Summary of the Twenty-Second Meeting of the International Task Force for Disease Eradication (II) January 14, 2014

The Twenty-Second Meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center from 8:30 am to 5:00 pm on January 14, 2014 to discuss the elimination of onchocerciasis and lymphatic filariasis (LF) in Africa. The Task Force members are Sir George Alleyne, Johns Hopkins University; Dr. Stephen Blount, The Carter Center; Dr. Mickey Chopra, UNICEF; Dr. Dirk Engels, World Health Organization (WHO); Dr. Donald Hopkins, The Carter Center (Chair); Dr. Julie Jacobson, Bill & Melinda Gates Foundation; Dr. Adetokunbo Lucas, Harvard University; Dr. Montserrat Meiro-Lorenzo, The World Bank; Professor David Molyneux, Liverpool School of Tropical Medicine (retired); Dr. Mark Rosenberg, Task Force for Global Health; Dr. Laurence Slutsker, Centers for Disease Control and Prevention (CDC); Dr. Harrison Spencer, Association of Schools of Public Health; Dr. Roberto Tapia, Carlos Slim Foundation; Dr. Dyann Wirth, Harvard School of Public Health; and Dr. Yoichi Yamagata, Japan International Cooperation Agency (JICA) (retired). Ten Task Force members (Blount, Engels, Hopkins, Jacobson, Molyneux, Slutsker, Spencer, Tapia, Wirth, Yamagata) attended this meeting, and two others were represented by alternates (Dr. Donald Bundy for Meiro-Lorenzo and Dr. Eric Ottesen for Rosenberg).

Presenters at the meeting included Drs. Mark Eberhard and Patrick Lammie, Centers for Disease Control and Prevention; Dr. Adrian Hopkins, Mectizan® Donation Program, Task Force for Global Health; Dr. Bridget Okoeguale, Federal Ministry of Health, Nigeria; Dr. Afework Haile Mariam Tekle, African Programme for Onchocerciasis Control, World Health Organization; and Dr. Ricardo Thompson, National Institute of Health, Mozambique. Dr. Stephen Blount also gave a brief update on The Carter Center's recent work to support elimination of malaria and LF on Hispaniola.

In its published report in 1993, the ITFDE became the first international body to recognize the potential eradicability of LF. The ITFDE reviewed LF again in 2002 and 2008, and onchocerciasis in 2001 and 2007. In 2002 The Carter Center and WHO also co-sponsored a conference on the eradicability of onchocerciasis.[1] When the ITFDE reviewed the eradicability of LF and onchocerciasis in Africa for the first time in 2011, it concluded that LF could be eradicated in Africa by 2020 if mapping of LF distribution and implementation of mass drug administration (MDA) for the disease were accelerated, but that eradication of onchocerciasis in Africa would "require surmounting several challenges", including finding an effective strategy for MDA in areas that are co-endemic for loiasis, as well as delineating and treating onchocerciasis in endemic zones that were still untreated.[2]

[1] Dadzie Y, Neira M, Hopkins D. Final report of the conference on the eradicability of onchocerciasis. *Filarial Journal*, 2003; 2:2.

[2] Anonymous. Meeting of the International Task Force for Disease Eradication, April 2011. *Wkly Epidemiol Rec*, 2011; 86:341—351.

Current Extent of Onchocerciasis, Lymphatic Filariasis and Loiasis in Africa

Onchocerciasis (river blindness) is caused by the parasite *Onchcocerca volvulus*, which is transmitted to humans by *Simulium* species black flies and occurs mainly in Africa. According to the latest published data available, approximately 130 million persons were at risk of the disease in 27 African countries in 2012 (Table 1). The three countries with the largest populations at risk are Nigeria (37 million), Democratic Republic of Congo—DRC—(30 million) and Ethiopia (8 million). The African Programme for Onchocerciasis Control (APOC) is delineating the transmission zones for the disease, including hypo-endemic areas and cross-border foci, especially in parts of East and Central Africa, work which should be completed in 2014 or 2015.

