



NIGERIA ONCHOCERCIASIS ELIMINATION PLAN



February, 2017

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Nigeria Onchocerciasis Elimination Plan

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EXECUTIVE SUMMARY

Nigeria, a sub-Saharan country, is located on Latitude 8⁰ E and Longitude 10⁰ N and spans a land mass of 923,768sq km. It is made up of six geo-political zones comprising 36 States, a Federal Capital Territory, and 774 Local Government Areas (LGAs). The national population is projected at over 170 million from the 2006 census.

Human infection with the filarial parasite *Onchocerca volvulus* (onchocerciasis, also known as 'river blindness'), one of the Neglected Tropical Diseases (NTDs) is of public health significance in Nigeria. More than 99% of all cases of onchocerciasis and onchocercal-related blindness are found in Africa; with Nigeria having the greatest burden of the disease (about 40% of the global population at risk). Nigeria has about 50 million persons in over 40,000 communities at risk. Blindness and severe skin manifestations are two major effects of the disease on affected populations with severe effects on affected communities. Onchocercal blindness is the world's fourth leading cause of preventable blindness after cataract, glaucoma and trachoma. The disease is significantly a disease of the poor with economic implications resulting in further impoverishment of affected communities, a challenge to the achievement of SDGs 2 and 3 and national developmental goals. It was, until recently, a major cause of blindness in many rural communities across the nation. Other socio-economic effects of infection with onchocerciasis include abandonment of farmlands leading to food insecurity; poor school attendance sometimes resulting from children having to drop out of school to assist blind parents/guardians; terrible itching and, skin disease and disfigurement leading to stigmatization. The infection is transmitted by several species of *Simulium* vector, black flies that breed in rapidly flowing streams and rivers.

The scenario is however changing given over two decades of interventions - mainly through annual mass administration of ivermectin (Mectizan^R) donated by Merck for treatment in endemic communities. Between 1990 and 1995, a series of mapping surveys were conducted which showed that onchocerciasis was prevalent in most States of Nigeria, except Rivers, Bayelsa, Lagos and Katsina. Nigeria accounts for the highest disease burden in sub-Saharan Africa with about 50 million people in over 40,000 communities at risk. Over 30 million Nigerians in more than 36,000 communities are being treated annually through

Mass Administration of Medicines (MAM) using Merck-donated ivermectin, coordinated through the Mectizan Donation Program (MDP). Several States and FCT have reached and maintained good geographic and therapeutic coverage for more than 10 years.

Following the emergence of evidence that onchocerciasis could be eliminated in Africa with Ivermectin, a national plan is now needed to guide Nigeria's progress towards interruption of human onchocerciasis by year 2020 and its ultimate elimination by year 2025. The goal of the onchocerciasis elimination agenda is to push transmission of *Onchocerca volvulus* infection to the point where the parasite population is irreversibly moving to its extinction in all onchocerciasis transmission zones by 2020, at which point all MAM can be halted. Ultimately, this plan will result in Nigeria obtaining WHO verification, by 2025, of country-wide transmission elimination. Post-elimination surveillance (Phase 3) will commence and continue beyond 2025.

The general objective of this document is to domesticate WHO 2016 onchocerciasis elimination guidelines to provide a national road map on the elimination of onchocerciasis transmission in Nigeria. This roadmap can be widely used at all levels, from policy makers to programme managers.

Stopping MAM will be considered when continuous MAM implementation with sufficient geographic and therapeutic coverage in the area during phase 1 (treatment phase) indicates it is safe to do so. Based on WHO guidelines, entomological and serological evaluations will be undertaken for the purposes of 1) assessing interruption of transmission either for stopping MAM, and 2) to confirm elimination of transmission after 3 - 5 years of post-treatment surveillance.

Assessments for the purpose of stopping MAM or for post-treatment surveillance will need to take into account local transmission dynamics. This may require separate evaluations in multiple areas in a single State (e.g. a separate evaluation for each river basin) or simultaneous evaluations in an adjoining State. **In the preparation of the national dossier for verification, the NOEC will pay close attention to assuring that data exist to support any WHO concerns that may arise pertaining to potential cross state transmission zones.**

ACRONYMS

ABR	Annual Biting Rate
APOC	African Programme for Onchocerciasis Control
ATP	Annual Transmission Potential
CBD	Community Based Distributor
CDD	Community Directed Distributor
CDI	Community Directed Intervention
CDTI	Community Directed Treatment with Ivermectin
DNA	Deoxyriboneucleicacid
ELISA	Enzyme Linked Immunosorbent Assay
FCT	Federal Capital Territory
FGN	Federal Government of Nigeria
FMOH	Federal Ministry of Health
IDSR	Integrated Disease Surveillance and Response
IEC	Information Education Communication
IVT	International Verification Team (under auspices of WHO)
LF	Lymphatic Filariasis
LGA	Local Government Area
MAM	Mass Administration of Medicine
MBR	Monthly Biting Rate
mf	Microfilariae
MoH	Ministry of Health

NOCP	National Onchocerciasis Control Programme
NOEP	National Onchocerciasis Elimination Programme
NGDO	Non-Governmental Development Organisation
NOEC	National Onchocerciasis Elimination Committee
NPC	National Population Commission
NTD	Neglected Tropical Disease
OV16	Recombinant antigen of <i>O. volvulus</i> used in serological testing
PCR	Polymerase Chain Reaction
PTS	Post Treatment Surveillance
RDT	Rapid Diagnostic Test
REA	Rapid Epidemiological Assessment
REMO	Rapid Epidemiological Mapping of Onchocerciasis
SAE	Severe Adverse Event
SBR	Seasonal Biting Rate
STP	Seasonal Transmission Potential
WHO	World Health Organization

FOREWORD

River blindness (Onchocerciasis) is a neglected tropical disease that poses public health challenge with about 50 million Nigerians affected or at risk. However, with the support of partners and the World Health Organization (WHO) African Programme for Onchocerciasis Control (APOC), the Federal Government in collaboration with the State governments, initiated and scaled up community education programmes and bolstered mass distribution of Ivermectin (generously provided by Merck) over the last 15 years.

These interventions have led to decreased levels of infection and very significant reduction in disease burden as results of several epidemiological assessments conducted over the past 4 years have indicated zero or low prevalence in selected foci.

We are at a threshold where, with a final push, over the next few years, onchocerciasis will be consigned to the annals of history. Just as we have eliminated Guinea Worm Disease, we look forward to being assessed by WHO for elimination of Onchocerciasis. Our vision is to reduce local Onchocerciasis infection and transmission to such low levels that its transmission can no longer sustain itself and treatment can be safely stopped without risk of recrudescence of infection and transmission. It is in consideration of this that structures have been established to drive the elimination process in Nigeria and ensure that set targets are met.

This document which was developed in collaboration with our partners and stakeholders, will serve as a strategic guide on the elimination of onchocerciasis transmission in Nigeria.

I wish to reiterate the commitment of the Federal Government of Nigeria to ensuring that Onchocerciasis is eliminated in Nigeria in line with the global targets.



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Honourable Minister of Health, Federal Ministry of Health

ACKNOWLEDGEMENT

On behalf of the Federal Ministry of Health (FMOH), I wish to thank the membership of the National Onchocerciasis Elimination Committee for their commitment and dedication towards the development of this guideline.

Also worthy of note is the commitment and support to the Government of Nigeria by individuals, donors and a coalition of Non-Governmental Development Organizations (NGDOs) for Onchocerciasis elimination; United Nation Agencies; African Programme for Onchocerciasis Control (APOC); Expanded Special Project for Elimination of NTDs (ESPEN); Sir Emeka Offor Foundation; Dr. Frank Richards of The Carter Center Atlanta; Dr. Emmanuel Miri - Country Representative, The Carter Center Nigeria; Dr. Vitalino Cama of CDC Atlanta; Dr. Rory Post - Honorary Professor London School of Hygiene & Tropical Medicine and Honorary Research Fellow, Liverpool John Moores University; Dr. Paul Cantey, Focal Person Onchocerciasis Elimination, WHO, Geneva and Professor Daniel Boakye of WHO, Ouagadougou. The financial, technical and logistic supports provided by these stakeholders are immensely appreciated.

I wish to commend the contributions of staff of National Onchocerciasis Elimination Programme and the entire NTDs for their support and active participation in the process of developing this document.



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CHAPTER 1: ONCHOCERCIASIS CONTROL IN NIGERIA

1.1. Background

Nigeria, a sub-Saharan country, is located between Latitudes 04-14^oN and Longitudes 03-15^oE. It spans a land mass of 923,768 sq km that stretches from the northern Sahelian climate through Savannah to Rain Forest and Mangrove swamp in the southern limit where it is bound by the Atlantic Ocean. It is further bounded by three countries namely: Cameroon in the east, Benin Republic in the west and in the north by Niger. On its North-eastern extremity is the Lake Chad that is central to Niger, Cameroun and Nigeria.

Nigeria is made up of six geo-political zones comprising 36 States, a Federal Capital Territory (Abuja), and 774 Local Government Areas (LGAs). The country operates a federal system of government with the Executive, Judiciary and a bicameral Legislative arm (the Senate and House of Representatives (FGN, 1999). The Federal Government of Nigeria (FGN) is headed by an elected President. Each federating unit (State) has three arms namely: Executive, Judiciary and Legislative. The State Government is headed by an elected Governor. Each State is made up of LGAs, the lowest administrative level of government. Each LGA is governed by an elected Chairman and a Legislative Council.

The national population census of 2006 gave the country's population as 140,431,790 (NPC, 2006). An annual population growth rate of 2.5% gave a projected population of over 170 million for 2015. The population distribution is as follows: 0-6months 4%, under 5 years is 20%, under 15 years is 47.6% and 15 years and above is 29.4%. The rural: urban population is at ratio of 45:55 (NPC, 2006).

1.2. Onchocerciasis Epidemiology

Human onchocerciasis (river blindness) is one of the Neglected Tropical Diseases that is of public health significance in Nigeria. Onchocerciasis is a parasitic disease caused by infection with the nematode worm *Onchocerca volvulus* (Crump, 2012). It is the world's second-leading infectious cause of blindness. The disease occurs in 35 countries: 31 in

Africa, 3 in Latin America and in Yemen (WHO, 2016). More than 99% of all cases of onchocerciasis and onchocerciasis-related blindness are found in Africa (WHO, 1995). Onchocerciasis is the world's fourth leading cause of preventable blindness after cataract, glaucoma and trachoma. The disease has been a major obstacle to agricultural development of fertile river valleys and the establishment of rural communities near rapidly flowing rivers in Africa (WHO, 2002).

The parasite is transmitted to humans by bites of certain *Simulium* species (black flies) that breed in fast flowing, well-oxygenated rivers and streams. It is in these streams and rivers that the female fly lays her eggs and the larval stage of the vector develop and pupate. Human populations living or working near vector breeding sites are at greater risk of infection.

In Africa it is only members of the *Simulium damnosum* complex and the *Simulium neavei* group which are known to transmit onchocerciasis (which is caused by *O. volvulus*), and the *S. neavei* group does not occur in Nigeria. However, other species of blackflies which will occasionally bite humans in Nigeria (for example *Simulium bovis* and *Simulium vorax*), but these are not known to be vectors of human onchocerciasis. *Simulium damnosum* s.l. is not a single species but a complex of sibling species. These are closely related species which are morphologically more or less indistinguishable but they are biologically incompatible (Vajime & Dumbar, 1975). In Nigeria there are known to be nine sibling species within the *S. damnosum* complex, and they probably all transmit onchocerciasis (Post et al., 2011). The distribution of disease is relegated to 'transmission zones' that are dependent on the presence of suitable numbers of vectors (and their associated ecology) and exposed infected humans.

In the human host, the adult worms of *O. volvulus* live mainly in subcutaneous nodules, which are often palpable, where the female worms (during their 9-14 years of active reproductive life) give birth to millions of microfilariae (mf). The mfs are predominantly found under the epidermis in subcutaneous tissues where they are picked up by female *Simulium* black flies during their blood meals. Microfilariae ingested by a vector can undergo two moults over the course of a week to become infective third stage filariform larvae, which can then be successfully transmitted to another person when the vector takes

another blood meal. No animal or environmental reservoirs exist for *O. volvulus*. An overwhelming majority of the skin dwelling mfs are never ingested by the female black flies; so these mfs eventually die in the human tissues after about two years. The dead mfs herald complex immunological manifestations leading to the dreaded onchocercal skin disease and intense itching, lymphatic complications (lymphadenitis resulting in hanging groin) and ocular lesions (impaired vision and blindness) as well as systemic manifestations. The socio-economic effects of the disease include: abandonment of farmlands leading to food insecurity; children dropping out of school to assist blind parents/guardians; skin disfigurement leading to stigmatization. Even when transmission is interrupted, adult worms that remain are a threat because they can re-establish transmission for 9-14 years (although there is strong evidence that MAM with ivermectin shortens worm lifespan to some degree). The current strategy against onchocerciasis that has been adopted by Nigeria is MAM to break the transmission cycle and maintain that condition for the duration of the lifespan of the adult worms in the human population.

