Monitoring and epidemiological assessment of mass drug administration in the global programme to eliminate lymphatic filariasis

A manual for national elimination programmes, second edition

World Health Organization

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Contents

Uganda: Tracking progress against lymphatic filariasis. The Bioline™ Filariasis Test Strip is a rapid diagnostic test used for qualitative detection of *Wuchereria bancrofti* antigen in human blood samples collected by fingerstick.

Preface

The Global Programme to Eliminate Lymphatic Filariasis (GPELF), launched by the World Health Organization (WHO) in 2000, had two strategic aims: to interrupt transmission of lymphatic filariasis (LF) through mass drug administration (MDA) and to alleviate the suffering of people affected by the disease. Through collective efforts of national governments, WHO and partners to implement the strategy, 21 countries have documented elimination of LF as a public health problem, more than 9.7 billion cumulative treatments have been delivered, and the estimated number of infections has been reduced by 74% globally *(1, 2)*. MDA has been implemented in 71 of the 72 countries considered to be endemic for the disease.

Monitoring and evaluation has been essential in generating evidence for programme decisions, such as when to start and stop MDA. WHO guidance on monitoring and evaluation was revised in 2005 and then again in 2011 to ensure the success of GPELF. In 2011, WHO published the *Monitoring and epidemiological assessment of mass drug administration: a manual for national lymphatic filariasis elimination programmes*, which introduced transmission assessment surveys (TAS) to standardize the strategy for deciding to stop MDA and to conduct post-MDA surveillance *(3)*.

Since 2011, countries have expanded MDA and implementation of TAS, and new MDA regimens have been recommended by WHO and used in countries. Additional challenges arise as countries progress towards elimination of LF as a public health problem and begin post-validation surveillance. To address these challenges, an updated framework for monitoring and evaluation was therefore necessary to improve programme decision-making and strengthen surveillance to sustain progress in elimination of LF. This second edition is based on the GPELF approach to reflect changing epidemiology, lessons learnt during extension of the programme and knowledge generated in operational research.

Aim of the manual

This revision and update of the 2011 guidance includes a new mapping protocol, adapted from the TAS, as a practical tool for determining when MDA is required in areas of uncertain endemicity. Best practices and new tools for monitoring MDA coverage are provided to ensure that MDA is delivered to all eligible people. Epidemiological monitoring surveys (EMS) have replaced pre-TAS and focus on the assessment of infection in the adult population. TAS has been strengthened by use of updated models of LF to more accurately measure the threshold below which transmission is assumed to be unsustainable, even in the absence of treatment. A protocol for measuring the impact of the new triple therapy regimen of ivermectin, diethylcarbamazine and albendazole (IDA) is included. More detailed guidance is provided for following up people found to be infected during surveys. Tools and guidance are provided to help national programmes mitigate persistent transmission, and new guidance is introduced, outlining possible platforms for post-validation surveillance. The use of integrated surveys is highlighted. The manual provides general guidance to national programmes and relevant background information on technical issues. Technical details and tools for implementing the guidance are provided in annexes. The diversity of the

epidemiology of LF and the unique programme situations encountered may not correspond to all of the categories or scenarios presented in this manual, and consultation with WHO continues to be recommended in such cases.

Intended readership

This manual is intended for managers of national LF elimination programmes; national, regional and district programme staff; development and technical agencies; nongovernmental organizations; regional programme review and technical advisory groups; and other organizations involved in supporting GPELF activities.

Methodology

Details on the methodology used to update the 2011 edition to this second edition of the manual, including declarations of interest and their management, can be found in Annex 1.

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Abbreviations

Ab	antibody
Ag	antigen or antigenaemia
CES	coverage evaluation survey
CFA	circulating filarial antigen
CI	confidence interval
DEC	diethylcarbamazine
DQA	data quality assessment
EA	enumeration area
EMS	epidemiological monitoring survey
EPIRF	Epidemiological Data Reporting Form
EU	evaluation unit
GPELF	Global Programme to Eliminate Lymphatic Filariasis
IDA	ivermectin, DEC, albendazole
IIS	IDA impact survey
IU	implementation unit
LF	lymphatic filariasis
LQAS	lot quality assurance sampling
MDA	mass drug administration
Mf	microfilariae or microfilaraemia
Mx	molecular xenomonitoring
NTD	neglected tropical disease
qPCR	quantitative polymerase chain reaction
PVS	post-validation surveillance
RDT	rapid diagnostic test
SCT	supervisor's coverage tool
SSB	survey sample builder
STH	soil-transmitted helminthiases
TAS	transmission assessment survey
iTAS	integrated TAS
WHO	World Health Organization

Glossary

The definitions given below apply to the terms as used in this manual. They may have different meanings in other contexts. The definitions are extracted from references *(3–5)*.

antibody (Ab)

A protein produced by the human immune system in response to a foreign substance (antigen) to fight off infection. An Ab reacts specifically with the antigen (Ag) that triggered its formation. Its function is to facilitate removal of the Ag from the body. In this manual, the term refers to Abs specific to *Wuchereria bancrofti*, *Brugia malayi* or *B. timori* in the bloodstream.

antigen (Ag)

Any foreign substance that stimulates the human immune system to produce Abs. In this manual, Ag refers to that specific to *W. bancrofti*.

antigenaemia

Circulation of an Ag in the bloodstream. A person with circulating filarial Ag specific to *W. bancrofti* in the bloodstream would be considered Ag positive or antigenaemic.

area endemic for *B. malayi, B. timori* or *W. bancrofti*

Geographical area with established transmission of the specific parasite indicated by the presence of infection (Ag or Mf).

critical cut-off value

A designated value used in a standardized survey to measure the threshold of infection prevalence and trigger a programmatic decision. In confirmatory mapping surveys, transmission assessment surveys (TAS) and IDA impact surveys (IIS), this value is estimated from the number of Ag- Ab- or Mf-positive cases.

drug coverage

Proportion of individuals, expressed as a percentage, in a specific population who ingested the MDA drugs.

elimination as a public health problem

Achievement of measurable global targets for both infection and disease. When reached, continued actions are required to maintain the targets and/or to advance to interruption of transmission.

elimination of transmission

Reduction to zero of the incidence of infection in defined areas, with minimal risk of reintroduction, as a result of deliberate work. Continued actions to prevent re-establishment of transmission may be required.

endemic area

Implementation unit (IU) or any subunit in which the average antigenaemia or microfilaraemia (Mf) positivity rate is ≥ 1% in the resident population.

enumeration area (EA)

The smallest area for which census population results are available.

epidemiological drug coverage

Expressed as a percentage, the proportion of individuals in the total population of an IU who have ingested the MDA drugs. The minimum effective coverage of the total population is considered to be 65%, but programmes should attempt to treat all eligible people where MDA is delivered and to exceed this number.

epidemiological monitoring survey (EMS)

A survey designed to measure whether the prevalence at sentinel and spot-check sites has been lowered below threshold levels. The EMS is used as the first part of a two-tier strategy for deciding to stop MDA. Once epidemiological criteria are met in sentinel and spot-check sites, the EU can conduct an IIS or TAS.

evaluation unit (EU)

An area selected for an epidemiological survey (EMS, TAS or IIS); may comprise several implementation units (IUs) or part of an IU.

geographical coverage

Proportion of administrative units in which MDA is being implemented, expressed as a percentage, out of all those that require MDA.