Table 1 2012 Status of Onchocerciasis and Lymphatic Filariasis Mapping and Treatments and Proportion of Households Owning at least One Insecticide Treated Bed Net in 47 African Countries

Country	Onchocerciasis (2012)^				Lymphatic Filariasis (2012)‡				% Household with 1 ITN (2011)§
	Mapped?	At-Risk Pop.	Treated	% treated	Mapped?	At-Risk Pop.	Treated	% treated	
Angola*	Y	1,212,200	430,329	35.5%	In Progress	12,090,000	--	0.0%	35
Benin (OCP/SIZ)	Y	3,304,364	2,768,062	83.8%	Y	3,747,913	656,329	17.5%	47
Botswana	--	--	--		--	--	--	--	34
Burkina Faso (OCP)	Y	219,298	186,040	84.8%	Y	16,779,208	12,437,078	74.1%	53
Burundi	Y	1,498,298	1,204,433	80.4%	--	Not Endemic	MDA not required	--	73
Cameroon*	Y	6,851,789	5,500,491	80.3%	In Progress	17,091,469	8,385,808	49.1%	61
Cape Verde	--	1,678,522	985,325	58.7%	--	Not Endemic	MDA not required	--	19
Centr. Afr. Rep*	Y	1,832,024	1,502,260	82.0%	In Progress	3,300,000	--	0.0%	17
Chad*	Y	2,086,183	1,718,974	82.4%	In Progress	7,270,000	--	0.0%	47
Comoros	--	Not Endemic	MDA not required		Y	514,110	--	0.0%	29
Congo*	Y	848,286	689,138	81.2%	Y	2,600,000	--	0.0%	10
Cote D'Ivoire (OCP)	Y	1,537,096	1,219,178	79.3%	In Progress	14,000,000	--	0.0%	61
D. R. Congo*	Y	30,379,763	23,126,855	76.1%	In Progress	49,140,000	--	0.0%	54
Egypt	N	Not Endemic	MDA not required		Y	No longer endemic	MDA stopped	--	--
Equatorial G.*+	Y	80,206	56,902	70.9%	Y	420,000	--	0.0%	56
Eritrea	N	Not Endemic	MDA not required		N	3,577,000	--	0.0%	73
Ethiopia*	Y	8,016,831	6,446,552	80.4%	In Progress	30,000,000	987,414	3.3%	90
Gabon*	Y	81,212	MDA not required		Y	1,290,600	--	0.0%	54

Gambia	N	Not Endemic	MDA not required		Y	1,200,000	--	0.0%	45
Ghana (OCP/SIZ)	Y	4,351,572	3,466,716	79.7%	Y	11,925,399	7,649,497	64.1%	38
Guinea (OCP/SIZ)	Y	2,694,390	2,236,136	83.0%	Y	6,067,135	--	0.0%	11
Guinea Bissau	Y	168,128	107,835	64.1%	Y	1,582,496	--	0.0%	58
Kenya	Y	Not Endemic	MDA not required		Y	3,421,741	--	0.0%	66
Liberia	Y	2,938,398	2,388,812	81.3%	In Progress	3,600,000	2,217,320	61.6%	44
Madagascar	N	Not Endemic	MDA not required		Y	18,602,379	907,295	4.9%	80
Malawi	Y	2,123,209	1,758,924	82.8%	Y	14,807,685	11,877,822	80.2%	53
Mali OCP	Y	4,844,513	3,956,909	81.7%	Y	16,166,882	10,373,698	64.2%	65
Mauritania	--	--	--		--	--	--	--	17
Mauritius	N	Not Endemic	MDA not required		--	Not Endemic	MDA not required	--	--
Mozambique	Y	Not Endemic	MDA not required		Y	17,114,949		0.0%	38
Namibia	--	--	--		--	--	--	--	74
Niger	Y	N/A	N/A		Y	12,467,592	8,926,672	71.6%	78
Nigeria*	Y	37,356,314	29,032,404	77.7%	In Progress	108,526,381	15,815,548	14.6%	46
Rwanda	Y	Not Endemic	MDA not required		--	Not Endemic	MDA not required	--	84
Sao Tome and Principe	N	Not Endemic	MDA not required		Y	410,000	0	0.0%	51
Senegal (OCP)	Y	N/A	OCP		Y	5,314,600		0.0%	60
Seychelles	N	Not Endemic	MDA not required		--	Not Endemic	MDA not required	--	--
Sierra Leone (OCP/SIZ)	Y	3,293,838	2,642,036	80.2%	Y	6,667,687	5,296,185	79.4%	86
South Africa	--	--	--		--	--	--	--	35
South Sudan*	--	5,707,037	2,473,693	43.3%	--	--	--	--	--
Sudan	Y	169,368	146,468	86.5%	In Progress	Endemic/No Data	0	0.0%	
Swaziland	--	--	--		--	--	--	--	63
Tanzania	Y	2,364,865	1,872,181	79.2%	Y	21,799,341	14,338,713	65.8%	90
Togo (OCP/SIZ)	Y	3,108,940	2,599,544	83.6%	UNDER SURVEILLANCE			0.0%	53
Uganda	Y	3,281,974	2,359,914	71.9%	Y	14,464,244	6,052,350	41.8%	59
Zambia	N	Not Endemic	MDA not required		In Progress	8,780,000	0	0.0%	40
Zimbabwe	N	Not Endemic	MDA not required		In Progress	6,000,000	0	0.0%	58
Total		**130,116,388**	**99,316,949**	**76.4%**		**440,738,811**	**105,921,729**	**24.0%**	**53%**

Information Sources:

*: Countries endemic for *Loa loa.*

Y: Mapping completed.