1.3 The Onchocerciasis Public Health Burden

Parsons first reported the presence of onchocerciasis in northern Nigeria in 1908 (Budden, 1956). In 1926, the mf of *Onchocerca volvulus* were observed in 55 prisoners in Kaduna. In a letter to the Director of Medical Services in 1937, Dr. J. L. Mcletchie reported ocular onchocerciasis among a group of elderly persons in the Adamawa province (Budden, 1956). However, only in the early 50s was the disease regarded with some seriousness (Patterson, 1974). Between 1951 and 1954, ocular onchocerciasis was prevalent in various parts of northern Nigeria, and was reported as the second leading cause of blindness (Budden, 1952). Distribution of the vector *Simulium damnosum* was found to be widespread in Sokoto, Niger, Adamawa, Benue, Kabba, and Zaria provinces with Abuja inclusive (Crosskey, 1956; Crosskey, 1957). Budden (1956) estimated the number of infected persons at 339,000, and about 20,000 blind due to onchocerciasis. Additional reports indicated presence of the disease in the southern part of the country (Jiya, 1998; NGDO, 2011).

In order to accurately establish the distribution of the disease in the country, between 1990 and 1995, a series of mapping surveys were conducted using the methods of

the Rapid Epidemiological Mapping of Onchocerciasis (REMO) and the Rapid Epidemiological Assessment (REA). These methodologies were developed by APOC and used extensively throughout sub-Saharan Africa. It should be noted that while REMO/REA have proven to be very useful tools for mapping hyper and meso - endemic areas of Onchocerciasis, they were not developed to detect active transmission in areas with low infection prevalence.

The results of these surveys indicated that the disease was present in all States of Nigeria, although in Lagos, Katsina, Bayelsa and Rivers it was not a significant health problem (FMOH, 2015). Nigeria accounts for the highest disease burden in sub-Saharan Africa with about 50 million persons at risk living in over 40,000 communities at risk. Until recently, it was a major cause of blindness in many rural communities across the nation.

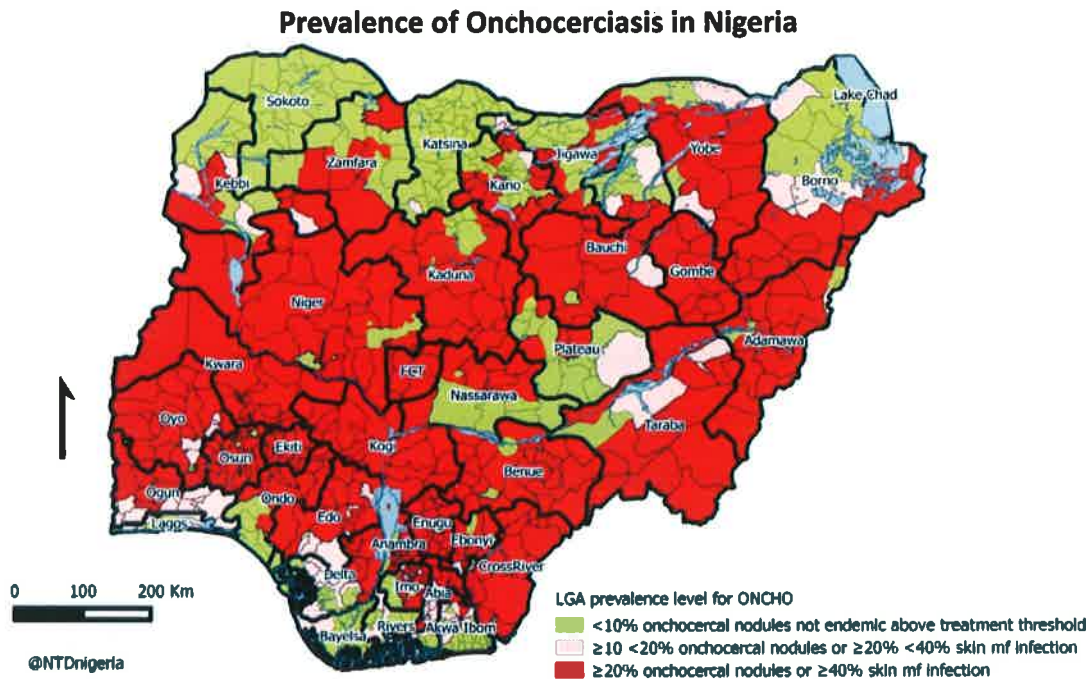


Figure 1: Pre-intervention Onchocerciasis prevalence map based on the Rapid Epidemiological Mapping for Onchocerciasis (REMO) approach (Source: APOC/FMOH, 1998)

1.4 National Onchocerciasis Elimination Committee (NOEC)

There is considerable evidence that onchocerciasis can be eliminated in Africa with Mass Administration of Medicines (MAM) using ivermectin (Diawara et al. 2009; Cupp et al. 2011b; Tekle et al. 2012; Higazi, 2013; Katarbarwa et al. 2014; Evans et al. 2014). MAM has

been on-going over almost two decades in Nigeria, with different States at different stages of interventions. In some places where treatment has been on-going consistently there is evidence that the transmission status has changed significantly with zero prevalence being recorded in evaluated villages (Tekle et al. 2012, Evans et al. 2014). In addition, with the 2015 closure of the African Programme for Onchocerciasis Control (APOC) and the 2016 release of new World Health Organization (WHO) guidelines for stopping MAM in onchocerciasis endemic areas (WHO, 2016), the Federal Ministry of Health (FMoH) was challenged to take on greater responsibility to drive the technical and programmatic process toward transmission elimination in Nigeria. Consequently, the Honourable Minister of Health in 2015 inaugurated a National Onchocerciasis Elimination Committee (NOEC) to report directly to his office in providing national guidelines and to oversee the process of assessing interruption of transmission, stoppage of MAM treatments, the post-treatment surveillance stage, and final preparation of a dossier to request national verification of elimination of onchocerciasis transmission in Nigeria from WHO.

A national plan is a *sine qua non* to guide the country's progress towards interruption of transmission of human onchocerciasis in Nigeria by year 2020 and ultimate elimination by year 2025. The guideline will also inform when to stop MAM where transmission of the parasite has been interrupted. This guideline will be invaluable in determining whether Nigeria has eliminated transmission of *Onchocerca volvulus* in compliance with international standards as captured in the WHO guidelines for stopping MAM and verifying elimination of human Onchocerciasis (WHO, 2016).

1.5. Co-endemicity between onchocerciasis and other NTD

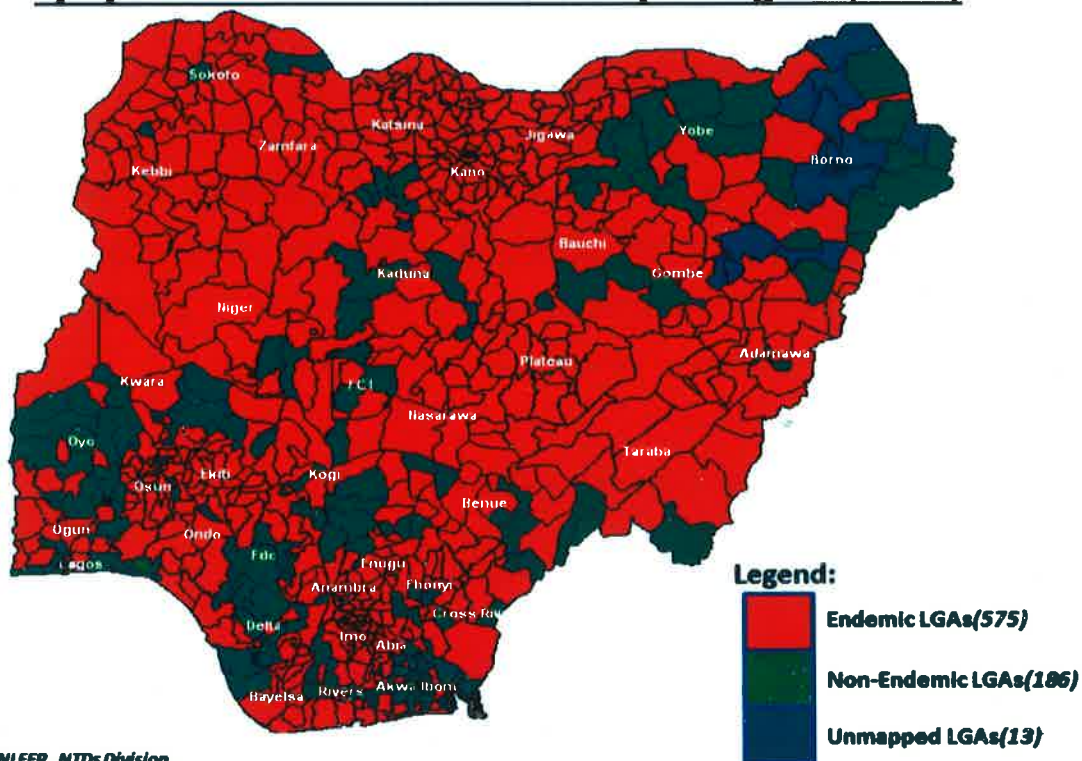
1.5.1. Co-endemicity with lymphatic filariasis (LF)

Lymphatic Filariasis is a parasitic disease caused by *Wuchereria bancrofti* and transmitted by mosquitoes mostly of the *Anopheles* species. Adult male and female *W. bancrofti* worms live in the human lymphatic channels, and fertilized female worms produce mf that enter the blood stream and circulate during the night. The common clinical signs include lymphoedema and elephantiasis of the extremities, febrile lymphadenitis attacks and hydrocele of the scrotum in men. Nigeria has the highest burden in Africa and is the third

most endemic country globally with 114 million people in 539 LGAs (Figure 2) are at risk of infection (over twice the number at risk for onchocerciasis). The National Lymphatic Filariasis Elimination Programme was established in 1997 with the objectives of interrupting transmission of the disease as well as managing morbidity and prevention of disability in victims by 2020. The transmission is interrupted by MAM with albendazole (generously donated by GWK) and (as with onchocerciasis) Mectizan.

Many States in the country are co-endemic for onchocerciasis and mapping results using rapid diagnostic tests for circulating LF antigens show co-endemicity of onchocerciasis with LF in 310 LGAs across the country. It is important to note that LF is also targeted for elimination in Nigeria, and ivermectin MAM is used (combined with albendazole) to break transmission of that parasite by 2020. As such the two elimination programmes require an important degree of coordination of field activities.

Lymphatic Filariasis Prevalence Map of Nigeria (Nov.'16)



Source: NOCP/NLFEP, NTDs Division
Dept of Public Health, FMOH Nigeria

Figure 2: Map of LF endemicity in Nigeria (2016).

complications in prolonged coma events. Only individuals with *Loa loa* mf densities >30,000/ml of blood are at risk of these serious adverse events (SAEs) (Gardon et al. 1997). Almost all *Loa loa* neurological reactions associated with MAM for onchocerciasis have been reported from MAM programmes in Cameroon and the Democratic Republic of Congo (Twum-Danso et al. 2003). For reasons currently unknown, neurological reactions have rarely been reported in Nigeria, despite years of ivermectin MAM in *Loa loa* endemic areas of southern Nigeria (Takougang et al. 2002, Twum-Danso et al. 2003, Ojurongbe et al. 2015). In fact, only one questionable neurological reaction has been reported (in the 2003 report by Twum-Danso) after well over 150 million treatment episodes provided over 19 years in *Loa loa* endemic areas in Nigeria.