IDA impact survey (IIS)

In areas where the triple therapy MDA regimen (ivermectin, diethylcarbamazine, albendazole) has been used, a survey designed to measure whether EUs have lowered the prevalence of infection to a level at which recrudescence is unlikely to occur, even in the absence of MDA.

implementation unit (IU)

The administrative unit in a country that is used as the basis for decisions about implementing MDA.

ineligible population

Group of individuals who are not qualified to receive anthelminthic treatment during MDA, determined by safety considerations.

interruption (elimination) of transmission

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 action to prevent re-establishment of transmission may be required.

lymphatic filariasis (LF)

A vector-borne disease in humans caused by infection with the filarial parasites *W. bancrofti, B. malayi* and *B. timori*. Infections damage the lymphatic vessels and impair vessel function, leading to clinical manifestations such as lymphoedema and hydrocoele.

lymphatic filariasis clinical case

A person living in an endemic country (or from an endemic country) with clinical characteristics of LF including lymphoedema, hydrocoele, chylocoele, chyluria and haematochyluria, for which other etiologies have been ruled out. Evidence of infection is not required to be considered a clinical case of LF.

lymphatic system

The network of nodes and vessels that maintain the delicate balance between the tissues and blood in humans. The lymphatic system is an essential component of the body's immune defence system.

mapping

An epidemiological survey to identify evidence of recent LF transmission and to decide whether MDA is required.

mass drug administration (MDA)

A modality of preventive chemotherapy in which anthelminthic medicines are administered to the entire at-risk population of an area (e.g. state, region, province, district, sub-district, village) at regular intervals, with the objective of clearing microfilariae (Mf) from the community and interrupting transmission of infection.

microfilariae (Mf)

Microscopic larval stage of LF parasites that circulates in the blood and is transmitted by mosquitoes.

microfilaraemia (Mf)

Presence of microfilariae in the blood.

morbidity

Clinical consequences of infections and diseases that adversely affect the health of individuals. LF causes chronic morbidity by damaging the lymphatic system, kidneys, arms, legs or genitals (especially in men).

neglected tropical disease (NTD)

A WHO-recognized group of more than 21, primarily infectious diseases that are mainly endemic in tropical climates, which often affect marginalized communities of society. Control or elimination of these diseases has historically been less of a priority than that of other major infectious diseases, such as malaria, HIV, tuberculosis and vaccine-preventable diseases.

net primary-school enrolment ratio

The number of children enrolled in primary school who are in the age group that officially corresponds to primary schooling, divided by the total population of the same age group.

preschool-aged children

All children between the ages of 1 and 5 years who are not yet attending (primary) school.

prevalence of infection

The proportion, expressed as a percentage, of individuals infected with a parasite species.

preventive chemotherapy

Use of anthelminthic medicines, either alone or in combination, as a public health tool against helminth infections. MDA is one modality of preventive chemotherapy.

recrudescence

An increase in the prevalence of LF infection in a defined area after being brought to below-threshold levels.

reported coverage

Coverage calculated from data reported by all drug distributors; census figures or previous reports from drug distributors are used to estimate the population denominator.

school-aged children

All children aged 6–15 years (usually), regardless of whether they are attending school. In some countries, enrolment may include individuals older than 15 years.

sentinel site

A community or similar geographical area selected for periodic collection of parasitological data to monitor the success of a programme. The same site should be maintained throughout a programme, until the level of infection is below target thresholds.

spot-check site

A community or similar geographical area selected for collecting parasitological data to complement data collected at sentinel sites. Spot-check sites that are considered to be at greatest risk for LF infection should be selected for each assessment. These could change during the programme.

surveillance

Ongoing, systematic collection and evaluation of data on the occurrence and spread of disease. The element of a programme for the discovery, investigation and elimination of continuing transmission, care of affected people, prevention and cure of infections and substantiation of claims of the absence of transmission.

surveyed coverage

Coverage measured by population-based survey sampling. Calculated as a percentage, the denominator being the total number of individuals surveyed and the numerator the total number of individuals surveyed who were identified as having ingested the medicine.

target population

The population in an IU targeted for treatment. For LF, the target population is the same as the eligible population, that is, individuals who are eligible to receive the drugs, according to criteria for drug safety. Usually represents 85–90% of the total population.

transmission assessment survey (TAS)

A survey to measure whether EUs have reduced the prevalence of infection to a level at which recrudescence is unlikely to occur, even in the absence of MDA.

validation

Documentation by WHO of a country's claim to have achieved elimination of LF as a public health problem and official recognition of their achievement.

Overview of changes since the 2011 edition

Table 1 lists the major technical revisions to the 2011 edition *(3)* of the manual and highlights changes in the current edition.

Table 1. Changes to the manual between 2011 and 2025

Technical issue	2011	2025	Justification for change
Description of biomarkers of lymphatic filariasis (LF) (section 3)	Limited detail provided.	Greater detail is provided, based on published literature, on LF biomarkers and their associated signals, diagnostics, limitations and in which programme phases the biomarkers are used (Table 3).	More details about LF biomarkers were needed, which stems from frequently asked questions by national programmes. This has been particularly relevant with the introduction of the ivermectin, diethylcarbamazine and albendazole (IDA) regimen in 2017. There has been no change since 2011 in the biomarkers recommended for programme decision-making which remains: ▪ presence of circulating filarial antigen (CFA) for *Wuchereria bancrofti.* ▪ presence of antifilarial antibody (Ab) for *Brugia* spp. ▪ presence of microfilariae (Mf) in the blood assessed by microscopy for *W. bancrofti* and *Brugia* spp.
Protocol for determining whether mass drug administration (MDA) is required (section 4)	Various methods can be used to determine whether MDA is required.	A confirmatory mapping survey should be used to determine whether MDA is required.	In the past, LF mapping protocols favoured simple approaches for rapid determination of eligibility for MDA and scaling up treatment in highly endemic areas. In some settings, this approach led to uncertain classification of endemicity and whether MDA was required. Confirmatory mapping surveys are a robust, standardized way for determining eligibility for MDA in areas of unknown endemicity.

