International Health 2021; **13**, **Suppl.1**: S39–S43
doi:10.1093/inthealth/ihaa077

The role of medicine donations in the global programme for the elimination of lymphatic filariasis

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Received 8 July 2020; revised 2 September 2020; editorial decision 16 September 2020; accepted 23 September 2020

World Health Assembly Resolution 50.29, adopted in 1997, committed the World Health Organization (WHO) and its member states to eliminate lymphatic filariasis (LF) as a public health problem. In 2000, to support this ambitious goal and the health ministries in the >70 LF-endemic countries, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) was created. The resulting WHO elimination strategy consists of two main components: to stop the spread of infection by interrupting transmission and to alleviate the suffering of affected populations (by controlling morbidity). The GPELF has brought together a broad global partnership of public and private actors, including three pharmaceutical companies with headquarters in three different continents. The medicine donations programmes from GlaxoSmithKline, MSD (trade name of Merck & Co. Inc., Kenilworth, NJ, USA) and Eisai have enabled significant achievements during the first 20 y of the GPELF and are positioned to provide essential contributions to the GPELF's goals for the next decade. As we celebrate the progress towards LF elimination during the GPELF's first 20 y, this article reflects on the factors that led to the creation of the three donation programmes, the contributions these programmes have made and some lessons learned along the way. We close by emphasizing our continued commitments to LF elimination and perspectives on the next decade.

Keywords: lymphatic filariasis, neglected tropical diseases, drug donation.

Introduction

Lymphatic filariasis (LF) is a disabling, neglected tropical disease (NTD), transmitted to humans by mosquitos, that has plagued societies for millennia.[1] The historical burden of LF has been widespread; in 2000, suspected transmission was ongoing in 80 countries, with an estimated 1.34 billion people at risk for infection and 120 million people infected.[2] However, a turning point occurred in the 1990s that paved the way for the potential global elimination of this long-existing, high-burden disease.

Interruption of transmission of LF can be achieved when the prevalence of microfilariae in the blood is reduced enough to halt the spread of the disease between humans via mosquitos.[3] A combination of albendazole and ivermectin, two anthelmintic medicines, administered together was shown to be a well-tolerated and highly effective treatment for preventing the transmission of LF at the community level.[4] Today this drug regimen is recommended as treatment through mass drug administration (MDA) in countries co-endemic with onchocerciasis, another NTD. Similarly, the combination of albendazole and another drug, diethylcarbamazine (DEC), was shown to result in a greater reduction of microfilaraemia than either of these two drugs administered as a single therapy.[5] Today, this is the recommended MDA regimen in countries endemic for LF but not onchocerciasis. To be successful, the recommended drug regimens must be administered once a year for at least 5 y, with coverage of at least 65% of the total at-risk population.[6] The effectiveness of these two different treatment options have proven to be highly advantageous given the risk factors for specific drug interactions in communities co-endemic for onchocerciasis, as discussed later in this article.

The evidence that these two-drug treatment strategies reduce microfilaraemia for many months, hence reducing transmission potential, and are well-tolerated through MDA in specific settings was an important contribution to LF being designated as a disease with the potential to be eliminated.[7] However, long-term access to the medicines was critically important to enable the

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required large-scale implementation of the two-drug treatment strategies.

Our commitments

Since 1987, MSD has operated the Mectizan Donation Program (MDP), a first-of-its-kind public–private partnership created to facilitate large-scale donation of the company's drug, Mectizan (ivermectin) for the treatment of onchocerciasis. The MDP was created following the unprecedented decision made by the company's chief executive officer (CEO) at the time, Dr Roy Vagelos, to donate Mectizan for the treatment of onchocerciasis to everyone who needs it for as long as needed. For >30 y, the MDP has facilitated the donation of Mectizan to communities in Africa, Latin America and Yemen, where onchocerciasis is endemic. MSD continues to operate MDP with the guidance of the independent Mectizan Expert Committee (MEC).[8]

A decade following the establishment of MDP, the CEO of SmithKline Beecham (now GlaxoSmithKline [GSK]) at the time, Jan Leschly, was seeking to establish a large-scale philanthropic effort aligned with the company's healthcare mission. The company was the original developer and manufacturer of albendazole. During a meeting with former U.S. President Jimmy Carter, who had been involved in the establishment of the MDP, Jan Leschly was inspired by the potential contribution that could be made through provision of albendazole.