A technique called the Rapid Assessment Procedure for *Loa loa* ('RAPLOA') was developed over a decade ago to quickly and noninvasively assess an area targeted for ivermectin MAM to assess the risk for *Loa loa* related SAEs. RAPLOA, which has been employed in 2014 and 2015 in areas of Nigeria by the FMOH, uses a questionnaire survey along with a photograph of a *Loa loa* worm in the eye to determine if the respondent has experienced a worm moving across the surface of his/her eye. If >40% of residents answer yes, then calibration research outside of Nigeria has shown that the prevalence of *Loa loa* microfilaremia is >20% in the community, and the likelihood of high density *Loa loa* (>30,000/ml) is >3% (Wanji et al. 2001; Diggle et al. 2007; Tekle et al. 2011; Zoure et al. 2011). According to WHO and the Mectizan Donation Programme (MDP), these criteria (RAPLOA>40%, and/or *Loa loa* microfilaremia>20% and/or high density *Loa loa* >3%) define an area at high risk for *Loa loa* neurological reactions (MDP, 2000; MDP, 2004; Diggle et al. 2007).

At its meeting in May 2015, the Nigeria Onchocerciasis Elimination Committee (NOEC) discussed *Loa loa* in Nigeria and the risk of SAEs with MAM. It noted that tens of millions of MAM ivermectin treatments for onchocerciasis have been given over the past two decades in CDTI programmes operating in *Loa loa* endemic areas of Nigeria. The NOEC noted that FMOH and partners have had no reports over this time-period of the central nervous system severe adverse events (CNS SAEs) compared to frequently observed CNS

SAEs in MAM programmes in *Loa loa* endemic areas in Cameroon and DRC (D'Ambrosio et al. 2015).

A recent survey of high intensity *Loa loa* in southern Nigeria used the *Loa* Cellscope in 110 villages with historical RAPLOA findings between 10-67%. The study found a maximum of only 11,429 mfs/ml in over 10,500 people examined; no individuals were found to have > 20,000 mfs/ml (TCC 2016, unpublished data). These findings indicate that in this part of Nigeria RAPLOA is not a predictor of populations at risk for CNS SAEs, and explains the lack of reports of such CNS SAEs in Nigeria. Ivermectin MAM is therefore safe in the six surveyed States (Edo, Delta, Anambra, Abia, Ebonyi and Enugu). Similar *Loa* Cellscope surveys are needed in other areas of Nigeria where onchocerciasis and high RAPLOA Loasis are co-endemic.

CHAPTER 2: SITUATION ANALYSIS AND CONTROL STATUS

2.1. Historical Perspective

Human onchocerciasis was first reported in Nigeria in 1909 when a certain disease pathogen, then known as *Filaria volvulus* was observed in four Nigerians at Lokoja but coming from Kabba, Onitsha, and Tola (Parsons, 1906). This was later followed by the first published record of black flies, captured by Dr. R. W. Gray in 1906 at Cross River (Austen, 1909). Several other reports such as the occurrence of microfilariae of *Onchocerca volvulus* in the skin of 55 out of 100 prisoners at Kaduna (Dyce, 1926); onchocercal nodules, visual impairment and total blindness in elderly people in Adamawa Province (Budden, 1956); Skin manifestation in Enugu, Eastern Nigeria; Ibadan, Southwest Nigeria; and Ikom, South South near Nigeria-Cameroon border (Nwokolo, 1950; Crosskey, 1979). These reports firmly established the presence of human onchocerciasis and its vector in Nigeria. Following these reports, the then government in existence initiates vector control measures along Enugu Oji River, Lokoja Mimi River, Kainji Lake, Kaduna and River Mawal down-stream, Garkida, and in Abuja Emirate (Crosskey, 1958; 1979; Davies, 1963; 1968; Walsh, 1968). Given the rising profile of the disease the WHO in the early 1970s opened a field office in Kaduna with the sole task of conducting research on and control of Onchocerciasis.

2.2. National Onchocerciasis Control Programme in Nigeria

It was in attempt to control the scourge of human onchocerciasis and the debilitating effects of the disease that the Federal Ministry of Health and Social Services established the National Onchocerciasis Control Programme (NOCP) in 1982. As a Division of the Department of Primary Health Care and Disease Control, NOCP, was made functional in 1986 and charged with the responsibility of coordinating all onchocerciasis control activities (including operational research) in the country.

Technical Advisory Committee (TAC) made up of reputable scientists from tertiary institutions was constituted to provide technical guidance to the NOCP (The TAC was later renamed the Onchocerciasis Steering Committee).

With the establishment of NOCP, and in realization of the need to have a comprehensive prevalence data on the disease for successful planning and implementation

of the control programme, NOCP initiated the first extensive and intensive nationwide prevalence survey in 1987/88-1990. This gave NOCP and indeed the international community the first evidence of the distribution of the disease in the country.

Suramin and diethylcarbamazine were used for treatment of the disease in the country but could not be used on a large-scale basis due to their toxicity and the complexity of the dosage schedules needed (Abiose, 1998). A major change occurred when ivermectin (Mectizan^R) was registered in 1987 and in an unprecedented move the manufacturers, Merck & Co. Inc. announced the donation of the drug “for as long as needed” for the treatment of human onchocerciasis (Meredith, Cross and Amazigo, 2012). This donation of ivermectin led to the reorganization of the NOCP in 1987, with task forces established at national, zonal and State levels, and State Onchocerciasis Control Units formed in the endemic States.

Several studies had demonstrated the effectiveness of ivermectin as a microfilaricide for reducing some ocular and dermal manifestations of the disease in infected individuals, as well as reducing transmission of the parasite (Meredith, Cross and Amazigo, 2012). Modeling studies predicted that elimination of infection and interruption of transmission was possible in some areas with ivermectin treatment, but that it might not be feasible in hyper endemic areas. Ivermectin was not macrofilaricidal (e.g., treatment did not immediately kill the adult worms), but it did impede the release of mf by adult female worms for a period of up to six months. In addition, it was determined that repeated treatment would increase the mortality of adult worms. An increased frequency of treatment (six monthly) accelerated the demise of adult worms, reduced the availability of mf to biting vectors, and thus enhanced the feasibility of elimination of onchocerciasis infection and transmission in most settings (Cupp & Cupp, 2005; Cupp, 2011b; Katarawa & Richards, 2014)

For a large scale implementation of Ivermectin treatment across in Nigeria, rapid assessment tool known as Rapid Epidemiological Mapping of onchocerciasis (REMO) was develop. This led to the first REMO mapping in Nigeria.

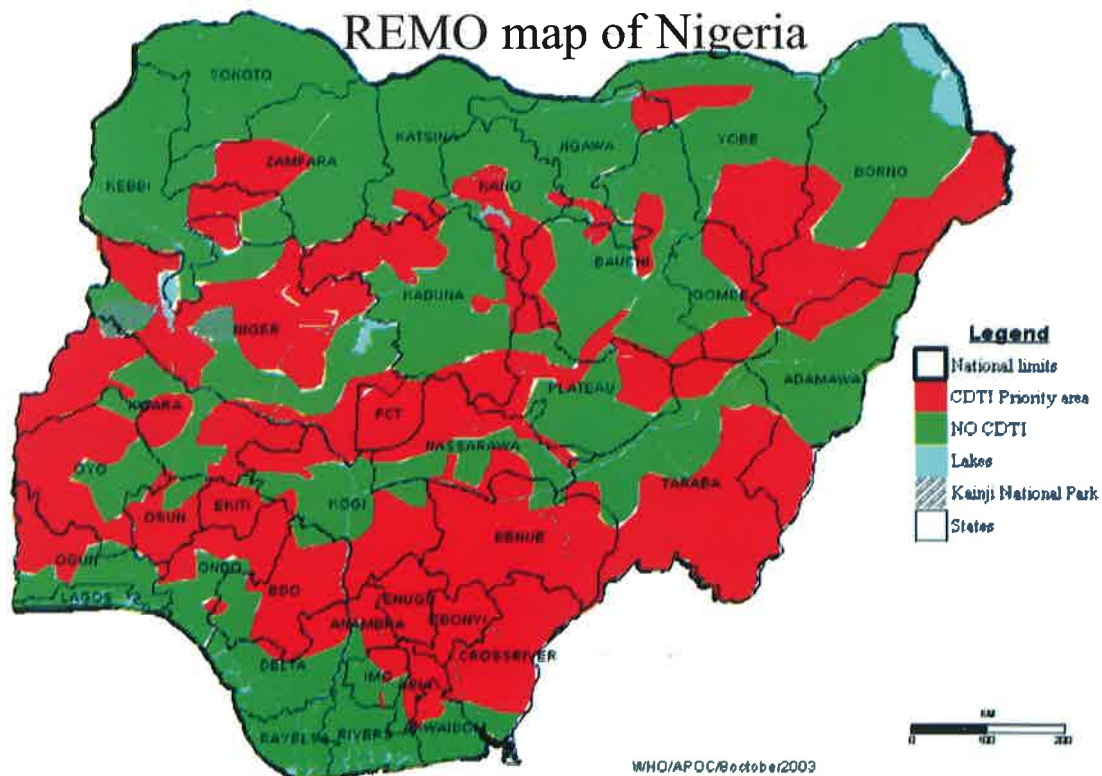


Figure 4: The rapid epidemiological map of onchocerciasis in Nigeria (WHO/APOC WHO (1998). Guidelines for analysis of REMO data using GIS. *TDR/TDF/COMT/98.3*, WHO Geneva.

2.3. The CDTI Strategy

2.3.1. Introduction of ivermectin in Nigeria and early involvement of NGOs

In 1989, after Merck's announcement of the donation of Mectizan^R, the International Eye Foundation (IEF) and Africare obtained a two year grant from the Public Welfare Foundation to support the Ministry of Health in distribution of ivermectin in Kwara State that included some areas in the present Kogi State (Pond, 1990) Ivermectin distribution in Kaduna State was also initiated in 1989 with support from Sightsavers (Tekle et al. 2012).

2.3.2. Mobile treatment

The first strategy for mass distribution of ivermectin in Nigeria was known as mobile treatment using health workers as teams that went into the affected communities to treat all eligible community members. This strategy had its challenges and drawbacks especially with the coverage, both therapeutic and geographic. Other challenges of this strategy

included the substantial cost of implementation both to the NGOs as well as the health system, the reluctance to take the drug by the people in some affected communities due to lack of good health education, and the reluctance of health workers to work in the remote areas where ivermectin was most needed. Treatment coverage was low because the working hours of health personnel coincided with the time people were on their farms, or had other community activities. The health workers did not spend enough time in the villages for communities to understand the purpose of their visit, recognize the potential benefits of ivermectin and the need for long-term use of the drug. Moreover, health workers were unavailable to take care of diverse events where and when they appear (Richards et al. 1996; Miri, 1998).

2.3.3. Community Based Ivermectin Treatment (CBIT)

The realization that the mobile strategy for distributing ivermectin to the communities was bound to be a failure motivated NGOs and health system to devise a new strategy of distributing ivermectin to affected communities, known as Community Based Ivermectin Treatment (CBIT). The CBIT strategy involved the training of Community Based Distributors (CBDs) by the health workers. A drawback in this approach was that the CBDs distributed ivermectin to the community members without the participation of the community leaders. The CBDs held their allegiance to the health workers who selected and trained them for the job. The CBIT strategy had an advantage over the mobile strategy because of the use of community based distributors who were selected from within the community by the health worker.

The CBIT approach was not found to be the best solution to building sustainable distribution of ivermectin because of:

- The dependence of the strategy on the health workers
- The absence of the roles and responsibilities of community leaders
- The absence of community engagement through community entry, advocacy, mobilization, health education and sensitization

- The absence of a sustainable system for procurement of ivermectin tablets from the MoH and delivery to the community level.

2.3.4. The Community Directed Treatment with Ivermectin (CDTI)

With the advent of APOC in 1995, WHO/TDR funded field research on the possibility of the community taking the responsibility for themselves of distributing ivermectin tablets. The communities needed to take ownership of the programme for it to be sustained, as ivermectin distribution might well be required for at least 20 years. In the APOC strategy known as community-directed treatment with ivermectin (CDTI), the community distributors (known as Community Directed Distributors - CDDs) had to be selected by the community within its own members and trained by the health workers. These CDDs, who lived within the community, could treat the eligible population (non-pregnant women and children over five years of age) at convenient time for both the CDD and the community members (APOC, 1998).

The concept of 'Community-Directedness' was introduced by the health services and its partners (NGDOs) in a participatory manner, highlighting community ownership from the onset. From then on, the community took charge of the process, usually through a series of community meetings where the CDDs were selected by the community members. CDDs were motivated (reimbursed) for their work in a way and at a scale determined by the community. The leaders and elders had roles and responsibilities such as storage of ivermectin with the village chief, and seeing that every eligible member of the community took his/her drug. The CDDs selected were trained in the community especially during a community meeting, combined with implementation by the selected community members (APOC, 1998).