Indicator assessed in sentinel and spot-check sites (section 6)	Threshold indicator: antigen (Ag) or Mf.	Threshold indicator of *W. bancrofti:* Ag and Mf. Assessment of Mf in all individuals with a positive rapid diagnostic test (RDT). Threshold indicator *Brugia* spp.: Mf.	In areas endemic for *W. bancrofti*, the recommended RDT identifies the presence of CFA of any adult worm, including worms that are infertile, dead or decaying. CFA in the blood represents Ag. It is difficult to determine whether Ag in adults represents a recent infection, is contributing to ongoing transmission or represents a prior infection, whereas Mf indicates potential ongoing transmission. As Mf is usually measured at night and is therefore logistically difficult, only Ag-positive people should be tested for Mf. Because of the test characteristics, it is assumed that anyone who is Ag negative is also Mf negative, and testing for Mf is not required.
Target population for sentinel and spot-check sites (section 6)	The target population for pre-transmission assessment survey (pre-TAS) is children aged ≥ 5 years.	The target population for epidemiological monitoring surveys (EMS) is people aged ≥ 20 years.	The change is proposed to improve the sensitivity of surveys to detect and respond to ongoing transmission. Adults are known to have a higher prevalence of Mf than children in areas of ongoing transmission. Measurement of Mf in children would result in an underestimate of the population prevalence.
Sampling method in sentinel and spot-check sites (section 6)	The method for selecting participants in pre-TAS is convenience sampling.	The method for selecting participants in EMS is random sampling.	Use of random sampling can provide an estimate of prevalence. A random sample is better than a convenience sample in that it can eliminate types of sampling bias that could lead to an incorrect decision about whether criteria have been met. Strengthening of EMS will prevent programmes from prematurely advancing to TAS or IDA impact survey (IIS), which are time- and resource-intensive.
Timing of sentinel and spot-check site assessments (section 6)	A pre-TAS is conducted 6 months after the last MDA.	An EMS is conducted 6 months after the last MDA in areas that received one- and two-drug LF regimens. An EMS is conducted no sooner than 9 months after the last MDA in areas that received IDA.	Research has shown that resurgence of Mf in infected people who received IDA was not detected 6 months after treatment but was detectable at 12 months. An EMS conducted 12 months post-IDA and above the threshold would delay the next round of IDA. MDA is often carefully planned according to school and other local calendars to maximize coverage of eligible groups. Thus, even minor disruptions to this schedule could be detrimental to the effectiveness of MDA or necessitate a long gap between IDA rounds. Long delays in MDA can lead to infection recrudescence. As in all public health approaches, a balance must be struck between what is operationally feasible and what is epidemiologically ideal. Conducting an EMS 9 months post-IDA was chosen to respect both parameters sufficiently.

Geographical area and size for surveys (sections 6, 7, 8)	Pre-TAS: implementation unit (IU) with 1 million people. TAS: evaluation unit (EU) with ≤ 2 million people.	EU for EMS, TAS and IIS with a total population < 500 000 people.	The change is proposed to improve the sensitivity of surveys to detect and respond to ongoing transmission. Surveys conducted in smaller EUs are less likely to result in misclassification of areas as passing and of stopping MDA too soon due to heterogeneous prevalence. EUs should comprise contiguous areas in which risk factors for LF transmission are homogeneous.
Target thresholds for prevalence in TAS (section 7)	In areas in which *W. bancrofti* is endemic and *Anopheles* or *Culex* is the vector, the target threshold Ag prevalence is < 2%. In areas in which *W. bancrofti* is endemic and *Aedes* is the primary vector, the target threshold Ag prevalence is < 1%. In areas in which *Brugia* spp. are endemic, the target threshold Ab prevalence is < 2%.	< 1% Ag (*W. bancrofti*) and Ab (*Brugia* spp.) prevalence target threshold for all vector and parasite species. The critical cut-off value for all vector species will be lower.	The change is proposed to improve the sensitivity of surveys to detect and respond to ongoing transmission. Programme experience of ongoing LF transmission in areas that passed the TAS based on the prior < 2% Ag and Ab threshold is documented. Published modelling simulations suggest that the LF transmission breakpoint for *Culex* and other vectors is < 2% Ag among children and 1% Mf in the total population. The aim of this change is to prevent premature cessation of MDA or late-stage TAS failures, both of which could delay or compromise elimination.
Targeted treatment (sections 7, 8)	Limited detail provided.	Guidance is provided on follow-up of individual infections detected during TAS or IIS. An additional response is outlined for clusters of two or more positives (TAS) or above the cluster-level critical cut-off value (IIS), with targeted MDA and steps after MDA.	This approach provides an actionable response to ongoing transmission at the sub-EU level. Studies have shown that clusters of two or more infected children are associated with a higher likelihood of ongoing community transmission.

Stop MDA survey specific to IDA (section 8)	Not applicable.	The IIS is introduced, which is a 30-cluster survey among adults aged ≥ 20 years using an RDT and collecting blood for Mf among those testing RDT positive. The survey indicator is Mf and the decision rule is based on the average Mf in the EU: < 1% (*Anopheles, Culex, Mansonia*) or < 0.5% (*Aedes*) and ≤ 2 clusters exceeding the threshold for positive adults.	IDA was recommended by WHO in 2017 with recognition of the need for a stop-MDA survey specific to the IDA regimen. While IDA is efficient in clearing Mf, CFA persists long after adult worm death or sterilization. Consequently, a standard TAS in children aged 6–7 years may not satisfy the TAS or EMS Ag threshold. The IIS is a more sensitive survey among adults, indicating that the average Mf prevalence in an EU is below the target threshold and that few, if any, hotspots of transmission remain.
Post-validation surveillance	Not elaborated.	Surveillance should be sustained for at least 10 years after validation using at least two of the following platforms: ▪ health facility screening; ▪ existing standard surveys; ▪ molecular xenomonitoring (Mx); and ▪ targeted surveys in high-risk areas or populations at highest risk.	Surveillance is essential to ensure that countries sustain their gains in eliminating LF. As the aim of the Global Programme to Eliminate Lymphatic Filariasis (GPELF) is to eliminate LF as a public health problem as a first step on the path to eliminating transmission, vigilance is required to ensure that the number of remaining infections in the post-validation phase does not increase above target thresholds, and, if infection emerges, that it is detected and addressed in a timely manner. The risk of recrudescence has been shown in models to be most common during the first 5 years after stopping MDA, but prevalence can be maintained for over 10 years at low levels without being eliminated. Additional evidence is required to confirm the ideal duration. Evidence from post-validation surveillance will be essential to further document elimination of transmission in certain settings. Appropriate strategies for surveillance are as unique as countries and programmes. Programmes should adapt these strategies to their own context and balance epidemiological rigour, operational feasibility and sustainability. Establishment of integrated surveillance platforms is therefore encouraged.

Ab, antibody; Ag, antigen; CFA, circulating filarial antigen; EMS, epidemiological monitoring survey; EU, evaluation unit; GPELF, global programme to eliminate lymphatic filariasis; IDA, ivermectin + diethylcarbamazine + albendazole; IU, implementation unit; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; Mx, molecular xenomonitoring; pre-Transmission Assessment Survey (pre-TAS); RDT, rapid diagnostic test; TAS, transmission assessment survey.

1. Eliminating lymphatic filariasis

1.1 Background

Lymphatic filariasis (LF) is one of the oldest and most debilitating neglected tropical diseases (NTDs). LF is caused by infection with one of three species of filarial parasites, *W. bancrofti, Brugia malayi* and *B. timori*, which are transmitted from person to person by mosquitoes. *Anopheles*, *Aedes* and *Culex* mosquitoes are the main vectors responsible for transmission. They serve as biological hosts that both develop and transmit the parasite during blood-feeding and establish the infection in humans. Hydrocoele, lymphoedema and elephantiasis are the overt, chronic, disabling consequences observed in people affected by these parasitic infections, which damage the lymphatic vessels.