N: Mapping not done.

SIZ: Special Intervention Zone (example: Onchocerciasis Control Programme (OCP) areas that had continued interventions after OCP closure in 2002).
United Republic of Tanzania Zanzibar reports transmission of LF interrupted and MDA stopped. It reports having no onchocerciasis.

^ Anonymous. African Programme for Onchocerciasis Control: meeting of national onchocerciasis task forces, September 2013. *Wkly Epidemiol Rec*, 2013; 88(50):533—544.

NOTE: Shaded countries were included in previous table but not referenced in the *Weekly Epidemiological Record* (No. 50, December 2013) data.

‡ Anonymous. Global programme to eliminate lymphatic filariasis: progress report for 2012. *Wkly Epidemiol Re*, 2013; 88(37): 389—400.

§ *World Malaria Report 2012*. Geneva: World Health Organization, 2012.

In Africa lymphatic filariasis (LF; elephantiasis) is caused by the parasite *Wuchereria bancrofti*, which is transmitted to humans in rural areas by *Anopheles* species mosquitoes that also transmit malaria and in urban settings and coastal areas of East Africa by *Culex* species mosquitoes. As of 2012, approximately 441 million persons were at risk of this disease in 33 countries (not including Sudan, which also is believed to be endemic) (Table 1). The three African countries with the largest populations at risk are Nigeria (109 million), Democratic Republic of Congo (49 million) and Ethiopia (30 million). Mapping of LF in Africa is expected to be completed in 2014.

Loiasis (Tropical Eye Worm) is caused by another filarial parasite, *Loa loa*, which is transmitted to humans by the bite of Tabanid (*Chrysops* species) flies. It occurs in 11 African countries (Table 1), where its coexistence with onchocerciasis and/or LF poses a serious potential risk to persons with high *Loa* microfilarial loads who receive treatment with ivermectin during MDA for either of those other filarial diseases. Persons with very high levels of *Loa loa* infection who are treated with ivermectin may experience serious adverse reactions, including coma and/or death.

Interventions for Onchocerciasis and Lymphatic Filariasis in Africa

At least five African countries have established national policies to eliminate onchocerciasis: Sudan (2006), Uganda (2007), Cameroon (2011), Ethiopia (2012) and Nigeria (2013); these represent 55 million, or 44% of all persons at risk of onchocerciasis in Africa. All African countries have been committed to eliminating LF for several years.

In 2012, approximately 99 million treatments for onchocerciasis were administered in Africa (Table 1), representing 76% (range by country: 35%-86%) of the 130 million persons at risk, which is slightly higher than the 74% overall coverage of treatments for the disease in 2009. According to APOC, whereas the goal for minimal coverage with MDA for onchocerciasis was 65% in the previous era of onchocerciasis control, in the present onchocerciasis elimination era that goal is now 80%. Approximately 105 million (24%) (range by country: 0%-80%) of the 441 million persons at risk were treated for LF in Africa in 2012 (Table 1), which is a modest increase from the 18% of persons at risk who were treated for LF in 2009, but is far below the

coverage needed in order to eliminate LF in Africa by 2020. Table 1 summarizes updated data on coverage of African populations with insecticide-treated bed nets, which reduce transmission of LF and malaria, showing that coverage with that intervention has improved significantly in Africa since 2009. The delay in reporting of authoritative annual statistics for onchocerciasis and LF and their treatments in Africa was noted and lamented during the discussion. A Task Force member suggested that perhaps a joint annual summary of data for onchocerciasis and LF should be published in WHO's *Weekly Epidemiological Record* a few months after each calendar year.

In areas co-endemic for loiasis, more evidence has emerged to support the efficacy of long-lasting insecticidal nets (LLINs) to interrupt LF transmission, while studies of MDA with albendazole alone (rather than albendazole and ivermectin), and of administering doxycycline treatment to destroy endosymbiotic *Wolbachia* bacteria and thereby kill adult *Wuchereria* parasites, are underway. Potential alternative interventions for onchocerciasis in areas where loiasis is co-endemic include distinguishing specific patients or sub-areas where high levels of *Loa* microfilariae prevent treatment with ivermectin, then using other treatments such as doxycycline in those individuals. Task Force members agreed that such provisional interventions should be deployed as soon as possible in as many areas as appropriate while improved or additional interventions are developed for such co-endemic circumstances.