The treatment of all eligible persons was accomplished by strategies agreed on by the community (usually either using house to house visits or central location distribution site). The community members were first mobilized and sensitized during a community meeting that they, the members themselves had responsibility for their health system. The community was in this way empowered and encouraged to take responsibility. This strategy

of drug distribution was shown in TDR studies to reach the highest coverages and to be most sustainable. The community, the health services and other partners have specific roles in supervising and supporting CDTI, especially in terms of provision of medicines and monitoring for adverse events.

2.3.5. Community Directed Intervention (CDI)

With the inclusion of other health interventions and commodities that communities needed (such as bednets for malaria and LF), 'CDTI' as a term was shortened to 'CDI' ('Community Directed Intervention'). Community-directed interventions are (as with CDTI) processes built on the experience of community members and thus enhance decision making and problem solving capacity. The community is the lead stakeholder in the provision of services, creating a sense of ownership, and thus enhancing the likelihood that the activities will be sustained, and integrated into the community's health agenda.

2.4. Status of Treatments

In 1997, the NOCP in partnership with the NGDO Coalition adopted the CDTI strategy with support from APOC. The CDTI strategy transferred most of the responsibility for onchocerciasis control to the affected communities and this strategy revolutionized the programme in Nigeria. It led to a massive increase in the number of health staff and community personnel trained, and treatments dramatically increased from about 6 million in 1996 to 35 million by 2014.

The partnership between the Ministry of Health and NGDO Coalition in Nigeria brought about increased and sustained treatment coverage, initiation and expansion of other community-based interventions, as well as the provision of CDDs, which is a huge personnel resource base at the community level contributing to strengthening health systems. It also facilitated access of funds from APOC (which closed in 2015) and the development and scale-up of other CDI interventions in Nigeria.

Over 45 million Nigerians in more than 36,000 communities are now being treated with annual MAM using the donated ivermectin (figure 5). This is 78% of the Ultimate Treatment Goal (UTG), which is calculated by using the treatment eligible population as the denominator. About 10 million Nigerians that were in areas previously classified as hypo-endemic areas are now being included in the UTG treatment target following the shift in FMOH policy from control to transmission elimination. Twenty six of the 31 States and FCT have reached and maintained adequate geographic and therapeutic coverage for more than 10 years. Many hard-to-reach communities are being covered (NOCP, 2013).

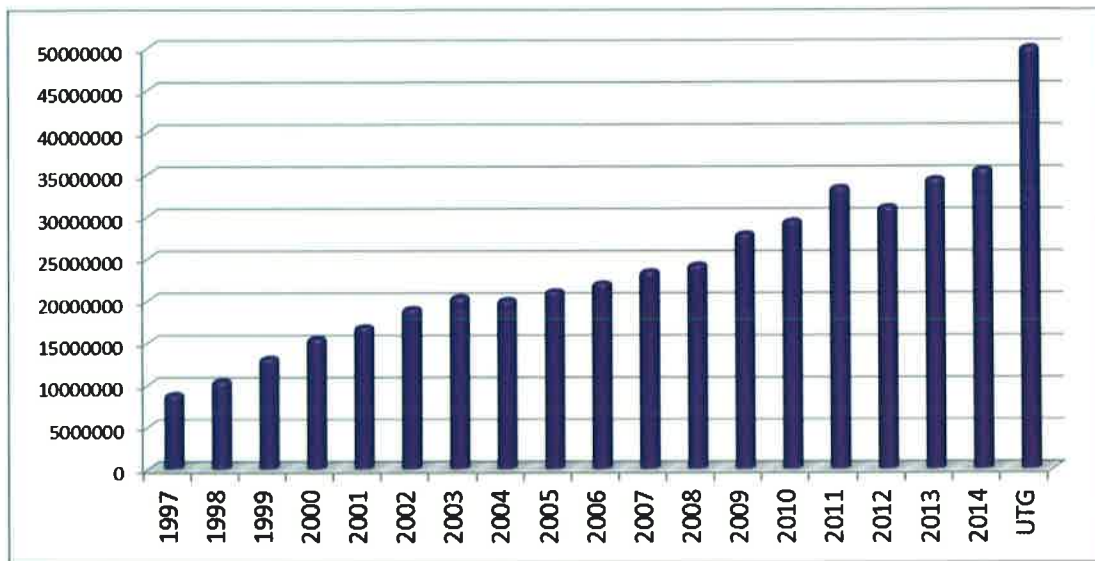


Figure 5: National treatments from 1997 - 2014

Ivermectin treatments in Nigeria are reported to have led to a reduction in symptoms of onchocerciasis and transmission (Abiose, 1998; Jiya, 1998; Emukah et al. 2004; Tekle et al. 2012; Evans et al. 2014). Epidemiological (skin snip) surveys supported by APOC have shown zero prevalence in Zamfara, Kaduna, Ebonyi, Enugu, Osun, Nasarawa, Plateau, Adamawa, Kebbi, Niger, and Kano following 12 to 16 years of Ivermectin treatment. However, very concerning areas of high prevalence have been identified on the Edo-Ondo border, Cross River, Kogi, Taraba and Ogun States (figure 6).

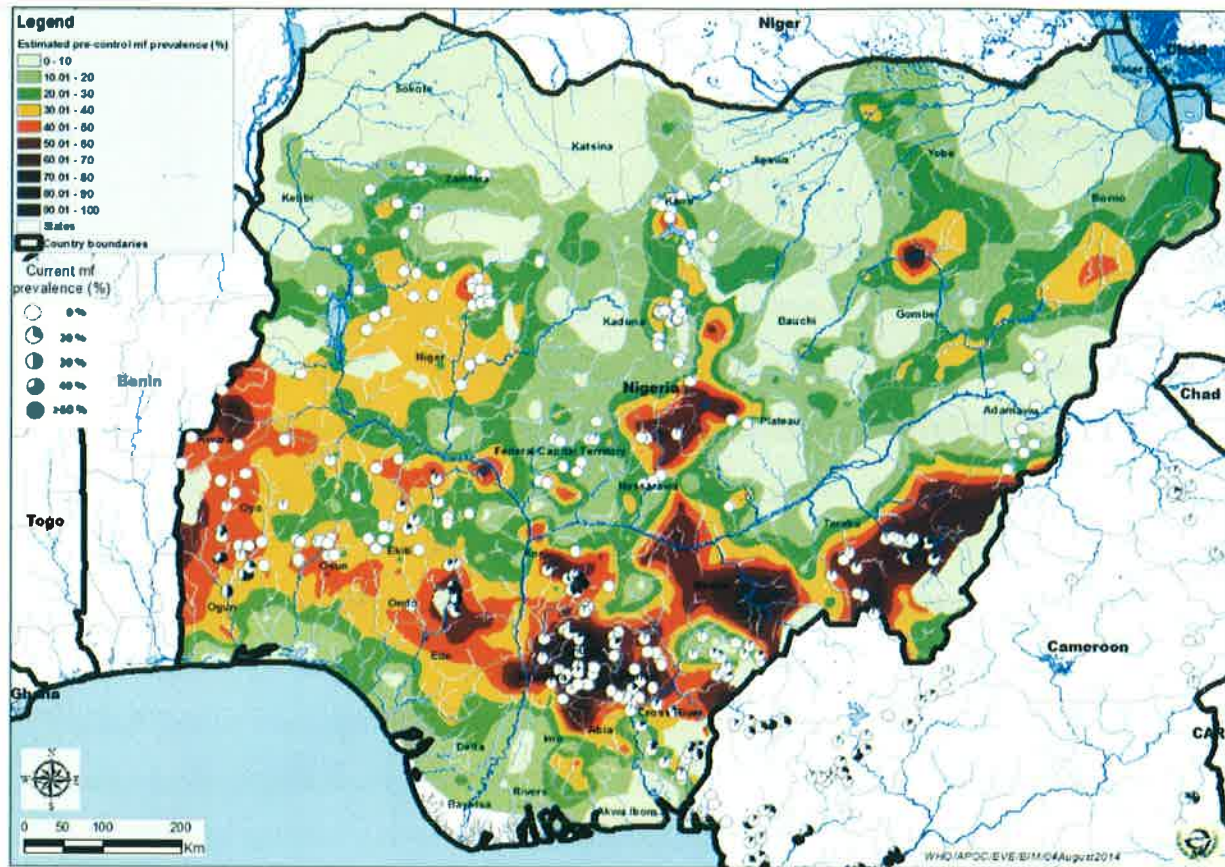


Figure 6: Epidemiological Evaluation Results (mf prevalence based on skin snips) in Nigeria as at August, 2014. Baseline coloring are modeled mf prevalence based on estimates from REMO nodule rates.

CHAPTER 3: THE ELIMINATION AGENDA

3.1. Elimination Context

WHO guideline on elimination of onchocerciasis (WHO, 2016) gives the road map to achieve elimination (figure 6). Longitudinal studies in Mali and Senegal were launched in 2005 to determine whether onchocerciasis could be eliminated by ivermectin MAM alone. The results provided the first empirical evidence in Africa that this was feasible in some endemic foci in Africa (Diawara et al. 2009; Traore et al. 2012). This 'proof of concept' was adopted by APOC to call for elimination of onchocerciasis transmission in most if not all of Africa. Based on this, the Joint Action Forum, which was the governing body for APOC mandated APOC to "determine when and where ivermectin treatment can be safely stopped and to provide guidance to countries on preparing to stop ivermectin treatment where feasible" (APOC, 2010). Since then, new studies have confirmed the feasibility of elimination of onchocerciasis (Zerroug et al. 2016; Katarbarwa, 2014). At the request of APOC, WHO Geneva formed an expert committee to revisit and update the 2001 WHO guidelines (WHO, 2001) for onchocerciasis elimination, a process that was completed and approved by the WHO Guideline Review Committee in 2016. These new WHO guidelines provide the primary orientation for this Nigerian Plan (WHO, 2016).

Figure 6 is taken from the new guidelines and show the conceptual framework for the elimination of onchocerciasis and its ultimate verification by an independent verification team (IVT) constituted under the auspices of the WHO. The Figure shows three arrows with define four stages on the roadmap to elimination as depicted in the WHO guidelines. The first stage (pre-suppression) is characterized by active transmission. The second stage (post-suppression) is characterized by no transmission but a reproductive capable adult worm population. The first and second stages are in the treatment phase. The third stage (transmission interrupted phase) is defined as the time after MAM has been stopped and PTS is in place. The fourth and final stage is after of 3-5 years of PTS with at least one PTS evaluation successfully completed.

The 2016 WHO guidelines come into operational and programmatic consideration at two points:

(1) When the decision is being made for MAM to be stopped (figure 10). In this context, what is being determined is whether onchocerciasis transmission has been suppressed by MAM long enough for the status of the *O. volvulus* adult worm population to be such that recrudescence of infection would be highly unlikely if MAM were stopped. In accordance to WHO guidelines, an assessment survey should be undertaken that establishes that;

- a) infective rates in vectors are $<1/2000$ as determined by O-150 PCR Pool Screen testing with 95% confidence (or if insufficient vectors can be collected to determine if the annual transmission potential [ATP] is < 20) and
- b) infection rates in children under 10 years of age (as determined primarily by OV16 antibody levels in ELISA) are $<0.1\%$ with 95% confidence.

If these conditions can be met, then onchocerciasis transmission is classified as having been 'interrupted' and MAM interventions can be stopped.

(2) The guidelines again come into consideration after the required 3-5-year post treatment surveillance (PTS) period needed to determine if recrudescence will occur; these assessments are primarily entomological. If no recrudescence occurs, then transmission is classified as having been eliminated. Post-elimination surveillance is still necessary for timely detection of recurrent infection, if a risk of reintroduction of infection from other areas remains (APOC, 2010).