Before widespread mapping and control, it was estimated that 120 million people globally were infected with filarial parasites *(6)*. A total of 72 countries have been considered endemic for LF, and 657 million people currently live in areas that require mass drug administration (MDA) *(1)*. LF is endemic in the Americas, African, Eastern Mediterranean, South-East Asia and Western Pacific regions of WHO.

An estimated 36 million people globally have clinically significant manifestations of LF *(7)*. These include approximately 17 million people affected by LF-related lymphoedema (or elephantiasis), which manifests as swelling of the limbs, breasts or genitals, and almost 19 million men affected by urogenital swelling, primarily hydrocoele. Lymphoedema and hydrocoele adversely affect personal and social life and limit occupational activities. Although these clinical manifestations are not often fatal, they lead to the ranking of LF as one of the world's leading causes of permanent and long-term disability *(8)*.

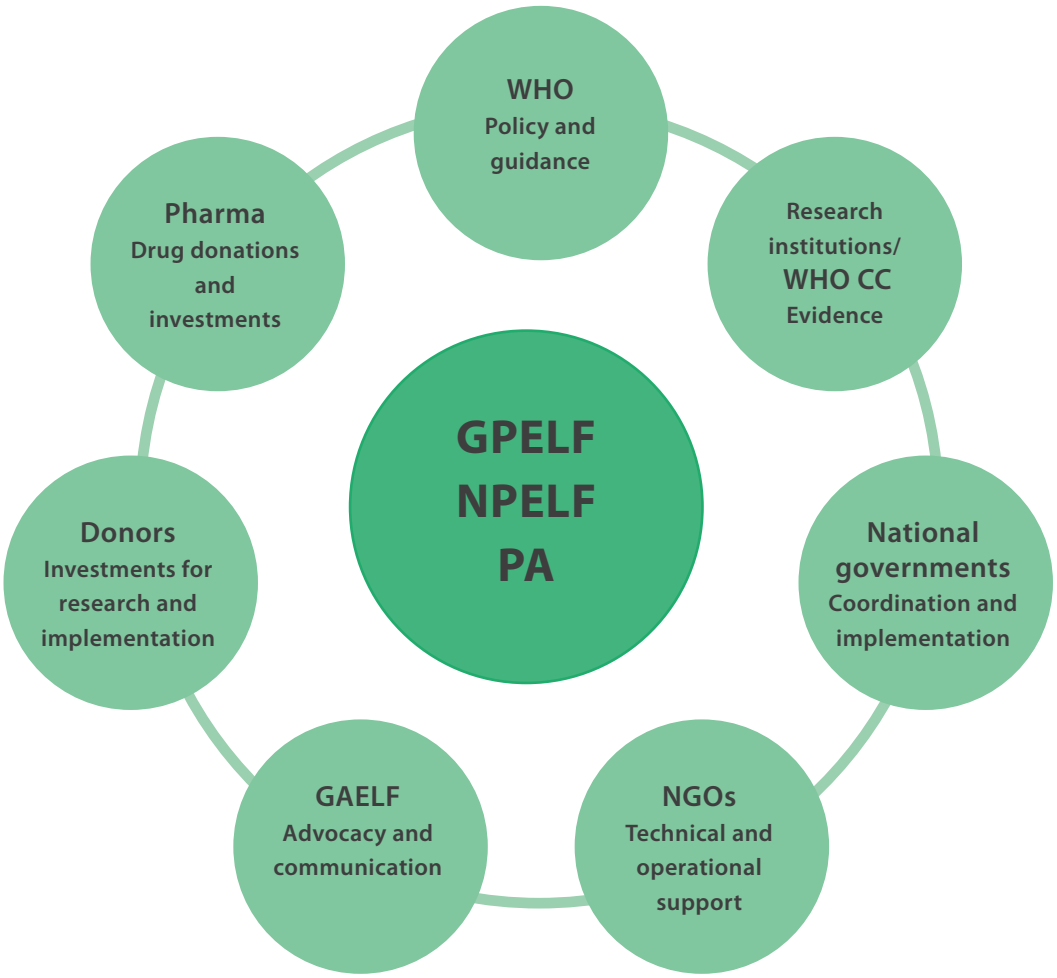
1.2 Partnership for impact

In World Health Assembly resolution WHA50.29 *(9)*, the world committed itself to eliminating LF as a public health problem. Shortly afterwards, WHO launched the GPELF to achieve that goal and to enhance solidarity among Member States, pharmaceutical industries, nongovernmental development organizations, bilateral agencies, donor agencies, academic institutions and WHO. The two aims of GPELF are to stop transmission of infection and alleviate suffering among people affected with hydrocoele and lymphoedema.

Since the start of GPELF, the number of infections has been reduced by 74% globally *(2)*. As of 2019, 51.4 million people were estimated to be infected *(2)*. The estimated burden of disease due to LF has also decreased, from 5.0 to 1.6 million disability-adjusted life years *(10)*. The decrease in numbers of cases of infection and clinical disease indicates an overall successful partnership in GPELF (Fig. 1), the effectiveness of the strategies recommended by WHO, leadership in implementation by national programmes, generous donations from the pharmaceutical industry, additional investments by bilateral donors and donor foundations, meaningful research conducted

by academic institutions, and the coordinated efforts of nongovernmental organizations to provide technical and operational support to GPELF at all levels *(11)*.

Fig. 1. Partnerships in the GPELF



GAELF, Global Alliance to Eliminate Lymphatic Filariasis; GPELF, Global Programme to Eliminate Lymphatic Filariasis; NGOs, nongovernmental organizations; PA, persons affected; NPELF, national programmes to eliminate LF; WHO, World Health Organization; WHO CC, WHO collaborating centres.

2. GPELF Strategic Framework

WHO's strategy is based on two components:

- stopping transmission of infection through MDA; and
- alleviating suffering and improving the quality of life of people affected by provision of a recommended essential package of care.

2.1 Stopping transmission

In order to stop transmission of LF in endemic countries, GPELF recommends MDA to treat all eligible people in areas where infection is present with regimens of effective antifilarial medicines. The objective of MDA is to clear microfilariae (Mf) from infected individuals in the community so that transmission cannot be sustained, even after MDA has been stopped. Repeated rounds of MDA are required, as the medicines target Mf and have limited impact on adult worms, which can continue to reproduce and release Mf until they die or become infertile.

The MDA regimen to be recommended depends on the co-endemicity of LF with other filarial diseases. WHO recommends the following MDA regimens *(4):*

- albendazole (400 mg) alone twice a year in areas co-endemic with loiasis;
- ivermectin and albendazole: ivermectin (200 µg/kg body weight) with albendazole (400 mg) in countries with onchocerciasis;
- diethylcarbamazine (DEC) and albendazole: DEC (6 mg/kg) and albendazole (400 mg); and
- ivermectin, DEC and albendazole (IDA): ivermectin (200 µg/kg) with DEC (6 mg/kg) and albendazole (400 mg) in certain settings (Table 2).

