Summary of Prioritized Research Needs

1) Define the duration and coverage of MDA necessary to achieve interruption of transmission in different epidemiologic/entomologic settings.
2) Determine the effect of the rate of upscaling on
   a) duration of MDA necessary to achieve interruption of transmission,
   b) cost of the program in the short- and long-term,
3) Identify the most effective social mobilization strategies for MDA in different settings,
4) Optimize MDA strategies for urban areas with low prevalence of infection,
5) Determine the duration and coverage of DEC-salt administration necessary to interrupt transmission,
6) Identify safe strategies for LF elimination in L. loa-endemic areas,
7) Assess the impact of LF elimination programs on health systems,
8) Identify the complementarities of specific targeted-disease programs that can promote linkages among the programs for coordinated implementation, monitoring, and evaluation,
9) Review outcomes and best practices both from ongoing LF elimination programs and from other, similar targeted-disease programs, and
10) Develop novel means of resource mobilization for upscaling national programs.

2.4.1 Overview

Program.

The GPELF was formulated in 1998\(^1\) with a goal to eliminate LF as a public health problem through focus on two principal targets:

1) interrupting transmission of the parasites that cause LF,
2) alleviating the suffering and preventing the morbidity caused by the infection.

For interrupting transmission, the two alternative strategies are

1) annual, community-wide two-drug distribution of albendazole with either DEC or Mectizan* (ivermectin) to at-risk populations until the criteria for stopping MDA are met (expected after 4–6 rounds of effective MDA coverage) or
2) exclusive use of table/cooking salt fortified with DEC for 1–2 years by at-risk populations.

For morbidity management, activities are designed to establish community home-based self care for people with lymphedema and to provide access to surgery for men with hydroceles/lymphoceles.

Progress.

By 2000, the first national PELF had been launched. By the end of December 2003, a total of 38 countries had established MDA programs based on albendazole and DEC, albendazole and ivermectin, or DEC-fortified salt; approximately 83 million people had been treated with these regimens and another 39 million with DEC alone.\(^2\) The total number of people who have benefited from hydrocolectomies or community-based self-care training is more difficult to ascertain at this time since many such programs are decentralized and still quite new.

The WHO estimates that by 2008 almost 800 million people in 70 countries will have been treated through MDAs.\(^3\) If this target is achieved, it would represent approximately 85% of the countries and 64% of the total-at-risk population in the GPELF. As some countries prepare to exit the GPELF after 4–6 years of MDA and new countries join the GPELF, critical questions continue to arise regarding the most effective and efficient ways to implement and manage the PELFs; these must be articulated and addressed to ensure achievement of the goal to eliminate LF by 2020.

2.4.2 Research Needs

Defining the general measures of successful program implementation.

Gauging the success or failure of national and global LF elimination programs depends on recognizing a number of overarching issues and addressing them directly through research studies early enough in the program for any necessary corrections to be made in a timely fashion. These researchable issues (also emphasized elsewhere in this document) are essential for successful implementation of the PELFs and include

- determining the feasibility of interrupting transmission of LF vis à vis successful elimination of LF as a public health problem in all countries,
- defining effective strategies to prevent recrudescence,
- developing tools to measure the reduction in incidence of LF morbidity, and
- assessing the impact of MDAs on geohelminth prevalence, on anemia and general health status of the population, on national health systems, and on other impact measures,
- proving the cost-effectiveness and cost-benefits of LF elimination programs.

Optimizing effectiveness of drug distribution strategies.

Drug distribution based on annual MDAs.

The impact of MDAs on LF elimination depends directly on the proportion of the total targeted population actually ingesting the drugs, not merely receiving them, and on the...
geographic completeness of the MDA in covering contiguous areas where transmission might be ongoing. Thus, it is imperative to identify those strategies leading to maximal MDA effectiveness by addressing, and in different epidemiologic settings, certain particularly critical issues, including

- the cost-effectiveness of directly observed drug administration compared to other indirect approaches to drug administration,
- the rates of MDA coverage as a function of the types of personnel distributing drugs, and
- the most effective techniques for communicating and managing adverse events related to the MDA.

Drug distribution based on DEC-fortified salt.