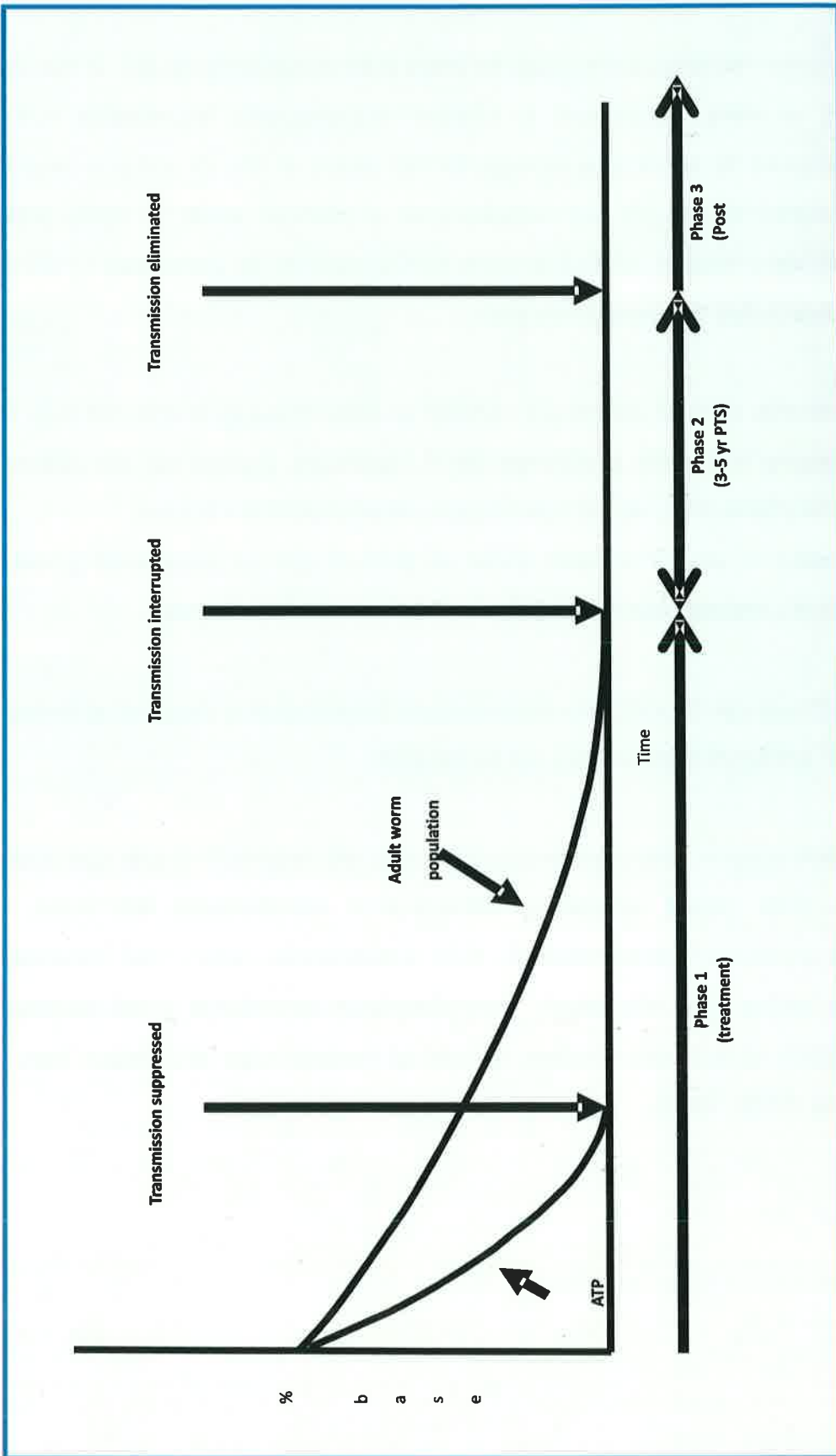


Figure 7: The 3 Phases of Onchocerciasis Elimination (WHO 2016)

3.2. Goals

The goals of the onchocerciasis elimination agenda in Nigeria are to reduce, by 2020, transmission of *Onchocerca volvulus* infection through MAM to the point where the parasite population is irreversibly moving to its demise/extinction in all defined onchocerciasis transmission zones in the country, and MAM will have been stopped nationwide. To achieve, by 2025, verification of nationwide elimination of onchocerciasis by a WHO IVT. Post-elimination surveillance (Phase 3) will likely need to continue until such point that onchocerciasis is eradicated.

3.3. The National Onchocerciasis Elimination Committee

The National Onchocerciasis Elimination Committee is constituted with the objective of providing technical advice to the Minister of Health on onchocerciasis elimination. The committee was formed to be aligned with the 2016 WHO guideline. "The health ministry establishes a national oversight committee to review programme data and validate that the criteria for interruption of transmission have been met." (WHO, 2016).

The NOEC was launched in 2015 and is composed of national and international experts, as well as Federal Ministry of Health staff. The committee's Terms of Reference are as follows:

•Provide technical advice on onchocerciasis elimination to the Federal Ministry of Health;

- a. What are the acceptable breakpoints for onchocerciasis elimination in Nigeria?
- b. What methods will be used to determine where and when these breakpoints have been reached?
- c. What are the best methods/modalities to ensure effective surveillance?

•Support the Government of Nigeria to develop a national guideline and road map for onchocerciasis elimination in Nigeria;

- a. What will be the guidelines for assessing and documenting elimination?
- b. What will be the road map for the country?

c. How much will it cost to provide evidence of elimination?

d. What are the sources of funding to support assessment of elimination?

• Assess where and when breakpoint have been reached and recommend to the Hon. Minister of Health the localities where ivermectin treatment can be safely stopped;

a. Where and when have the breakpoints been reached?

b. What steps would be followed in stopping treatments?

c. What is the overlap with the interventions for other PC-NTDs particularly LF?

• Support the government in the preparation of the country's dossier for verification of Nigeria as having eliminated the transmission of onchocerciasis infection nationwide;

a. What documents/information requirements would be needed?

b. What documents/information requirements are available, and at what level?

c. How can these documents/information requirements be collected and collated?

d. How can these documents/information requirements be prepared for submission?

Over the course of four meetings in 2015 - 2016 the NOEC launched its work with respect to its TOR in developing this Guideline, in collaboration with the FMOH. NOEC intends to review annual progress of the national elimination effort and update the country onchocerciasis status as defined herein, using a visual table colour coded by State, LGA, or focus according to the four stages of elimination depicted in the WHO guidelines. Further, the committee will assesses where and when breakpoint has been reached and recommends to the Hon. Minister of Health the localities where ivermectin treatment can be safely stopped. It will support the preparation and submission of the country's dossier for verification of Nigeria as having interrupted the transmission of onchocerciasis infection nationwide.

3.4. National Nigeria Guidelines for the Elimination of Onchocerciasis

3.4.1. General Objective

The purpose of this guideline is to provide a road map on elimination of onchocerciasis transmission in Nigeria to the FMOH, which could be used broadly, from policy makers to programme managers at all levels.

3.4.2. Specific objectives

- a. Provide detailed guidelines, aligned with WHO recommendations, to programme managers on the 3 phases of the road map: treatment, stopping ivermectin treatments and post treatment surveillance.
- b. To define and delineate transmission zones and evaluation units with respect to oncho elimination in the country.
- c. Develop strategies to be applied in relevant areas to ensure that the interruption of transmission is achieved in all endemic transmission zone, including launching of twice per year treatments, focal vector control, and any other needed intervention dictated by the epidemiological situation and the need to meet the 2020 and 2025 goals.
- d. Provide guidance on how to institute post-treatment surveillance for an appropriate period to demonstrate no recrudescence of transmission so that elimination can be declared; and
- e. Provide guidance on post elimination surveillance for timely detection of recurrent infections, especially if a risk of reintroduction of infection from other areas or neighbouring countries remains.

Table 1: Strategic Targets in 36 states and FCT 2016 - 2020

	Indicators	2016	2017	2018	2019	2020
1	Complete mapping/delineation of oncho endemic areas and the population at risk.	30 (81%)	37 (100%)			
2	Conduct assessments to re - classify States transmission status.	17 (52%)	37 (100%)			
3	Begin implementation of oncho MAM where required including loiasis co-endemic areas.	37 (100%)				
4	Achieve 100% geographical coverage of MAM in Oncho endemic areas of all States	17 (52%)	37 (100%)			
5	Initiate twice per year treatments where required	1 (0%)	9 (26%)	17 (52%)	37 (100%)	
6	Conduct more than 10 annual or 5 twice per year rounds of MAM in endemic States with at least 80% coverage	5 (13%)	5 (13%)	9 (26%)	17 (52%)	37 (100%)
7	Pass WHO criteria for stopping MAM	0 (0%)	0 (0%)	5 (13%)	9 (26%)	17 (52%)
8	Enter post -treatment surveillance (MAM of ivermectin for both onchocerciasis and lymphatic filariasis stopped)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (13%)
9	States completing PTS, country submits dossier	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

3.5. Status of Onchocerciasis in Nigeria and Colour Coding

Given the WHO guidelines and in the light of the status of States, the NOEC has defined a color coding system (figure 8 and table 2). A change in States' color status shall be applicable only after fulfilling the requirements as spelt out in algorithms described in this document and in consultation with the NOEC.

Based on available information and the results of APOC ONCHOSIM modelling, States at the time of the writing of this document have been color-categorized as:

- 1) Green-Transmission Eliminated (0);
- 2) Ash-Transmission Interrupted (0);
- 3) Tan-Transmission Suspected Interrupted (5);
- 4) Red-Transmission Ongoing (8);
- 5) Yellow-On track for elimination by 2025 based on ONCHOSIM (13 including FCT), and 6) Blue-No data/Information (11).

These States are shown by color in the map (figure 8).

It is noted that within a State a Local Government Area (LGA) level micro analysis will indicate that some LGAs within an overall State color code could have classifications that include the Tan, Red, and Yellow color codes described above. Further technical documents will be developed by the FMOH to guide State-level LGA focused elimination activities.

Nigeria Onchocerciasis Elimination: States Classification in 2016

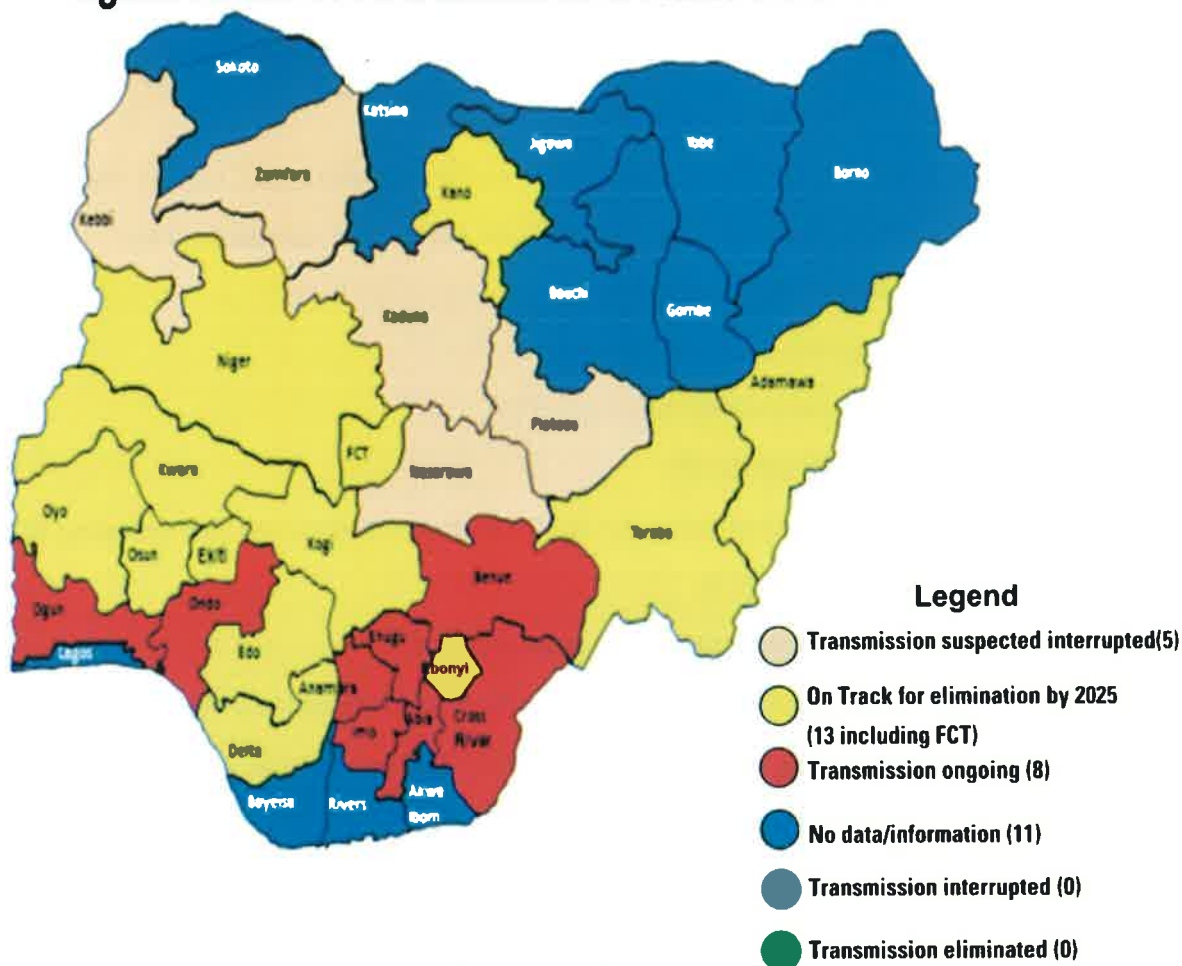


Figure 8: Status of Onchocerciasis in Nigeria in 2016.