The number of rounds required depends on the following factors *(12):*

- the initial prevalence of infection,
- the combinations of parasites and vectors,
- the density of vectors,
- the efficiency of the MDA regimen in reducing the prevalence and density of Mf,
- the proportion of the population that ingests the medicines during each MDA round and
- the proportion of the population that is never treated.

The minimum effective coverage of the total population is considered to be 65%, but programmes should attempt to treat all eligible people where MDA is delivered and exceed this number *(13)*. Mathematical models suggest a much higher probability of achieving elimination targets when coverage is > 80% in each round *(14, 15)*.

Table 2. MDA regimens to eliminate LF

In countries endemic for LF but with neither onchocerciasis nor loiasis
WHO recommends annual IDA in the following settings: ▪ IUs that have not started or have conducted fewer than four effective rounds with DEC and albendazole; ▪ IUs that are not below epidemiological thresholds in sentinel and spot-check site surveys or in TAS despite meeting drug coverage targets; and ▪ communities in which post-MDA or post-validation surveillance identified infection, suggesting local transmission. WHO recommends annual DEC and albendazole in all other settings.
In countries co-endemic for LF and onchocerciasis
WHO recommends annual ivermectin and albendazole in countries where LF is co-endemic with onchocerciasis. WHO recommends biannual ivermectin and albendazole in areas in which biannual distribution of ivermectin is already being delivered for onchocerciasis elimination.
In countries co-endemic for LF and loiasis
WHO recommends biannual albendazole in IUs where LF is co-endemic with loiasis and ivermectin has not been distributed for either onchocerciasis or LF.

DEC, diethylcarbamazine; IDA, ivermectin + diethylcarbamazine + albendazole; IU, implementation unit; LF, lymphatic filariasis; MDA, mass drug administration; TAS, transmission assessment survey; WHO, World Health Organization.

Source: WHO *(4)*.

Exclusive use of table or cooking salt fortified with DEC for 1–2 years was a successful approach used in China *(16, 17)*. DEC-fortified salt was effective in reducing the prevalence of Mf in settings in which it was used exclusively *(18)*. There is no recent evidence of successful use of DEC-salt on a large scale or nationwide.

In some settings, vector control is recommended to supplement MDA and to accelerate interruption of LF transmission *(19)*. Integrated vector management prioritizes use of resources for vector control to control many vector-borne diseases and could be used to complement MDA in LF elimination programmes during both MDA and surveillance *(20–22)*.

2.2 Alleviating suffering

To alleviate suffering and improve the quality of life, GPELF proposes that access to an essential package of care be provided for every person affected by the chronic manifestations of LF in all areas where the disease is present *(23)*. The package should include:

- treatment for episodes of adenolymphangitis;
- guidance in applying simple measures to manage lymphoedema to prevent progression of disease and debilitating, inflammatory episodes of adenolymphangitis;
- surgery for hydrocoele; and
- treatment of infected people with antifilarial medicines.

Surgery can alleviate most cases of hydrocoele *(24)*. People with lymphoedema must have access to care throughout their lives, both to manage the disease and to prevent progression to more advanced stages. Clinical severity and progression of the disease, including acute inflammatory episodes, can be reduced and prevented with simple measures of hygiene, skin care, exercises and elevation of affected limbs *(25, 26)*. The essential package of care for LF management should be integrated into primary health-care services to ensure its sustainability. Interventions to reduce stigmatization, ensure optimal mental health and inclusion of affected people in society are also important *(27)*.

2.3 Programmatic steps

The following strategic monitoring and evaluation framework consisting of a series of programmatic steps is intended to show national NTD programmes how to implement, monitor and evaluate WHO-recommended interventions for stopping the spread of infection and measuring when elimination targets have been achieved *(28)*.

Step 1 (mapping). Epidemiological surveys are conducted to identify evidence of transmission and to determine whether MDA is required.

Step 2 (MDA). Mass treatment of all eligible people in all areas where warranted according to WHO guidelines, and monitoring of both coverage and impact, with the following approaches:

- drug coverage observed during and after every MDA to monitor implementation;
- periodic assessment of drug coverage with WHO monitoring and evaluation tools during and after distribution;
- serological and parasitological surveys conducted at sentinel and spot-check sites after the recommended number of MDA rounds, as necessary; and
- robust epidemiological surveys to assess the prevalence of infection in an EU after the recommended number of MDA rounds, as necessary, to determine whether the level of infection has been reduced to one at which it is unlikely that transmission is sustainable.

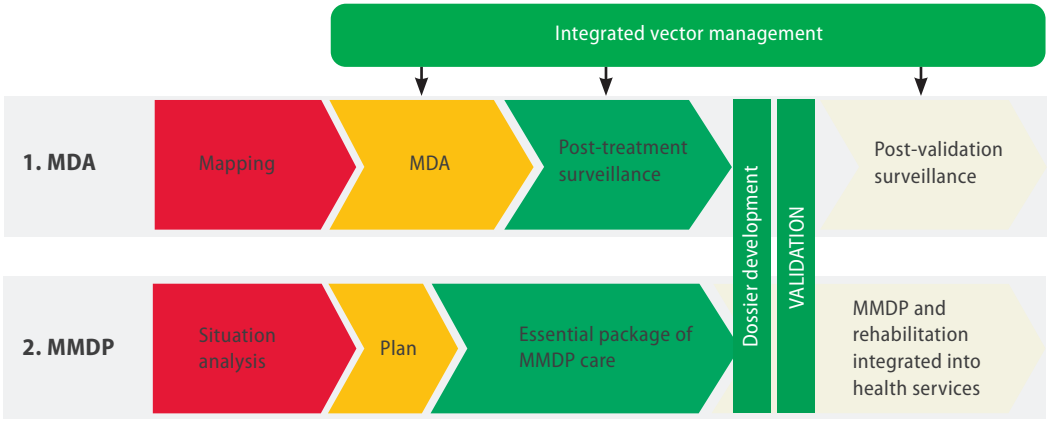
Step 3 (post-treatment surveillance). Repeated surveys and other integrated activities are used to monitor infection levels for 4–6 years after MDA has been stopped.

Step 4 (validation). A detailed independent review of documented historical, programme and epidemiological evidence submitted in a dossier by a country that claims to have met the criteria for the elimination of LF as a public health problem.

Step 5 (post-validation surveillance [PVS]). National LF elimination programmes do not end after MDA has been discontinued or after acknowledgement that a country has achieved elimination as a public health problem. Programme staff and resources must be maintained to continue surveillance and response activities, and health-care systems must continue to care for people who are affected. Surveillance and response should be integrated during this phase for sustainability and health systems strengthened for continuation of care for lymphoedema and hydrocoele. Activities during this phase may generate evidence for elimination of transmission.

Fig. 2 illustrates the GPELF Strategic Framework for stopping the spread of LF infection and alleviating suffering among people with the disease. Vector control, when used appropriately, can supplement activities to interrupt transmission *(29)*.

Fig. 2. GPELF Strategic Framework for stopping the spread of LF infection and alleviating suffering due to the disease



MDA, mass drug administration; MMDP, morbidity management and disability prevention.