As the highest endemic country for onchocerciasis and for LF in Africa, a representative from Nigeria (estimated 160 million population in 2013; which has targeted onchocerciasis and LF for elimination by 2020) was invited to describe the status of efforts to combat those two diseases and malaria. Nigeria has completed mapping for onchocerciasis in all 36 states and the Federal Capital Territory (FCT), and mapping for LF is also complete in all administrative areas except Borno State, where mapping is expected to be completed in 2014. Approximately 30.5 million (80%) of 38.3 million Nigerians at risk of onchocerciasis received MDA in 2012, while reportedly only 19.9 million (18%) of 108.5 million Nigerians at risk of LF received MDA in 2012. In the largest insecticide-treated bed net campaign in history, Nigeria distributed almost 58 million LLINs to all administrative areas between 2009 and 2013. With assistance provided by The Carter Center, in March 2012 Nigeria's Federal Ministry of Health convened a meeting to discuss coordination of action against malaria and LF, and it will publish Guidelines for Malaria-Lymphatic Filariasis Co-Implementation in Nigeria in early 2014.

Evidence of Impact of Interventions

There is now significantly more evidence available, including from Senegal, Mali, Nigeria, Sudan and Uganda, to show that transmission of onchocerciasis can be interrupted in Africa, most often by using mass distribution of ivermectin once (Senegal, Mali)[3] or twice (Sudan)[4] per year, or by annual mass distribution of ivermectin and control of the vector *Simulium neavei*

[3] Diawara L et al. Feasibility of onchocerciasis elimination with ivermectin treatment in endemic foci in Africa: first evidence from studies in Mali and Senegal. *PLoS Negl Trop Dis* [electronic resource], 2009, 3(7):e497 doi: 10.1371/journal.pntd.0000497.

[4] Higazi et al. Interruption of Onchocerciasis Transmission in the Abu Hamed Focus, Sudan. *Am J. Trop Med Hyg* 2013; 89: 51-57.

(Uganda)[5] thus also showing the value of flexible approaches to interventions and combinations of interventions. Additional proof that transmission of LF can be stopped by annual MDA with ivermectin and albendazole and/or by mass distribution of LLINs is also now published from Togo[6] and Nigeria[7,8]. APOC believes interruption of onchocerciasis transmission will be most problematic and require the longest time (from now), in Central African Republic, Democratic Republic of Congo, and South Sudan.

A consortium led by WHO is analyzing and developing cost projections for implementation of current interventions envisioned to eliminate both diseases by 2020.

In Mozambique, mapping of onchocerciasis revealed that many areas that are hypo-endemic for that disease had already received MDA for LF (which also treated onchocerciasis) for several years. The Mozambique experience illustrates the importance and utility of overlaid maps showing distribution of onchocerciasis, LF and loiasis at district level. See also paper by Okorie et al on microstratification overlap mapping in Nigeria.[9] It also highlights the need to measure the impact of MDA treatments for one disease on the other.

The ITFDE noted the continued progress achieved by the Onchocerciasis Elimination Program for the Americas (OEPA) where, in 2012 Colombia became the first country to be verified by WHO as having eliminated onchocerciasis, and where all but two of the 13 originally endemic foci (in southern Venezuela and adjacent northern Brazil) in the Americas have interrupted transmission. As in the Americas, attention to transmission in cross-border foci is an important rationale and justification for the regional approach being taken to eliminate onchocerciasis and LF in Africa.

Research Needs

Better diagnostic tools are needed in order to assess when MDA can be safely halted, to confirm whether transmission has been eliminated, and to find the last cases of disease. It appears at least one improved diagnostic tool will become available for general use later in 2014, namely an Ov16/Wb123 biplex rapid diagnostic test that is anticipated to be suitable for dual surveillance of onchocerciasis and LF infections. It was also suggested that detailed maps of the genomes of *Onchocerca* and *Wuchereria* parasites might be useful tools for tracing sources of parasites (the genome of *Onchocerca volvulus* has been mapped already).