The scientific data on ivermectin and albendazole combination therapy for LF was already under review by expert committees (i.e. MEC) at the time. This combination was particularly relevant for communities where LF and onchocerciasis are co-endemic, as the use of DEC poses the risk of serious side effects. Ivermectin and albendazole provided a well-tolerated treatment option for LF in communities where these two diseases are co-endemic.[4] Further, the MDP provided an existing platform to facilitate drug distribution in these communities.

In January 1998, GSK announced their commitment to donate enough albendazole directly to the World Health Organization (WHO) for every country that needs it until LF is eliminated as a public health problem.[9] In October 1998, MSD committed to expand its unlimited donation of Mectizan for onchocerciasis for the elimination of LF in Africa and Yemen, where onchocerciasis and LF co-exist.[10]

These unlimited donations complemented the efforts of many partners who had come together to support global elimination through the Global Programme to Eliminate Lymphatic Filariasis (GPELF) and, specifically, to support endemic countries to collectively achieve the global target to eliminate LF by 2020.[11] For >20 y, GSK and MSD, through the MDP, have coordinated their donations of albendazole and Mectizan.[12]

DEC is used in combination with albendazole in LF-endemic countries not co-endemic for onchocerciasis. The discovery and clinical use of DEC originated in the late 1940s with the pioneering work by Hewitt and Hawking.[13,14] After several decades of successful use, by the late 2000s the insufficient quality and supply of DEC hindered efforts for global LF elimination. Subsequent to a meeting between Eisai's CEO, Dr Haruo Naito, and then WHO Director General, Dr Margaret Chan, in November 2010, Eisai announced its commitment to supply DEC tablets for the treatment of LF. Eisai's development of DEC was immediately initiated to fulfil the needs of the GPELF.[15] A global team was assembled and processes for manufacturing, validation and quality control and assurance were developed in order to prepare and submit a dossier to the WHO for prequalification (PQ). These activities were for the most part centred in Eisai's Vizag plant in India, the largest LF-endemic country. The WHO PQ was secured in August 2013; an important milestone given that it was the first WHO PQ ever provided for treatment of an NTD. Subsequently, in October 2013, Eisai implemented manufacturing and distribution of donated DEC tablets to LF-endemic countries.

Our expanded commitments

By the mid-2010s, much success had been achieved through the implementation of the two-drug therapies, resulting in a significant reduction in the global burden.[16] However, as the 2020 global target for LF elimination grew closer, it was evident that several countries would not achieve elimination by this date. These countries were eager to identify alternative treatment options with the potential to accelerate their progress toward elimination. Around this same time, evidence from recent research had demonstrated that the addition of ivermectin to the currently recommended combination of DEC and albendazole could accelerate progress toward elimination more efficiently than the DEC and albendazole combination alone and was equally well tolerated. Specifically, with this three-drug combination, evidence showed the microfilaraemia declined rapidly and the absence of microfilaria in the peripheral blood of patients persisted for significantly longer than with the two-drug combination.[16]

In response, the WHO revised the treatment guidelines for LF elimination to recommend a triple therapy of ivermectin, DEC and albendazole (IDA) in some settings to accelerate elimination.[17] To support the implementation of IDA in certain recommended settings, MSD once again expanded its donation of Mectizan to provide up to an additional 100 million treatments per year through 2025 to support the elimination of LF in countries where onchocerciasis is not endemic. Eisai, GSK and MSD are coordinating the donation of their medicines to facilitate the effective implementation of IDA.