2.4 Neglected tropical diseases road map and the GPELF targets for 2030

In 2021, a new road map for NTDs was published, which outlined new, cross-cutting and disease-specific targets for NTDs in the next decade *(30)*. Progress in achieving the GPELF targets will be key to achieving two cross-cutting NTD targets: (i) a 90% reduction in the number of people who require interventions against an NTD; and (ii) 100 countries having eliminated at least 1 NTD.

The technical indicators used to validate elimination of LF as a public health problem are as follows *(31)*.

1. In all areas in which LF is endemic, the level of infection is reduced below a target threshold at which transmission is considered unsustainable. The first elimination milestone for a country is that 100% of endemic areas have successfully passed a TAS or IIS and have stopped MDA. Countries must then demonstrate a sustained reduction of infection below the threshold for at least 4 years after MDA is stopped.

2. Documentation of readiness to provide morbidity management and disability prevention, specifically:

- The (reported or estimated) number of patients with lymphoedema and hydrocoele by IU or similar health administrative unit;
- the availability of the recommended essential package of care in all areas with known patients (100% geographical coverage); and
- the readiness for and quality of services in designated facilities.

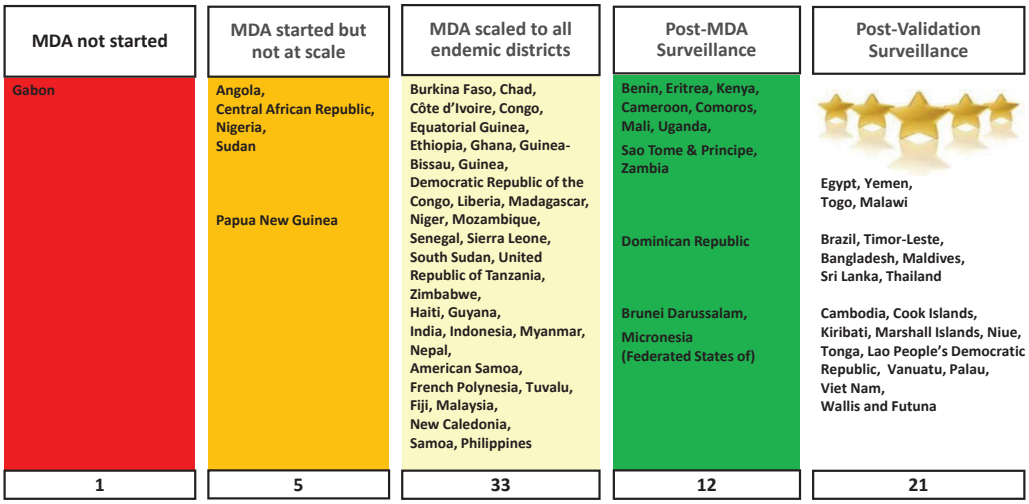
Box 1. GPELF 2030 targets

The specific targets established for GPELF by 2030 are:

- 80% of endemic countries have met the criteria for validation of elimination of LF as a public health problem.
- 100% of endemic countries implement post-MDA or post-validation surveillance.
- Reduction to 0 of the total population requiring MDA.

Significant progress was made in MDA between 2000 and 2023, with more than 943 million people reported to have been treated at least once *(1)*. The status of the 72 LF-endemic countries in delivery of MDA and in reducing the prevalence of LF to meet the validation criteria is presented in Fig. 3 *(1)*. In 2023, 39 countries were considered to require MDA; MDA had not started in one country; and MDA had been implemented in some but not all endemic IUs in five countries. In 2023 or previously, 33 countries had delivered at least one round of MDA in all known endemic IUs, and 12 countries had stopped MDA nationally but had not yet met the criteria for validation. Twenty one countries have been validated by WHO as having eliminated LF as a public health problem.

Fig. 3. Country status in implementation of MDA for LF elimination, 2024



MDA, mass drug administration.

The GPELF Strategic Framework is intended to guide national programmes systematically through each programmatic step. Effective monitoring and evaluation are important throughout the lifespan of the LF programme. This manual outlines the standard activities recommended for monitoring and evaluation of interventions and for providing evidence for making important decisions to move from one step to the next towards validation of elimination as a public health problem. While this global guidance is intended to standardize decision-making, it will not be applicable in every situation. National programmes are encouraged to consult WHO on specific challenges outside the situations considered in this document.

3. Diagnostic tools

The choice of diagnostics for monitoring and evaluating the progress of national programmes in eliminating LF depends on the sensitivity and specificity of the tools, the feasibility of using them in the field, the technical skills required and the cost *(32, 33)*. The diagnostic tools available to assess the impact of MDA include:

- thick blood smears (60 µL, in 3 parallel lines of 20 µL each) to detect the presence of Mf;
- tests to detect *W. bancrofti* CFA, representing antigenaemia;
- tests to detect filarial Ab for *Brugia* spp.; and
- quantitative polymerase chain reaction (qPCR) techniques to detect parasite DNA in humans and mosquitoes.

There are no key differences in available biomarkers between the 2011 and 2025 editions of the manual; rather, this second edition provides greater detail about the LF biomarkers and their use by national programmes. Their epidemiological use in monitoring and evaluation is further described in subsequent sections of the manual. Consult WHO for information about available diagnostic tests that detect these biomarkers and which have been validated through the WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases *(34)*.

3.1 Biomarkers

LF is a parasitic disease caused by three main species of filarial nematodes: *W. bancrofti, B. malayi* and *B. timori*. The complete life cycle of a parasite depends on development stages in both the definitive human host and the intermediate vector mosquito *(35)*. Definitive diagnosis of infection requires identification of adult worms or Mf in infected people *(36–39)*; however, detection of adult worms is difficult and is not usually done. Biomarkers that are used as an alternative to adult worms are listed in Table 3 and described below. The progression of their appearance in the human host after initial exposure varies *(40)* (Fig. 4).