3.6. Strategies for Fast-tracking Elimination

Various countries and ivermectin distribution programmes have adopted or are in the process of adopting several strategies to fast-track the elimination process, mainly through increased number of yearly rounds of ivermectin MAM. In some areas, vector control activities have also been implemented. However, ivermectin monotherapy in onchocerciasis-endemic areas retains a central place. Twice-yearly treatments have been initiated in the Americas (CDC, 2013) and parts of Africa (Diawara et al. 2009; Traore et al. 2012; Zerroug et al. 2016; Katarbarwa, 2014). This approach has resulted in the elimination of transmission in four countries in the Americas (Colombia, Ecuador, Mexico and Guatemala) after as few as 11 six-monthly treatments (Cupp et al. 2011b; Cupp et al. 2011a; CDC, 2013). Foci have been eliminated in Sudan using twice per year treatment (Zarroug,

2016) and Uganda using twice per year treatment plus vector control/elimination (Katarawa, 2014; Uganda Onchocerciasis Elimination Expert Advisory Committee, 2016), together resulting in over 900,000 persons freed from onchocerciasis. In Nigeria, twice per year ivermectin treatment (alone or in combination with albendazole for LF elimination) will be at the centre-stage for fast-tracking the process of elimination in areas determined to be unable to reach 2020 and 2025 goals.

The following measures shall be undertaken to achieve the elimination of onchocerciasis in the country:

1. Setting a goal of consistently achieving 100% geographic coverage and a minimum of 80% therapeutic coverage in all target/endemic areas in the country. This requires programmatic adjustments required for improving ivermectin treatment coverage in areas with inadequate/sub-optimal coverage.
2. Twice per year treatment should be instituted when assessments indicate a State or parts of a State are not on track to reach the 2020 and 2025 goals using annual treatment. These include;
 - i) previously untreated areas,
 - ii) areas where OV16 rates in children >5%, and
 - iii) any other data considered by the FMOH and NOEC to be relevant to indicate the need for more twice per year MAM.

Prior to instituting twice per-year treatments in a locality, health workers and community directed distributors will be appropriately trained, and the communities targeted health educated and well-mobilized regarding the change in treatment frequency.

3. Justification for twice per year treatment will be provided to MDP. Medicines requests to WHO will be submitted by April to ensure that drugs are available in the first quarter of the following year.
4. Consider and implement vector control through ground larviciding or clearing of vegetation in breeding sites where it would be cost effective and environmentally acceptable to support reaching the 2020 and 2025 goals.

The States of Borno, Bauchi, Gombe, Yobe, Akwa Ibom, Jigawa, Sokoto, Lagos, Rivers, Bayelsa and Katsina have been categorized in the Blue classification because:

- No evaluation for onchocerciasis has been previously conducted using rapid epidemiological mapping of Onchocerciasis (REMO), or
- no evaluation has been conducted since the commencement of MAM or
- parts of the States have not been mapped for onchocerciasis, or,
- there are areas with environmental changes after REMO was conducted that might have resulted in permissiveness for onchocerciasis transmission (vector breeding), or
- parts of the States were previously classified by REMO as hypo and non-endemic.

Reclassification of Blue States is a high priority and must be completed as quickly as possible. Mapping procedures used in Blue areas must be able to detect active transmission including in low infection prevalence areas. Protocols using IgG4 antibody testing in children to the recombinant OV 16 antigen will be used instead of skin snips or nodule rates. This approach, using either OV16 rapid diagnostic tests (RDT) or ELISA, is designed to map out areas previously classified as hypo and untreated non-endemic areas in Nigeria as well as areas where environmental changes have been suspected to permit breeding of vectors. Thresholds in children to be used are higher than those defined in the Onchocerciasis Elimination Guidelines to reduce sample sizes and decrease the time required in the assessment. Seroprevalence > 1% in children ≥ 5 years <10 years will be the indication for launching mass drug administration (MAM).

Programmatic actions and assessments required in the six color-coded categories of transmission status are shown in Table 2.

Table 2: Colour coding of transmission status

Colour	Transmission status	Tools for evaluation	Indicator(s)	Reclassification or programme actions
Blue	a) No evaluation since after commencement of MAM/MAM b) Areas previously classified hypo or non-endemic for onchocerciasis by REMO/REA, or where environmental changes favour the transmission of onchocerciasis	OV16 RDT or ELISA in children below 10 yrs.	>5% ≥1 - =5% <1%	Classify as Red and treat twice per year Classify as Yellow if area already under MAM otherwise classify as red and treat twice per year Classify as Tan or non-endemic
Red	Ongoing transmission	OV16 RDT or ELISA in children below 10 yrs.	>5% 1-5% <1%	MAM changes to twice per year treatment; and vector control where feasible in line with national guideline Classify as Yellow Classify as Tan
Yellow	On track for interruption by 2020	OV16 RDT or ELISA in children below 10 yrs.	>5% ≥1 - =5%	Classify as Red Stay Yellow ; MAM continues, but may be fast tracked by twice per year treatment; vector control where feasible in line with national guideline Classify as Tan <1%

Tan	Suspected interruption	transmission	Conduct stop MAM assessment a. OV 16 ELISA testing of children <10 yrs. (at least 2,000/State) and b. PCR of flies (a total of at least 6,000 flies from at least 3 catching sites per State in transmission zone)	1a. <0.1% of the children in the State and 1b. <1 infective fly per 2,000 flies and/or ATP <20 If 1a and 1b are not met:	Stop MAM, classify as Ash, enter PTS Continue MAM, as per Flow Chart for stop MAM (Figure 10)
Ash	Post Treatment Surveillance (PTS): time needed to verify that transmission was interrupted. No MAM of ivermectin occurs during this period.		After 3-5 years in PTS PCR of flies, from a total of = 6,000 flies from =3 catching sites per State in transmission zone	a. <1 infective fly per 2,000 flies and/or ATP <20 and b. >1 infective fly per 2,000 flies and/or ATP <20	a. Transmission eliminated, reclassify as green b. Conduct sero -survey in children <10 years and follow decision tree and reclassify according (Fig 8)
Green	Transmission eliminated: begins Post Elimination Surveillance		Repeat evaluation every 3-5 years: a. OV 16 ELISA testing of children <10 yrs. (= 2,000/State) OR b. PCR of flies (a total of =6,000 flies from =3 catching sites per State in transmission zone)	To be determined	Post elimination surveillance continues.
			After all States achieve this classification the national dossier is compiled, followed by request for WHO verification		

3.7. Elimination Process

Stopping MAM will generally be considered by the FMOH and the NOEC only after continuous MAM implementation with acceptable geographic and therapeutic coverage during phase 1 (treatment phase) indicates it is safe to do so.

Four steps are required to stop MAM and launch phase 2 (post-treatment surveillance):

Step 1: The Federal Ministry of Health establishes an oversight committee independent from the national programme to address matters concerning onchocerciasis elimination. (This is already satisfied by the establishment of the NOEC).

Step 2: The NOEC advises the country to stop MAM according to the recommendations contained in WHO 2016 guidelines (Figure 8). It considers the success of MAM delivery and achievement of adequate coverage, the results of any assessment results conducted during Phase 1, the status of treatment for lymphatic filariasis and/ or any recrudescence issues of each focus, including cross-border risk with neighbouring States and countries, to determine the length of post-treatment surveillance (PTS) that can extend over the 3–5 year period. Areas successfully completing this evaluation will be color coded Ash for 'Transmission Interrupted'.

Step 3: Once MAM is halted and the PTS period is launched, as per the 2016 guidelines, primarily entomological PCR-O150 DNA test will be used to assess if recrudescence has occurred over the 3-5 year period (Figure 9). However, the O v-16 serology testing of children aged ≥ 5 and < 10 years (and if required PCR in skin snips of OV-16 positives) could be used if insufficient black flies are collected. Areas successfully completing this evaluation will be color coded Green for 'Transmission Eliminated'.

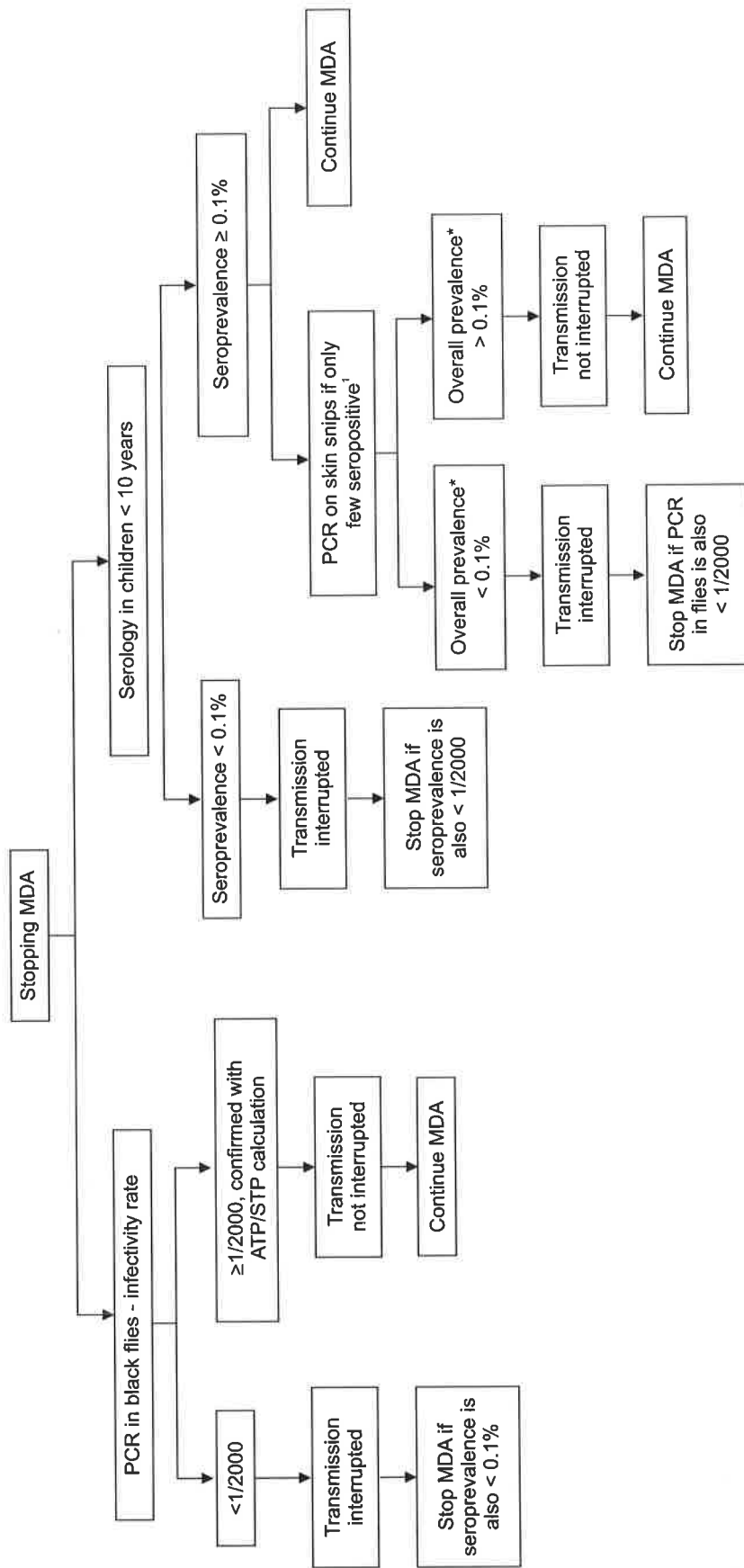
Step 4: The NOEC assists the national programme in the documentation of the elimination process of each transmission zone (States) as it completes its PTS period and moves from Ash to Green (the elimination stage). The NOEC will ultimately

assist the national programme to prepare the country report once all States have completed the PTS period.