Demonstration of the effectiveness of annual single-dose treatment with antifilarial drugs opened the door to new programmatic options for the elimination of LF, but barriers to the successful implementation of programs based on annual mass treatment still include 1) the difficulty of developing an infrastructure capable of distributing the drugs; 2) the need to achieve very high coverage levels; and 3) diminished compliance because of adverse reactions associated with the death of the parasite.

Use of salt fortified with DEC is an alternative program strategy avoiding many of the difficulties associated with tablet-based MDAs. Fortified salt (as recognized already in salt iodization programs) can be delivered to populations without developing new, dedicated drug distribution systems, and the DEC-salt (generally 0.2–0.3% w/w) is an effective microfilaricide that is rarely associated with adverse reactions. Furthermore, since fortification techniques for DEC and iodine are similar, incorporation of DEC-fortification into existing salt iodization programs appears very feasible. Finally, DEC-fortified salt represents an especially attractive programmatic option in situations where traditional approaches to tablet distribution are likely to be problematic, e.g., in rapidly expanding urban areas where health infrastructure and social services are particularly strained.

Because of the potential value of a DEC-fortified salt strategy, operational research studies are very much needed to address a number of important issues, including the

- duration and population-coverage of DEC-fortified salt required to achieve interruption of transmission,
- cost-effectiveness of DEC-fortified salt in urban areas compared to traditional MDA strategies to achieve interruption of transmission, and
- best strategies to address the regulatory and supply issues associated with the use of DEC-salt.

Program implementation in urban areas.

Both the strategy and details of program implementation in urban environments are likely to be very different from those in rural settings. The experience to date with MDA activities in cities is limited, and the challenges for achieving success are great. Therefore innovative research efforts will be required

- to develop techniques for appropriate sentinel site selection in highly urbanized areas,
- to compare the cost-benefit of conducting an MDA in highly urbanized areas with low LF prevalence with conducting a focal, targeted approach to pockets of endemicity.

Program implementation in L. loa-endemic areas.

Loiasis is endemic in forested areas of west and central Africa. While classical presentation includes transient, localized angioedema and occasional migration of a worm subconjunctivamente, the majority of infected persons have no recognizable signs of infection. Because central nervous system reactions (encephalitis/encephalopathy) may rarely occur in highly microfilaremic (> 30,000 mf/mL of blood) persons with loiasis after treatment with microfilaricidal drugs (including ivermectin), use of such drugs for onchocerciasis or for LF in areas coendemic for loiasis provides a major (or in some instances, a currently insurmountable) programmatic challenge. Since this situation is posing an effective block to MDA implementation for LF in vast areas of Africa, research is urgently needed for

- a rapid individual diagnostic tool for L. loa that gauges the risk for post-treatment serious adverse events,
- a safe and effective pre-treatment strategy for slow reduction of L. loa mf levels in endemic countries,
- assessing the potential for insecticide-treated nets to promote LF elimination in L. loa-endemic areas in the absence of a safe chemotherapy for MDA,
- defining the risk-benefit of MDA for LF elimination in L. loa-endemic areas.

Program upscaling/downscaling.

For most national LF elimination programs, upscaling from pilot activities to programmatic coverage of their entire at-risk populations has provided enormous implementation challenges. While many of these challenges are purely programmatic, there are still important researchable issues whose resolution would greatly aid these expanding programs, including

- the effect of the rate of upscaling on
  a) the number of MDA rounds required to achieve success,
  b) the cost implications in the short-term and long-term,
  c) the number of rounds of MDA needed to achieve interruption of transmission in settings with different initial mf prevalences,
  d) the most effective training materials to support upscaling,
  e) the most effective advocacy and fundraising strategies to link program needs with sources of support.

Although GPELF efforts to date have focused principally on the initiation or upscaling of programs, soon countries or regions of countries will be nearing the end of their projected 4–6 annual rounds of MDA. Assessment of the LF situation at that point might identify residual pockets of infection and lead to activities that might be termed mopping up, consolidation, termination of residual foci, or downscaling. Operational research should be undertaken in mature programs
• to determine the safest and most effective strategies for judging when to stop the MDAs,
• to identify residual foci of transmission and to implement appropriate, targeted intervention,
• to assess consequences of terminating the LF elimination program on the entomology, epidemiology, and clinical aspects of other endemic diseases in the community.