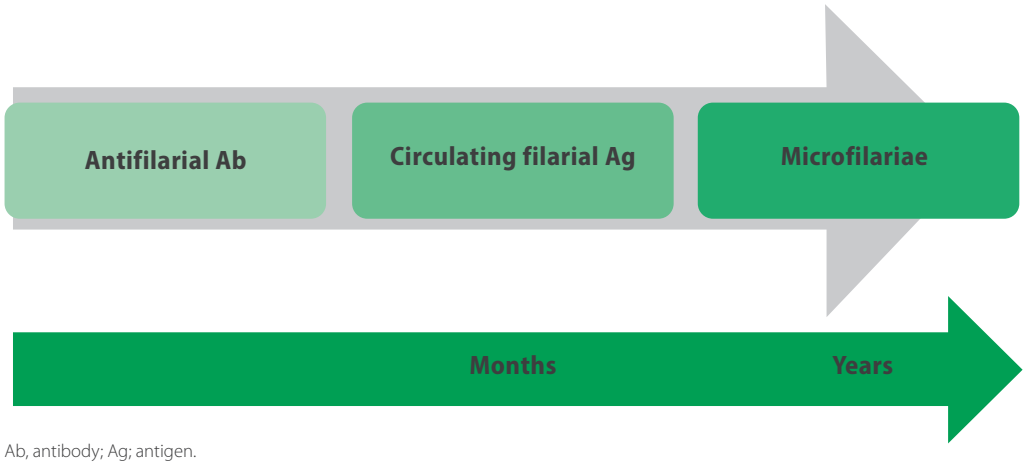
Table 3. Available biomarkers of LF

Signal	Biomarker	Diagnostic(s)	Description	Limitations	Programme stage
Parasite in the vector	L3 larvae in mosquitoes	Dissection *(35)* and reverse transcriptase-polymerase chain reaction[a] *(41, 42)*	▪ Measure of transmission potential ▪ Highly specific	▪ Dissection requires skilled technicians ▪ Reverse transcriptase-PCR requires laboratory capacity and specialized equipment ▪ Ability to trap sufficient mosquitoes varies	MDA Surveillance
	Filarial DNA	qPCR[a] *(43–49)*	▪ Proxy for Mf in humans ▪ Highly specific	▪ qPCR requires laboratory capacity and specialized equipment ▪ Ability to trap sufficient mosquitoes varies ▪ Need standardization of sampling strategies *(50)* ▪ Need validation and standardization of methods	MDA Surveillance
Parasite in humans	Microfilariae	Blood smear *(51)*	▪ Direct measure of infection ▪ Highly specific	▪ Requires microscopy capacity ▪ Low sensitivity to detect Mf after treatment ▪ Requires night blood collection in most settings	Mapping MDA Surveillance
	CFA	Lateral flow assay *(33, 52–57)*; enzyme-linked immunosorbent assay[a] *(33, 58)*	▪ Measure of *W. bancrofti* adult worm Ag in blood ▪ In children, CFA is a marker of incident infection and recent transmission ▪ Strongly correlated with Mf but more sensitive than Mf detection ▪ Rapid tests available for field use (see Annexes 6–7) ▪ Highly specific	▪ Presence does not confirm viability of adult worm to reproduce ▪ No CFA test available for *Brugia* spp. ▪ CFA persists after treatment, and its presence alone in adults may not be sufficient for making a decision to stop MDA *(59, 60)*	Mapping MDA Surveillance
	Filarial DNA	qPCR[a] *(48, 49, 61)*	▪ Measure of parasite DNA ▪ Highly specific	▪ qPCR requires laboratory capacity and specialized equipment ▪ Sensitivity to detect parasite DNA is comparable to detection of Mf by blood smear but lower than sensitivity to detect CFA after treatment *(33)* ▪ Requires night blood collection in most setting	MDA Surveillance
Host immune response	Antifilarial Ab	Lateral flow assay *(33, 62–66)*; enzyme-linked immunosorbent assay[a] *(32, 33, 65, 66)*	▪ Measure of host immune response ▪ Ab responses in children may be a marker of incident exposure or infection and, hence, signify recent transmission ▪ Rapid test available for field use	▪ Difficult to distinguish recent exposure from past exposure or infection ▪ Tests often not specific enough *(65, 67)*	Surveillance

Ab, antibody; Ag; antigen; CFA, circulating filarial antigen; L3, third stage larvae; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; PCR, polymerase chain reaction; qPCR, quantitative polymerase chain reaction.

[a] Not routinely used in programmes.

Fig. 4. Progression of appearance of biomarkers in human hosts



Ab, antibody; Ag; antigen.

3.2 Blood smears

Examination of a stained blood smear for Mf reveals whether a person has microfilaraemia *(51)*. In areas with nocturnally periodic Mf, accurate diagnosis is best achieved with blood collected during the hours of peak presence (22:00–02:00 h) *(51, 68)*. Blood samples should not be collected before 21:00 h. Accurate diagnosis requires careful preparation and staining of slides and correct identification of Mf by skilled microscopists. During examination of blood slides for Mf, 10% of negatives and all positives should be re-read by experienced technicians for quality control. The prevalence of Mf is calculated as the proportion of blood smears found positive for Mf from the following equation:

$$\frac{\textit{Number of individuals whose slides are positive for Mf}}{\textit{Number of individuals examined for Mf}} \times 100$$

When initial testing is done by Ag or Ab and blood smears are prepared only for people who test positive, the denominator should be the total number of people examined for Ag or Ab. Additional details of measurement of Mf prevalence are provided in section 6.3.5. Annexes 3, 4 and 5 outline the recommended procedures for detection and identification of Mf in the blood.

3.3 Tests for circulating filarial Ag

CFA from adult *W. bancrofti* worms is nearly always present in people with Mf and in infected people who are amicrofilaraemic and asymptomatic. Thus, the results of CFA tests are a more sensitive measure of infection than those used to detect Mf. CFA, indicating antigenaemia, is detectable in peripheral blood at any time of the day. Diagnostic tests for CFA are available only for *W. bancrofti* and not *Brugia* spp. People who are treated with antifilarial medicines retain CFA in the blood for several months or years while the adult worms and Mf die and disintegrate *(59, 60, 69, 70)*. Tests of CFA may therefore still be positive despite a significant reduction in Mf levels. Annexes 6 and 7 provide detailed instructions for use of CFA tests.

3.4 Antifilarial Ab tests

Repeated exposure to filarial parasites may induce certain Abs in people, even if a true infection does not occur. Infected people, both microfilaraemic and amicrofilaraemic, have elevated levels of Abs, but the results of Ab testing do not distinguish between current and past infection *(40, 71)*. Nevertheless, detection of Abs in children demonstrates recent exposure to filarial parasites. Diagnostic tests to detect antifilarial Ab are available for *Brugia* spp. and W. *bancrofti*. Currently, Ab tests only for *Brugia* spp. are used to guide progamme decisions *(32–34, 62, 65, 66, 72)*.

3.5 Quantitative polymerase chain reaction

Techniques for detecting parasite DNA in human blood are available yet not routinely used. Molecular xenomonitoring (Mx) which consists of direct assessment of parasites in vector mosquitoes by PCR techniques *(41, 73, 74)* can be used to detect the presence of the parasite in vectors and shows a strong linear correlation of Mf prevalence in humans *(75)*; however, it may not be a direct measure of infectivity or of current rates of parasite transmission *(43–49, 61)*. Potential programmatic uses of Mx are being considered by WHO (see section 10.3.3).

3.6 Procurement of diagnostic tests

WHO maintains global coordination of procurement of LF diagnostic tests used in the GPELF to ensure a steady supply and to forecast demand. To improve access to LF diagnostic tests, limited resources have been provided to WHO to procure recommended LF diagnostic tests on behalf of endemic countries. National programmes may request such subsidized LF diagnostic tests as follows:

- In collaboration with WHO country and regional offices and partners, national LF elimination programmes develop a plan for WHO-recommended LF surveys and complete eligibility and planning forms, when applicable. Ensure that the number of tests required is sufficient for the estimated sample size of planned surveys. Please indicate the date by which tests are required in the country and the date of the planned activities.
- Submit the plan and forms with a formal request from the ministry of health to WHO through the WHO country office, with copies to regional office focal points.
- WHO will conduct a technical review of the plan and either proceed with procurement or return to the programme with questions for clarification.
- Answers to questions or clarifications should be addressed and submitted to WHO.
- For some diagnostics, the manufacturer requires an annual "No objection certificate" or letter for importation.