Step 5 The country submits its official request for WHO verification of national elimination of onchocerciasis transmission, together with the country report, to WHO through the appropriate WHO regional office. After receipt of the country report, WHO constitutes an international verification team (IVT) that will visit Nigeria and assess the programme results with respect to nationwide transmission elimination

Figure 9

Decision tree for stopping MDA as elimination programmes transition from phase 1 (treatment) to phase 2 (post-treatment surveillance) using both PCR in black flies and serology in children aged under 10 years

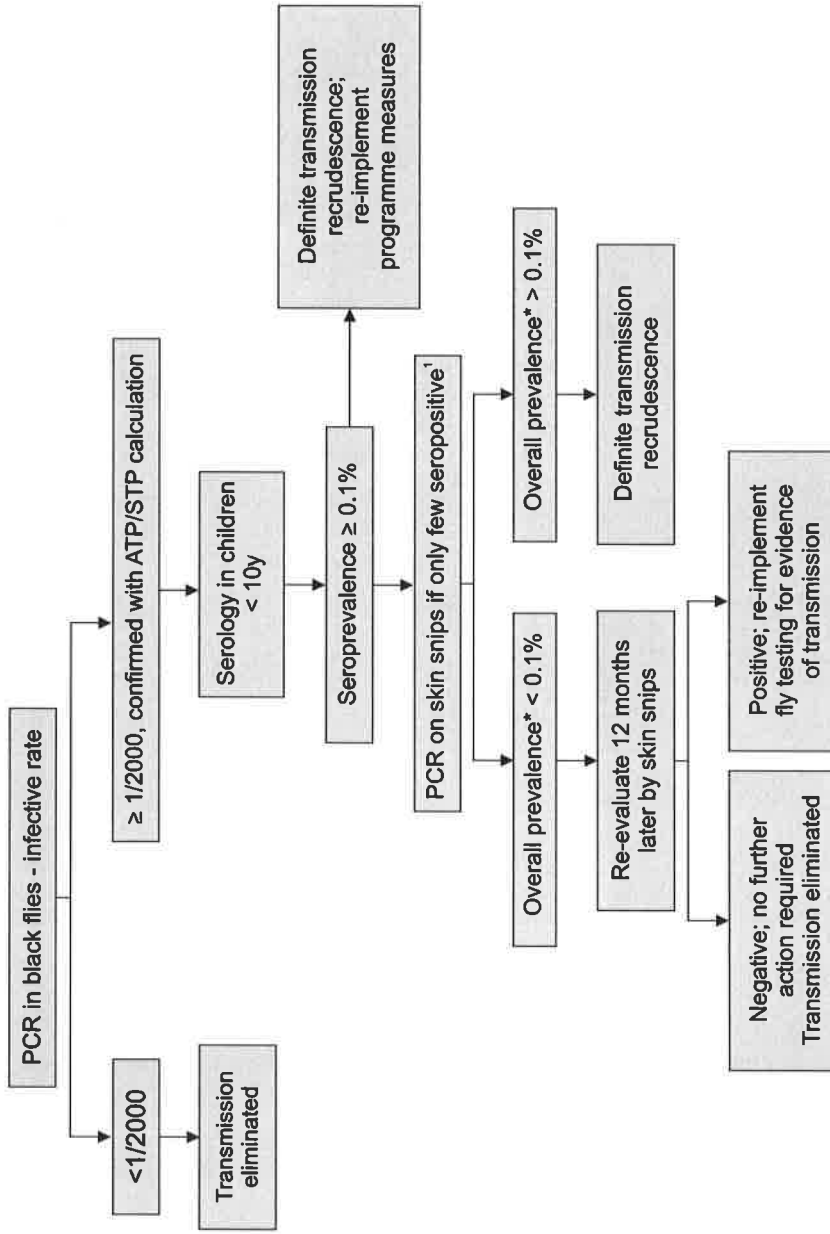


ATP, annual transmission potential; MDA, mass drug administration; PCR, polymerase chain reaction; PTS, post-treatment surveillance; STP, seasonal transmission potential

1. Few is defined here as below 10.

* Overall prevalence: the number of seropositive children minus the number of seropositive children who tested negative at PCR on skin snips, divided by the number of children who were tested for serology.

Figure 10 Post-treatment surveillance decision tree for the detection, confirmation and response to a potential recrudescence event (modified from Program Coordinating Committee and OEPA Staff, 2012 (20))



ATP, annual transmission potential, MDA, mass drug administration; PCR, polymerase chain reaction; PTS, post-treatment surveillance; STP, seasonal transmission potential

1. Few is defined here as below 10.

* Overall prevalence: the number of seropositive children minus the number of seropositive children who tested negative at PCR on skin snips, divided by the number of children who were tested for serology.

3.8. Coordination of the Onchocerciasis Elimination Process with the Elimination of LF

In areas under MAM for onchocerciasis and/or LF, activities of the two programmes should be closely coordinated. Areas with MAM for onchocerciasis that are also co-endemic for LF should add Albendazole as soon as possible. Stop-MAM surveys for onchocerciasis may be conducted to determine if interruption of onchocerciasis transmission has been achieved (to classify into Ash). However, the final PTS assessment for onchocerciasis (to classify from Ash to Green) can only be conducted after ivermectin MAM for LF has stopped. Decisions to stop LF MDA involve following WHO Transmission Assessment Surveys that evaluate 6-7 year old children with rapid diagnostic tests for LF antigenemia (WHO, 2011). Integrated LF onchocerciasis assessment is encouraged where practicable.

CHAPTER 4: ASSESSING INTERRUPTION (ASH) AND ELIMINATION (GREEN) OF TRANSMISSION IN NIGERIA

All colour classifications in these Nigerian guidelines are based on NOEC determinations except Ash and Green, which are based on the latest WHO guidelines (WHO 2016). Careful documentation of assessments to make Ash and Green determinations are critical for successful verification of the country. They are based on entomological and serological evaluations with statistically valid confidence intervals, as described in this chapter. WHO recommends that for stopping MAM, the entomological and serological evaluation should be performed in the same quarter of the year. In Nigeria, both evaluations should be conducted within a one year period.

4.1. Transmission Zones

A transmission zone (focus) is the geographical area where transmission of *Onchocerca volvulus* occurs by locally breeding vectors. "A defined and circumscribed area that contains the epidemiologic and ecological factors necessary for onchocerciasis transmission." It can be regarded as a natural ecological and epidemiological unit for interventions and assessments.

Assessments of interruption of transmission either for the purpose of stopping MAM or confirming absence of transmission after 3 - 5 years of post-treatment surveillance will be conducted based ideally on identified transmission zones (States). Decisions to stop MAM in any given State transmission zone after assessments shall take into consideration situations in adjoining States.

4.2. Guidelines for Assessing Transmission Interruption (classification into Ash category)

The WHO flowchart for this assessment is given in figure 9.

4.2.1. Entomological evaluation by PCR technique (pool screening)

This evaluation is used to determine the level of infective stages of *O. volvulus* larvae (L3 stage) in female black flies. It shall be based on PCR amplification of parasite-specific DNA (O-150 repetitive fragment), and detected with an *O. volvulus* specific probe.

Dissection of blackflies to determine infection is not recommended given that other (animal) species of *Onchocerca* are not properly distinguishable by microscopy, and also because dissection often fails to detect *Onchocerca* larvae when they are rare.

The upper bound of the 95% confidence interval of the prevalence of infective flies as measured by PCR should be less than one infected black fly for 1000 parous flies (< 1/1000) tested, representing a prevalence of less than 0.1% or one infected black fly in 2000 of all flies examined (assuming a parous rate of 50%), equivalent to a prevalence of less than 0.05%.

A minimum of 6,000 black flies collected from a transmission zone must be tested and all found to be free of infective larvae to ensure that the upper bound of the 95% confidence interval is met. If less than 6,000 flies are collected, the Seasonal Transmission Potential (STP) / Annual Transmission Potential (ATP) will be determined using the pool-screen algorithm. In order to pass this element of the assessment, the STP/ATP values should be <20 L3 larvae/person/year.

4.2.2. Serologic (OV-16 ELISA) testing of children

This method determines the presence of IgG4 antibodies to the antigen Ov-16 in children at least 5 years and less than 10 years of age. The objective of this evaluation is to determine if children have been infected with the *O. volvulus* parasite. A seroprevalence rate of <0.1% (with 95% confidence) is used to assess this criterion. If small numbers of children (<10) are found to be seropositive, their infections may be confirmed by PCR (O-150) testing of skin snips from seropositive children. If snips are negative, this is acceptable for meeting the <0.1% criterion and MAM may be stopped. Those PCR negative children shall be tested again 1.5 years later by skin snip PCR. If positive, they have to be treated according to clinical practices approved in Nigeria.

4.2.2.1. Number of children to be tested

Generally, a sample size of 2,000 children is needed to detect a prevalence of less than or equal to 0.1 % at the upper bound of the 95% confidence interval.

For a finite population with 1,100–2,000 children to be examined, the number of children to be tested is estimated based on the WHO guidelines:

Table 3: Proportion of finite target population that must be tested to conclude that the prevalence in the entire target population is < 0.1% when none of the sample tested is positive

Total population size (children < 10 y)	Maximum number of positives allowed in total population of children < 10 y	Actual allowed upper bound of prevalence (%)	Number of sample size to be tested
1750	1	0.057	1663
1500	1	0.067	1425
1260	1	0.080	1188
1100	1	0.090	1045

When the eligible population of children less than 10 years of age is below 1,100, then all eligible children in that focus should be tested according to the 2016 WHO guidelines.

4.2.3. Criteria for stopping MAM

Both the entomological and serological criteria need to be met:

<1/2000 infectivity rate in black flies

AND

Infection rates in children <0.1% (Figure 10)

If the assessment fails, FMOH and NOEC shall determine next steps for such States, LGAs, and transmission zones.

4.3. Onchocerciasis and Lymphatic Filariasis overlap

Stopping the treatment for onchocerciasis in areas co-endemic with Lymphatic Filariasis (LF) will take into consideration the treatment rounds for LF. LF treatment generally requires 5 to 6 years of yearly treatment reaching the threshold of > 65% therapeutic coverage for each round over this period. After this period, a Transmission Assessment Survey (TAS) is conducted in an endemic area to determine if treatment for LF can be stopped. Therefore, if an endemic LGA has reached a point where ivermectin treatment can be stopped for the

purpose of onchocerciasis but LF treatment has not reached a point where it can be stopped, the treatment with ivermectin will continue until LF treatment can be safely stopped. This implies that all co-endemic LGAs/areas of onchocerciasis and LF overlap should be spelt out clearly before any decision is made to stop MAM.

Interruption of onchocerciasis transmission may be assessed in LF areas, and based on that assessment a color may be assigned as 'Ash.' However the time count for the 3-5 year PTS period (needed to achieve Green color) will not start until all ivermectin MAM, both for onchocerciasis and LF, has stopped.

4.4; Assessment to end Post treatment surveillance (PTS) and classify as 'Transmission Eliminated' (Green)

The process for assessment during PTS is shown in figure 9. The use of entomological evaluation by O-150 PCR technique (pool screening) of blackflies (*Simulium* species) as described above for stopping MAM (Ash color classification) is again needed after 3-5 years to determine if elimination has been achieved. In case of insufficient or absence of flies, ATO and/or OV-16 serology test on 2,000 children under 10 years should be used instead.

4.5. Post Elimination Surveillance

After achieving elimination (classification from Ash to Green), there is still need for a routine surveillance system for timely detection of possible recrudescence, or reintroduction of infection from other areas where the infection still occurs. Theoretically, this surveillance will continue until global eradication is achieved (see Table 2).

CHAPTER 5: PREPARING FOR VERIFICATION

In preparing for WHO verification of elimination of onchocerciasis transmission from Nigeria, the country must have completed all the steps leading to successful completion of, and documentation of, post treatment surveillance (PTS) of phase II (WHO, 2016).