Disability prevention (disease management).

Many of the general issues and researchable questions dealing with morbidity management and disability prevention activities have been outlined elsewhere (Section 2.3), especially relating to the most suitable indicators for monitoring effectiveness of compliance, coverage, physical health outcomes, psychological health outcomes and socioeconomic outcomes. Additionally important, however, especially for its effect on the overall success of PELF implementation would be information derived from research to determine the

• impact of having or not having a morbidity/disability component in the national PELF on the success of LF elimination efforts, and
• impact of providing or not providing hydrocele/lymphocele surgery on the success of LF elimination efforts.

Social mobilization.

The majority of people infected with LF have no visible manifestations, and as a result, community perceptions of how people get affected are distorted. Therefore, the majority of the people in the communities where MDA is targeted are often indifferent and not motivated to take the drugs, believing they are neither affected nor at risk of being affected. Social mobilization is therefore of paramount importance to get communities to participate in the MDA. Model simulations indicate that high coverage, likely more than 80% of the total population, is essential during each annual MDA for interruption of transmission to be attained after five years; indeed, most areas in countries where social mobilization has not been accorded much importance have shown poor treatment coverage. It is therefore important that effective social mobilization is maintained throughout the duration of MDA.

To address this challenge, WHO introduced in some countries a social-mobilization approach termed COMBI (Communication for Behavioral Impact), based on a mixture of five communications interventions: public/government mobilization, community mobilization, interpersonal communication, advertising, and point-of-service promotion. It is meant to be a planning tool and serves as a framework for guiding the planning and development of appropriate, behaviorally oriented communications and social mobilization strategies that are culturally acceptable and country specific. A key aspect of the approach is the recruiting of private advertising agents to work on the communications while volunteer drug distributors are trained to be motivators for drug administration.

High drug coverage rates have been attained in countries where COMBI has been applied, but at in other places where classic social mobilization has been conducted based on knowledge, attitudes, and perceptions (KAP) and other social science studies, results have also been good. Therefore, it is important that social mobilization research be carried out

• to assess and compare cost-effectiveness, usefulness, and value-for-investment between the classical social mobilization methods and the more costly COMBI approach,
• to determine the factors that motivate populations to accept the drugs in various geographic, social, and cultural settings,
• to determine the factors that ensure or promote the maintenance of the motivation to continue taking the drugs each year of the annual MDA in various geographic, social, and cultural settings, and
• to develop effective social marketing strategies to maximize acceptance of DEC-fortified salt in countries where it is used.

Integrating LF elimination with other disease control programs.

Many parasitic and other infectious diseases have overlapping spatial distribution, with similar vectors and environmental determinants. Such scenarios are particularly common in the tropics and subtropics, home to the world’s least developed countries, where these overlapping, pervasive infections play an essential role in perpetuating the vicious cycle of poverty. Historically, to address these infections, disease-specific control programs (vertical programs) have been set up, most operating within the national health system, and thus drawing from the same pool of available resources and personnel for their field-level operations. What have become obvious are not only the great opportunities but also the compelling need of the national health systems to decrease the costs and burden of the multiple vertical programs by integrating or packaging as many of these activities as possible.

Successful recent precedents for effective integration of programs focused on specific diseases include the programs for Integrated Disease Surveillance (to coordinate surveillance of communicable diseases), Integrated Vector Management (aiming at the control of vector-borne diseases by combined approaches that are sustainable, cost-effective and have an impact on transmission), a new targeting of neglected diseases by WHO through providing neglected communities with an integrated solution to their disease-control problems, and a number of national programs now in the early stages of integrating control of such diseases as LF, onchocerciasis, geohelminths, schistosomiasis, trachoma, and others.

Many uncertainties remain, about which control programs can be effectively linked or packaged, depending particularly on the geographic and age distributions of the diseases and on programmatic similarities or complementarities. Because, however, the potential savings to the health systems and the populations they serve are so great, research to address those uncertainties should be urgently addressed by

• determining the specific program components that can be feasibly linked in implementing multiple disease-targeted programs,
• identifying the most effective tools and methodologies for monitoring integrated health interventions,
• determining the cost-effectiveness of integrated disease control programs,
assessing the feasibility and impact of integrating targeted disease programs with the primary health care system.

2.4.3 References