In addition to the commitments of donated medicines, Eisai, GSK and MSD provide financial grants and technical support for LF elimination. For example, the companies are collaborating with the Bill & Melinda Gates Foundation and the WHO to deliver LF test strips (Filariasis Test Strips [FTSs]), a rapid diagnostic test recommended for mapping, monitoring and transmission assessment surveys for LF elimination. As acknowledged in the new WHO 2030 Roadmap for NTDs, availability of diagnostics facilitates more effective and targeted treatment, potentially saving years of community-level treatment and providing an important tool to validate disease elimination.[18]

Reach and achievements

The reach of the GPELF has been expansive and incredibly successful.[19] In 2018 alone, 62.5% of the 892.9 million people

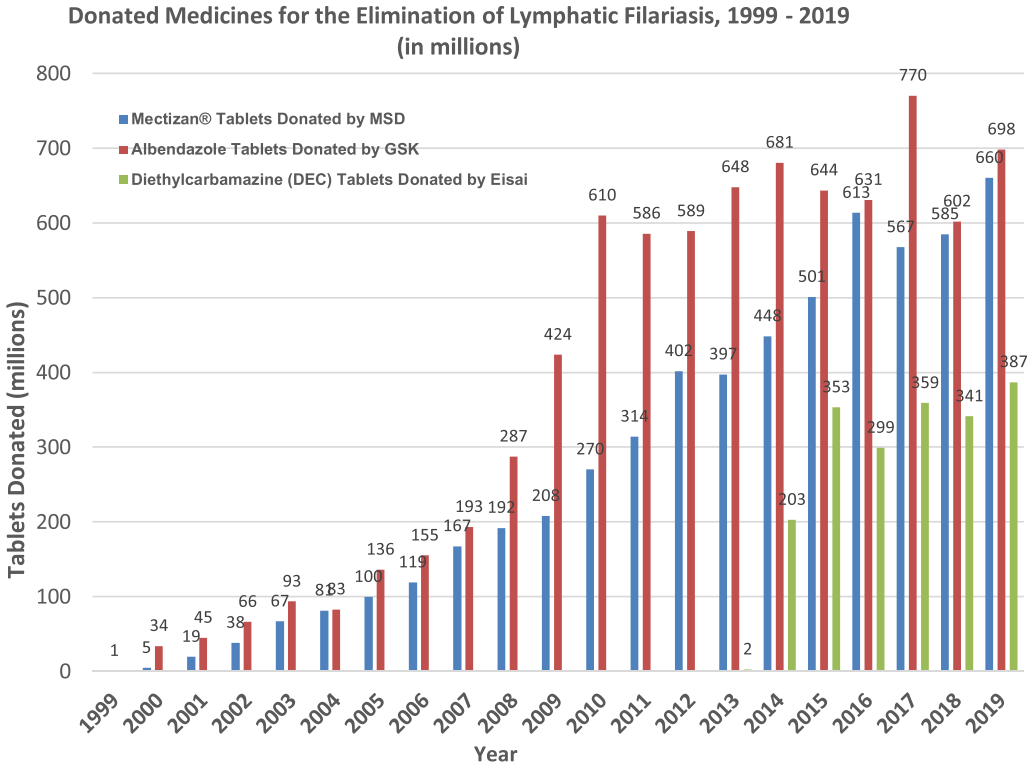

Figure 1. Donated medicines for the elimination of LF, 1999–2019 (Eisai, GSK, MSD).

