the expansion
 - the resources for that expansion are adequate
6. Technical capacity present already or a clear statement of how such capacity will be created
7. Guaranteed exemption from fees or counter-part payments to cover customs duties, acceptance and clearance; evidence of mechanisms in place for appropriate drug handling and warehousing
8. A plan for impact assessment on transmission in a subset or sentinel group of the treated population
9. The capacity to adequately identify, manage, report and monitor serious adverse experiences with the drugs being used.

5.3 Approval Process

The specific steps in the process of approving Applications for the supplies of donated albendazole (to be used with ivermectin or DEC) in National Programmes to Eliminate Lymphatic Filariasis can be outlined as follows.

1. The Ministry of Health (MoH) sends the Application it has prepared to WHO;
2. The WHO Secretariat reviews the Application for *administrative* completeness; if incomplete, communication with the MoH will lead to completeness;
3. When the Application is *administratively* complete, the WHO Secretariat will send the Application to members of the Programme Review Group (PRG);
4. PRG members will review the Applications for programmatic content and for satisfying essential public health and filariasis elimination issues;
5. PRG members return the Applications and their critiques to WHO;
6. The WHO Secretariat consolidates comments and critiques on the Application for a general review at the next PRG meeting (held 2-4 times per year);
7. At the PRG meeting, the Application either will be approved or will be referred to the WHO Secretariat to work with the country to satisfy programmatic uncertainties in the original Application; the WHO Secretariat will either clarify these uncertainties simply through direct communication or will work through a technical consultant, as appropriate;
8. The MoH will revise its original Application to satisfy the concerns of the PRG, and the WHO Secretariat will summarize the actions taken and forward the revised Application to the PRG members;
9. PRG members will review the revised Application and recommend either that the WHO Secretariat consider the Application approved or that the Application be reviewed again at the next PRG meeting;
10. When the Application is finally approved by the PRG, one of two courses will be followed:
 - If no ivermectin is required for the national Programme, the Application will be processed for implementation of the albendazole donation and the shipping process;
 - If ivermectin is required, the Application will be sent to the Mectizan® Donation Program (MDP) for evaluation and recommendations according to its requirements; when the Application has been approved by the MDP, the process of implementing the donation and shipping of both drugs will begin.
11. Requests for re-supply of drug each year will require the MoH to submit to WHO an annual report (see below) which will be reviewed by the PRG (and MDP where ivermectin is involved) before the requests for re-supply are approved.

6. PROGRAMME IMPLEMENTATION AND REPORTS

6.1 Initiation of Programmes

Programmes will be implemented according to the details of the individual country Plans of Action and Application forms. For larger countries, initiation of activities will usually take place in a limited area where the practical technical and logistical issues can be addressed on a smaller scale before the Programme is expanded country-wide.

6.2 Reporting Procedures

Each year, the Ministry of Health responsible for the Programme to Eliminate Lymphatic Filariasis (PELF) in each country will submit to WHO an annual report on the progress achieved. These reports will focus primarily on process indicators dealing with the success of the distribution of the drugs to the target populations. They will be reviewed by the Programme Review Group (and by the Mectizan® Donation Program when ivermectin is used), and re-supply of drugs will be recommended if the programme operations are satisfactory.

Reports on the overall public health impact of the PELF will focus on the decreases in the microfilarial and infection rates and on the social and economic impacts of the treatment programmes. Of necessity, these assessments will be made only after several years of programme activity and will follow standardized protocols whose specific guidelines have been established through WHO.

In the event that any Severe Adverse Experience (SAE) is encountered during the treatment programmes, a Severe Adverse Experience Report form must be completed immediately and returned to WHO and SmithKline Beecham (and in areas where ivermectin is being used in conjunction with albendazole, the Mectizan® Donation Program's Serious Adverse Experience Form must also be completed and returned to that Programme and to Merck & Co., Inc.). Thorough investigation of any Severe Adverse Experience is mandatory in all National Programmes to Eliminate Lymphatic Filariasis.

The collective experience of all of the National Programmes to Eliminate Lymphatic Filariasis that are undertaken will be consolidated in order for use in both programme enhancement and impact assessment. This consolidation will be carried out not only through reviews of individual programme reports but also through Regional and Sub-Regional meetings of National Programme Directors and their staffs.

Appendix 1

A. Those countries (with recognized lymphatic filariasis) where it is safe to use DEC in lymphatic filariasis elimination programmes are:

African Region

Cap Verde
Comoros
Gambia
Kenya
Madagascar
Mauritius

Réunion
Sao Tomé & Príncipe
Seychelles
Zambia
Zimbabwe

Region of the Americas

Brazil
Costa Rica
Dominican Republic
Guyana

Haiti
Suriname
Trinidad & Tobago

South-East Asia Region

Bangladesh
India
Indonesia
Maldives

Myanmar
Nepal
Sri Lanka
Thailand

Eastern Mediterranean Region

Egypt
Oman
Somalia

Western Pacific Region

American Samoa
China
Cook Islands
Federated States of Micronesia
Fiji
French Polynesia
Kiribati
Malaysia

Papua New Guinea
Philippines
Republic of Korea
Samoa
Tonga
Tuvalu
Vanuatu
Viet Nam

B. Those countries where ivermectin should be used instead of DEC are:

African Region

Angola
Benin
Burkina Faso
Burundi
Cameroon
Central African Republic
Chad
Congo
Côte d'Ivoire
Democratic Republic of the Congo
Equatorial Guinea
Ethiopia
Ghana
Guinea Bissau

Liberia
Malawi
Mali
Mozambique
Niger
Nigeria
Senegal
Sierra Leone
Togo
Uganda
United Republic of Tanzania
Gabon
Guinea

Eastern Mediterranean Region

Sudan
Yemen

Appendix 2

Broad anti-parasite effectiveness⁺ of single doses of the drugs used in programmes to eliminate lymphatic filariasis

Ivermectin		Albendazole	
Ascaris	4 +	Ascaris	4 +
Strongyloides	4 +	Strongyloides	2 +
Enterobius	3 +	Enterobius	3 +
Trichuris	1+/2+	Trichuris	1+/2+
Hookworm	1 +	Hookworm	4 +
Larva migrans (cutaneous)	4 +	Larva migrans (cutaneous)	3 +
Onchocerciasis	4 +	Cysticercosis	*
Lice	3 +	Hydatids	*
Scabies	4 +	Giardia/Trichomonads	*
		Micro-/Crypto-sporidia	*

+ Graded qualitatively on a scale 1+ to 4+ (most active).

* Effective but requires more than a single dose of albendazole.