[5] Lakwo et al. The disappearance of onchocerciasis from the Itwara focus, western Uganda after elimination of the vector *Simulium neavei* and 19 years of annual ivermectin treatments. *Acta Tropica* 2013; 126:218—221.
[6] Sodahlon et al. A Success Story: Togo Is Moving toward Becoming the First Sub-Saharan African Nation to Eliminate Lymphatic Filariasis through Mass Drug Administration and Countrywide Morbidity Alleviation. *PLoS Negl Trop Dis* 2013; 7(4): e2080. doi:10.1371/journal.pntd.0002080.
[7] Eigege et al. Long-lasting insecticidal nets are synergistic with mass drug administration for interruption of lymphatic filariasis transmission in Nigeria. *PLoS Negl Trop Dis* 2013; 7(10): e2508.
[8] Richards et al. Community-wide distribution of long lasting insecticidal nets can halt transmission of lymphatic filariasis in southeast Nigeria. *Am J. Trop Med Hyg* 2013; 89: 578-87.
[9] Okorie et al. Lymphatic Filariasis in Nigeria; Micro-stratification Overlap Mapping (MOM) as a Prerequisite for Cost-Effective Resource Utilization in Control and Surveillance. *PLoS Negl Trop Dis* 2013;7(9):e2416. doi: 10.1371/journal.pntd.0002416.

In a brief discussion of research pertaining to the development of drugs that would be effective against the adult stages of the parasites (macrofilaricides), it was noted that the Bill & Melinda Gates Foundation is supporting new uses of existing drugs (e.g., ivermectin and albendazole), including increased dosages and frequency of administration; new drugs such as flubendazole; doxycycline for LF (4 weeks) and onchocerciasis (6 weeks); and screening of new drugs in on-going efforts to identify a practical way to kill adult parasites of either or both diseases and so shorten the time needed for elimination.

Conclusions and Recommendations

1. There has been significant progress in efforts to eliminate onchocerciasis and lymphatic filariasis (LF) in Africa since the ITFDE first discussed this topic (collaborative assault on these two diseases in Africa) nearly three years ago. There is increased evidence that both diseases are eradicable, the feasibility of onchocerciasis elimination in Africa has been embraced by APOC, at least five African governments have established national goals of onchocerciasis elimination, and coverages with MDA for both diseases and LLINs have also improved.
2. Interventions against both diseases provide exceptional value for money, are relatively inexpensive (given the generous donations of drugs), are pro-poor and help to alleviate poverty directly, but both programs are still neglected financially, especially the efforts to eliminate LF.
3. In order to meet the current goals to eliminate LF by 2020 and onchocerciasis by 2025, mapping of LF and supplemental mapping of hypo-endemic onchocerciasis areas need to be completed by 2014 and 2015 respectively, while available funding and interventions for elimination of LF need to be scaled up much more rapidly.
4. The ITFDE believes that the logic for "fusion" of onchocerciasis/LF/malaria programs at local, national and continental levels in Africa is compelling, with mutual benefits such as the additional impact of MDA with ivermectin for LF or onchocerciasis on malaria, the impact of LLINs on transmission of LF and malaria, and the impact of MDA with ivermectin and albendazole for LF on onchocerchiasis, in addition to the operational efficiencies expected from such coordination.
5. There is new evidence of safe interventions to stop transmission of LF in areas where *Loa loa* is endemic, and potential strategies for doing so for onchocerciasis as well, but more research on the latter is needed urgently.
6. The ITFDE endorses support for interventions against the entire package of Preventable Chemotherapy (PCT) Neglected Tropical Diseases (NTDs), but urges special attention to increased support for onchocerciasis and LF, which are being targeted for elimination of transmission. Within the campaign against LF and onchocerciasis in Africa, only three countries—DRC, Ethiopia and Nigeria—account for over one-third and over one-half of the burden respectively of those two diseases in Africa, and should thus be considered priorities for early assistance.

7. Given the complexity of associated technical issues, there is need for authoritative, clear, sound, and timely advice to countries on technical aspects related to elimination of onchocerciasis and LF in Africa, such as uptake of flexible new strategies or of interventions shown to have worked elsewhere; criteria for deciding when to stop MDA for either or both diseases; and monitoring during post treatment surveillance, for example.
8. More useful diagnostic tools for assessing the prevalence of LF and onchocerciasis have been developed and are expected to be deployed more widely soon after more validation studies are completed. The Bill & Melinda Gates Foundation also is investing heavily in supporting efforts to identify effective macrofilaricides for adult *Onchocerca* and *Wuchereria* parasites, including testing existing drugs, screening new compounds, and testing combinations of drugs, but a practical macrofilaricide is not expected for either parasite in the near future.
9. The Task Force notes the ongoing development of cost projections for joint implementation of LF and onchocerciasis elimination programmes and urges these to be completed and made available as soon as possible to inform discussions with donors.
10. The Task Force commends Nigeria for its progress in combatting onchocerciasis, LF, and malaria, and congratulates the Federal Ministry of Health of Nigeria on its soon to be published Guidelines for Malaria-Lymphatic Filariasis Co-Implementation in Nigeria.