globally requiring community-level treatment for LF elimination received it. The cumulative number of treatments provided since 2000 now exceeds 7.7 billion, delivered to >910 million people at least once.[11] Along with the contributions from many partners supporting the GPELF, the medicine donations from Eisai, GSK and MSD are an important contribution to this reach. Over 20 y, GSK has donated 8 billion albendazole tablets to 66 endemic countries, MSD has donated >2 billion treatments (totalling 5.7 billion tablets) to 40 countries and over >6 y, Eisai has donated 2 billion DEC tablets to 28 countries. Figure 1 illustrates the annual contributions for the last 20 y. As mentioned in the previous section, the commitments from the three companies extend beyond medicine donations. The investments in diagnostics have allowed coordinated procurement of >2 million FTSs for 40 countries in the past 5 y.[19]

Sustained interventions over the past 20 y have provided a significant public health impact through the GPELF. The population requiring treatment for LF has declined by 42% where infection prevalence has been reduced and communities no longer require treatment.[19] The WHO has validated 17 countries as having eliminated LF as a public health problem and 6 others are in post-treatment surveillance, on their way to validation (see Figure 2).

It is important also to acknowledge what we, the donating companies, have gained from our engagement in the GPELF. As a partner in this global coalition, we have built strong, lasting relationships among ourselves as well as with many other key stakeholders. We have been able to demonstrate externally our organizational commitments to the global community through our long-standing and even expanded investments. And, importantly, our donation programmes are motivational for our employees, exemplifying the impact of our science and our global supply chains on public health.

Key lessons

Reflecting on the last 20 y and confronted by the scope and scale of what was being proposed to achieve the global elimination of LF as a public health problem—the coordinated annual delivery and co-administration of two, and now in some settings three, different drugs to more than a billion people annually in >70 countries—it was abundantly clear that the mission was beyond the scope of any single organisation. Thus, from the outset of the programme, it was widely accepted that the programme would only be successfully accomplished through a broad coalition of partners each bringing their unique comparative advantage and expertise to the benefit of national programmes and the communities in need. The Global Alliance to Eliminate Lymphatic Filariasis (GAELF) was also formed in 2000 to support the GPELF. It consists of 72 national endemic country programmes, private sector and non-governmental organizations, academic and research institutes and international development agencies. GSK, MSD and Eisai are some of the many partners working together as a coordinated global community to achieve LF elimination. Through this partnership, many lessons have been learned—some challenging, others enlightening. Here we highlight some of what we

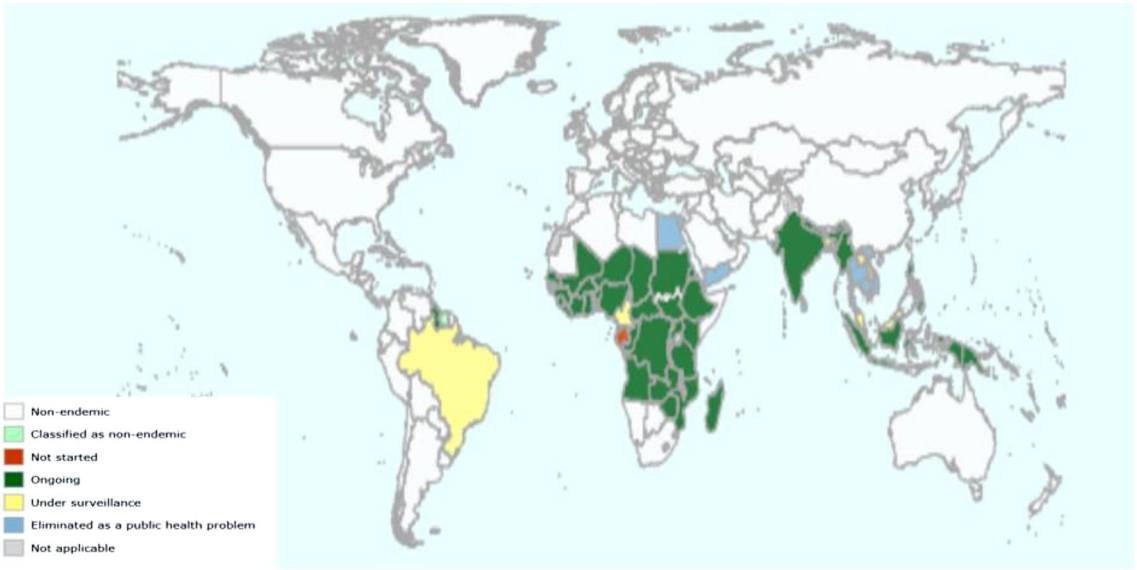

Figure 2. Distribution of LF and status of Preventative Chemotherapy (PC) in endemic countries.[25]