5.1. Country Processes

The NOEC will internally review and accept all the reports describing the first four steps of the process. In doing this, the NOEC will provide an independent internal validation of the archived documents required by WHO for its verification of onchocerciasis elimination. These documents will be organized and filed in a manner that they will be accessible to the WHO international verification team (IVT). These documents should include: CDDs registers, treatment reporting forms at all levels, supervision, baseline information for each State or transmission zone, monitoring and evaluation reports, data on ivermectin treatment and coverage assessment reports, historical reports of onchocerciasis in Nigeria, and published reports in the medical literature. Other materials may include IEC materials, advocacy kits, fliers and facts sheets.

Subnational transmission elimination targets are important internal milestones and can result in enhanced public/political goodwill and additional government/donor funding to achieve national onchocerciasis elimination and verification. The NOEC process of internally validate elimination, and assuring its careful documentation at State or transmission zone level in Nigeria, should be as rigorous as the future IVT visit. Subnational transmission assessments will not involve WHO directly and so must be owned and managed by Nigeria. The information reviewed by the NOEC will form the basis for the national transmission elimination dossier, and as such must align with the WHO verification process.

5.2. WHO processes

The WHO verifiable bench marks or indicators have been described in detail in this national guideline. The interruption of disease transmission will be assessed and determined based on these indicators

In line with the onchocerciasis elimination guideline, a national dossier will be prepared and submitted to the WHO Regional Office (AFRO) together with an official request for verification from the Honorable Minister of Health.

This country report should include the following sections:

- a. Introduction and History
- b. Baseline data
- c. Maps
- d. MAM Duration and Coverage
- e. Evaluation results, focuses especially on documentation of Ash and Green determinations
- f. Results of NOEC internal validation procedures
- g. Publications

CHAPTER 6: BUDGET

A total sum of about N3.7 billion will be required to implement and fast-track activities for elimination as well as conducted needed assessments based on this guideline for the years 2016 - 2020 (tables 4 and 5).

Table 4: Summary Budget for National Activities

State	Coordination, Partnership & Advocacy	Planning and Resource Mobilization	Scale-up Interventions	M&E, Research
Abia	15,394,867	6,153,657	44,518,623	18,557,120
Adamawa	23,110,497	8,949,405	79,066,158	28,172,500
Akwa ibom	20,934,731	6,936,105	54,803,810	20,365,460
Anambra	20,874,125	5,978,499	46,139,877	18,854,560
Bauchi	17,125,146	5,797,520	64,013,405	21,720,880
Bayelsa	5,000,000	4,909,407	0	17,968,320
Benue	17,905,058	7,743,727	53,238,300	21,962,060
Borno	10,551,858	4,103,407	82,297,351	23,043,900
Cross river	19,595,943	6,393,330	50,037,960	17,593,980
Delta	10,963,126	3,384,015	43,131,944	15,359,980
Ebonyi	15,924,354	5,950,677	47,744,909	15,272,580
Edo	19,595,943	6,393,330	50,015,460	18,454,980
Ekiti	13,671,660	4,634,134	44,945,554	15,765,980
Enugu	17,026,065	5,676,706	52,322,217	21,940,580
FCT	10,575,552	4,040,144	32,980,309	15,636,960
Gombe	17,566,649	4,365,745	80,524,032	25,503,380
Imo	18,476,614	8,055,633	58,753,098	24,673,400
Jigawa	14,908,058	6,471,991	50,406,488	17,831,868
Kaduna	14,099,552	4,901,752	63,664,634	20,151,100
Kano	17,757,843	6,038,602	107,288,668	34,376,800
Katsina	16,445,854	7,127,873	6,000,000	16,162,168
Kebbi	13,800,243	5,824,002	52,301,837	13,792,380
Kogi	14,738,608	4,049,573	55,812,541	14,105,000
Kwara	12,572,556	4,661,426	47,712,896	17,203,880
Lagos	11,919,087	5,814,014	8,000,000	18,993,210
Nasarawa	13,704,365	5,158,920	12,000,000	18,341,880
Niger	16,650,658	5,090,722	99,815,090	28,499,080
Ogun	14,170,671	5,801,018	63,397,454	21,403,280
Ondo	13,831,433	3,150,119	49,232,351	16,503,460
Osun	23,696,446	5,497,705	53,813,970	20,220,460
Oyo	19,060,885	7,303,549	52,418,569	20,100,920
Plateau	16,636,617	5,535,614	9,000,000	20,750,416
Rivers	16,126,593	5,140,008	6,000,000	18,863,820
Sokoto	16,061,494	5,168,171	9,000,000	19,459,900
Taraba	13,588,347	5,423,320	56,457,128	19,998,280
Yobe	17,047,669	5,535,614	64,979,707	21,512,080
Zamfara	10,033,002	4,904,220	39,210,493	13,869,220
National HQ	62,547,275	35,600,173	22,256,256	207,558,917
Totals	643,689,446	243,663,826	1,813,301,085	940,544,739

Table 5: Summary Budget for Federal level activities/inputs only

Key Activities	2016	2017	2018	2019	2020	Total
Mapping	0	0	0	0	0	
MAM	512,939	546,527	567,789	592,199	473,759	2,693,212
Capacity Building	3,936,506	4,131,322	3,472,875	3,820,163	4,202,179	19,563,044
Coordination	3,489,238	3,670,028	4,037,031	4,440,734	4,884,808	20,521,839
Partnerships	316,462	262,037	272,231	288,896	231,117	1,370,742
Review Meetings	5,909,961	6,296,961	6,541,935	6,942,399	5,553,919	31,245,175
Advocacy	2,228,532	1,802,111	1,826,989	1,973,270	1,578,616	9,409,519
Planning	1,021,432	1,088,318	1,130,657	1,199,870	959,896	5,400,173
Review of Policies	8,000,000	8,000,000	4,500,000	4,700,000	5,000,000	30,200,000
Supervision & Monitoring	10,370,372	11,187,948	11,540,918	8,651,591	6,921,273	48,672,101
Serological Evaluation	5,761,318	6,215,527	6,411,621	7,052,783	7,758,062	33,199,310
Entomological Evaluation	17,283,953	18,646,580	19,234,863	21,158,350	23,274,185	99,597,931
Surveillance	1,866,225	1,959,776	2,057,582	2,160,341	1,728,273	9,772,196
Operational research	2,019,507	2,120,482	2,226,507	2,337,832	1,870,265	10,574,593
Data management	207,690	2,516,188	228,978	1,549,961	1,239,969	5,742,786
Totals	62,924,134	68,443,804	64,049,976	66,868,388	65,676,319	327,962,621

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APPENDIX 1: DEFINITIONS

Annual transmission potential

A value calculated as the product of the annual biting rate, the proportion of black flies with infective-stage *Onchocerca volvulus* larvae and the mean number of infective larvae per infective fly. The value refers to the approximate number of infective larvae any one individual may be exposed to in a year. Current evidence suggests that at an annual transmission value of less than 20 in an endemic onchocerciasis focus is not sustainable.

Case of human onchocerciasis

An individual in whom there is evidence of current infection with *Onchocerca volvulus*.

Case definition of human onchocerciasis

An individual who presents with:

- fibrous nodules in the subcutaneous tissue

and

- laboratory confirmation of the presence of *Onchocerca volvulus* microfilariae in skin snips (microscopy or polymerase chain reaction)

or

- the presence of viable *Onchocerca volvulus* adult worms in excised nodules

or

- the presence of living microfilariae in the eye as determined by slit lamp or other examination.

Control

A reduction of the incidence, prevalence, intensity, morbidity and/or mortality of disease as a result of deliberate efforts. Continued interventions may be required to maintain this reduction.

Elimination

The reduction to zero of the incidence of infection caused by a specific pathogen in a defined geographical area, with minimal risk of reintroduction, as a result of deliberate efforts; continued actions to prevent re-establishment of transmission may be required.

When elimination of the parasite is confirmed, the endemic area enters the phase of post elimination surveillance.

Endemic onchocerciasis focus

An area within a country where a local cycle of *Onchocerca volvulus* transmission is maintained and gives rise to local infections; that is, where the basic reproductive rate exceeds 1 (apart from temporal fluctuations). Endemicity is stable where the incidence of the infection shows little or no increasing or decreasing trend over time.

Endemic foci

(And transmission zones) can be classified as having (i) active transmission, (ii) suppressed transmission; and (iii) interrupted transmission.

Countries are classified as:

Endemic; when *Onchocerca volvulus* transmission and infection are present; or post-endemic; when a country with a previous history of endemic onchocerciasis is officially confirmed as having successfully completed a post-treatment surveillance period of at least 3–5 years of interrupted transmission in all its previously endemic onchocerciasis foci.

Eradication

The permanent reduction to zero of the global incidence of infection caused by a specific pathogen as a result of deliberate efforts, with no risk of reintroduction. Sometimes a pathogen may become extinct, or may still be present in confined settings such as laboratories. Eradication requires a formal certification process.

Incidence

The rate at which new cases occur in a given population within a defined time interval.

Interruption of transmission of *Onchocerca volvulus*

The permanent reduction of transmission in a defined geographical area after all the adult worms (and microfilariae) in the human population in that area have died, been exterminated by some other intervention, or become sterile and infertile.

Map Legend

This represents the colours of various stages of elimination map as shown in figure 8

- Tan – Transmission suspected interrupted
- Yellow – on Track for elimination by 2025
- Red – Transmission on going
- Blue – No data/information
- Grey – Transmission interrupted
- Green – Transmission eliminated

Morbidity

The presence of disease manifestations of the skin (such as dermatitis, especially pruritus and depigmentation) and of the eye (including keratitis, corneal opacities, iridocyclitis, chorio-retinitis, optic neuritis and blindness) caused by *Onchocerca volvulus* parasites.

Ov-16

A recombinant *Onchocerca volvulus* antigen to which IgG4 antibodies are produced and detectable using immunological methodologies. The critical threshold for interruption or elimination of transmission is an upper bound of the 95% confidence interval of less than 0.1% confirmed seropositivity to Ov-16 in children under 10 years of age.

Polymerase Chain Reaction

A biochemical method in molecular biology to amplify a single or a few copies of a piece of DNA across several orders of magnitude, generating millions to billions of copies of a particular DNA sequence.

Poolscreen

A software program that employs a statistical model to calculate the probability of infection of an individual black fly with *Onchocerca volvulus* from the number of positive pools and the size of the pools using the results of polymerase chain reaction. The model takes into account the biting rate, the fly density and the infection rate to calculate estimates of annual transmission potential (or seasonal transmission potential) and associated 95% confidence intervals. The critical threshold for interruption or elimination of transmission is an upper bound of the 95% confidence interval of the point estimate of the prevalence of black flies carrying infective larvae of 0.05%, calculated by the results of polymerase chain reaction from testing the head of the vector in which L3s are found.

Post-treatment surveillance

The period of at least 3–5 years after the end of treatment during which ongoing surveillance is conducted to document that interruption of transmission has occurred and there is no recrudescence of infection.

Prevalence

The proportion of the host population infected at a particular point in time.

Ro (basic reproductive rate)

A measure of the reproductive success of the parasite population. Endemic onchocerciasis requires a basic reproductive rate equal to or greater than 1; any intervention which aims to eliminate onchocerciasis must achieve a state where this rate is below 1 for a sufficient period of time (usually defined by the reproductive lifespan of the parasite). Corresponding values are the threshold biting rate (that is, the vector density below which *Onchocerca volvulus* cannot remain endemic) and the population breakpoint (that is, the parasite density below which onchocerciasis cannot remain endemic).

Seasonal transmission potential

A value calculated as the product of the seasonal biting density, the proportion of flies with infective-stage larvae and the mean number of infective larvae per infective fly. The seasonal transmission potential may be equal to or slightly less than the annual transmission potential.

Sentinel site (community)

A hyper endemic community pre-selected by some programmes where in-depth epidemiological evaluations take place at regular intervals (before treatment starts and at set intervals thereafter).

Suppression of transmission (or conditional interruption of transmission)

The absence of infective larvae (L3s) in the *Simulium* vector population. Infectivity can be suppressed through drug (ivermectin) pressure, despite the potential for re-initiation of transmission through the presence of a population of adult worms capable of producing microfilariae if the drug pressure is removed.

Transmission zone (equivalent to a transmission focus)

A geographical area where transmission of *Onchocerca volvulus* occurs by locally breeding vectors and which can be regarded as a natural ecological and epidemiological unit for interventions. In Nigeria the adopted transmission zone is the state (region) based on the river systems.

APPENDICES

APPENDIX 2: CONTRIBUTORS

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