consider to be key learnings that have benefitted our companies, the LF national programmes and the GPELF.

- Independence from demand/supply decisions: Establishing independent review committees and collaborating with the WHO has been critical in providing industry a neutral operational space regarding decisions on the supply of therapeutics. Independence from the decision-making process is important to avoid the perception of company bias towards any country or geographic region.
- Coordination of supply chains: In a resource-constrained environment, integration of programme function is key to efficiency and affordability. Establishing processes to coordinate and monitor international and country-level supply chains has had a significant positive impact on both manufacturing and supply efficiency and in-country programme function. In response, the NTD Supply Chain Forum was established as a public–private partnership in 2012 to serve as a common platform for engagement of supply chain experts from the WHO, pharmaceutical companies, non-governmental organizations, donor organizations, ministries of health and logistics providers. The Forum created 'NTDeliver' as a centralized information system for storing annual requests and shipping information related to donations to further mitigate these issues.[20]
- Operational research: While the GPELF was launched on sound empirical evidence, there were, and remain, questions that require dependable cost-effective solutions to address current and future programmatic challenges.[21] Consequently, pharmaceutical partner engagement extends beyond just the supply of therapeutic products. Industry partners continue to engage with and invest financially in the dynamic and highly productive NTD research community. Robust and dependable programme evaluation processes that result in sustainable programme closure and effective, affordable post-validation surveillance systems will be crucial to inform the complex planning and manufacturing adjustments needed to support drug requirements as the global programme evolves over the next decade.
- Programme adaption to support to new tools: As new evidence emerges from operational research and experiential learning, partners need to be flexible to adapt and respond, as needed, to support new strategies and tools to accelerate progress toward global elimination targets.
- Monitoring, evaluation and visibility of achievement: Raising awareness, both within industry and with external stakeholders of the health and economic impacts that drug donations have achieved is important for supporting long-term programme sustainability. Donation programmes require substantial financial resources that must be allocated at the expense of other company priorities. In many LF-endemic countries, health ministries face stark choices on the allocation of limited financial resources among many competing public health conditions. Making the case for continued investments requires demonstrated measurable progress toward stated public health objectives. Strong national programmes that align with global targets and include rigorous monitoring and evaluation indicators are critical for providing the rationale for sustained investment in LF elimination.[22]

The next decade

2020 is a pivotal year for the LF community. In addition to GPELF's 20th anniversary, this year also marks the launch of the WHO 2030 NTD Roadmap, setting new ambitious targets for the elimination of LF for the next decade.[18] We are committed to continuing to support endemic countries through our donation programmes and as active partners in the global programme. While there are many unknowns on the path to the global elimination of LF, including what the full scope of the impact of the coronavirus disease 2019 pandemic will be,[22–24] we recognise the strong partnership that has been built over the last 20 y to support the GPELF

will be invaluable to manage them.[25] As it has in the past, this partnership will enable our companies and the LF community to collectively monitor, evaluate, adjust and respond as needed.

Authors' contributions: All authors contributed to the development, drafting and review of this manuscript.

Acknowledgements: None.

Funding: The publication of the papers within this supplement were supported by MSD, GSK and Eisai through the Mectizan Donation Program (MDP) and the Global Alliance for LF Elimination (GAELF).

Competing interests: None declared.

Ethical approval: Not required.

Data availability: The data underlying this article will be shared on reasonable request to the corresponding author.

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