National programmes are encouraged to submit requests well in advance. It may take 12 weeks between the time of raising a procurement order until delivery to the country.

3.7 Future availability of diagnostic tools

Programmes must have high-quality diagnostic tools. The WHO Diagnostic Technical Advisory Group for Neglected Tropical Diseases, formed in 2019, is responsible for reviewing and prioritizing the requirements of NTD programmes for diagnostics, defining use cases and the target

product profiles for such tools, working with national NTD programmes and partners in test development and validation, and advising WHO on adoption of new tools and use of existing tools. A development framework for target product profiles was established and is used to guide a standardized approach to development of new tests *(76)*. Two target product profiles have been developed within the framework to standardize the characteristics necessary for better diagnostics for monitoring the impact of IDA and for surveillance *(77, 78)*. As new tools for LF programmes are developed, rigorous laboratory evaluation and field validation will ensure that alignment with programme needs is maintained. WHO will inform national programmes of any changes in recommended diagnostic tools.

4. Mapping

Mapping, the first programmatic step in LF elimination, is used to assess the disease situation in a country and to identify areas in which MDA is required by determining where active transmission is occurring. When a national LF elimination programme is started, a situation analysis should be conducted of the ecological (e.g. altitude), geographical (e.g. proximity to known endemic areas), clinical (evidence of hydrocoele and/or lymphoedema) and sociological conditions that could affect the likelihood of ongoing LF transmission. The analysis allows rough classification of areas as endemic, non-endemic or of unknown endemicity.

The previously used method of baseline mapping by purposeful sampling of two villages considered to be at higher risk was useful for rapid identification of highly endemic areas. When more areas of unknown endemicity were targeted for mapping, however, this method led to inconclusive results, and it was concluded that a more robust method was required to determine eligibility for MDA *(79)*. Therefore, a new approach, confirmatory mapping surveys, was developed, which provides more information about LF transmission than the conventional mapping method, particularly in areas of low endemicity, and can be used to assess recent transmission as a basis for deciding whether MDA is warranted. This approach is recommended for baseline mapping in areas of unknown endemicity and to confirm endemicity in areas that were previously mapped *(80, 81)*.

4.1 Planning a confirmatory mapping survey

Mapping begins with identification of the IU for MDA in the country. An IU is the administrative unit in a country for which a decision to administer MDA is made to stop indigenous transmission *(82, 83)*.

Usually, the choice of administrative level that will constitute an IU is made at national level. In most countries, the "region" is considered the first administrative level and the "district" the second. Usually, a district is identified as the IU; however, the choice is influenced by feedback from lower administrative levels on how LF is distributed. If filarial infection is focal, a lower administrative level may be chosen as the IU, whereas a higher administrative level may be chosen if infection is more widespread.

4.1.1 Where a confirmatory mapping survey should be conducted

Identification of areas in which MDA might be required involves a review of a combination of:

- unpublished and published data on LF, including routine programme data on adjacent endemic areas;
- population movement between endemic and non-endemic IUs in the country;

- hospital records of hydrocoelectomy; and
- unpublished and published data on LF vectors or vector density (e.g. the malaria programme if the vector species is the same).

The review should be based on several sources of information to ensure comprehensive understanding of potential transmission in each IU. Programmes should review initial data on areas that have not received MDA to determine whether there is enough evidence to classify an IU as non-endemic. In areas in which the results of initial mapping results were indeterminate (e.g. positive cases were identified, but the number did not exceed the threshold for starting MDA) or the initial mapping was poorly implemented (e.g. poor selection of high-risk sites or uncertainty about the accuracy of diagnostic results), confirmatory mapping might be necessary. Programmes are encouraged to consult WHO if they are uncertain about whether additional mapping is necessary.

A confirmatory mapping survey is designed for use in the following situations:

- baseline mapping of IUs of unknown endemicity in which transmission is suspected;
- confirmatory mapping of IUs that were previously determined to be non-endemic or low-endemic (< 1% Mf or Ag) but in which there is suspicion of recent ongoing transmission; and
- confirmatory mapping of IUs for which the results of previous mapping were indeterminate.

4.1.2 Implementation of a confirmatory mapping survey

In areas in which *W. bancrofti* may be endemic, initial mapping of LF is undertaken with an RDT to detect Ag (section 3). Programme managers should be aware that testing for Mf is not as sensitive as testing for Ag; therefore, countries in which Mf is used to identify IUs that require MDA should consult WHO to decide whether confirmatory mapping with Ag is necessary in areas with an infection level below the threshold of classification as endemic. It is not appropriate to assess Mf in a mapping survey in which children are sampled, as this indicator is slow to develop in infected individuals, and the absence of Mf in children is not sufficient evidence of lack of transmission. If use of Mf as the mapping indicator is necessary, the survey population should be adults. Table 4 presents guidance on sample sizes and critical cut-off values for confirmatory mapping of Mf in adults.

In areas where *Brugia* spp. are endemic, initial mapping has been done with use of blood films to measure levels of Mf in older school-aged or adult populations. For a confirmatory mapping survey, a rapid test can be used to detect anti-*Brugia* Abs, if available, with the same cut-off point as for Ag (see section 3). If the level of either Ag- or Ab-positive samples is > 2% or those of Mf are ≥ 1%, the area is designated as requiring MDA to eliminate LF transmission.

Table 4. Sample sizes for confirmatory mapping among adults when Mf is used as the indicator

Target population size (adults aged ≥ 20 years)	Systematic sampling design		Cluster sampling design		
	LQAS sample size (n)	Critical cut-off value	Sample size	No. of clusters	Critical cut-off value
1 000	506	1	759	Divide the sample size for a cluster survey by the average number of adults per enumeration area (EA), and round up to the nearest integer. If the integer is < 30, the number of clusters is 30.	1
1 200	520	1	780		1
1 400	530	2	795		3
1 600	594	2	891		3
2 000	606	2	909		3
2 400	614	2	1228		4
2 800	678	2	1356		4
3 200	684	2	1368		4
3 600	688	2	1376		4
4 000	690	2	1380		4
5 000	696	2	1392		4
6 000	762	3	1524		6
8 000	766	3	1532		6
10 000	770	3	1540		6
14 000	774	3	1548		6
18 000	776	3	1552		6
24 000	778	3	1556		6
30 000	778	3	1556		6
40 000	842	3	1684		6
49 999	842	3	1684		6
50 000	846	3	1692		6

EA, enumeration area; LQAS, lot quality assurance sampling.

4.2 Conducting a confirmatory mapping survey

4.2.1 Survey design

A confirmatory mapping survey when Ag or Ab is used as the indicator is based on a school survey platform. It is designed to provide a geographically representative estimate of LF transmission in the IU and thus provide greater confidence in determining whether MDA is necessary. Either systematic or cluster sampling may be used, depending on the number of schools in the IU. The survey is designed to estimate (with known probabilities of error) whether the average prevalence of LF infection among older school children in the IU is below, at or above a threshold for Ag or Ab positivity of 2.0%.

4.2.2 Target population

The target population for a school-based confirmatory mapping survey is pupils in upper grade primary school, who are typically aged 9–14 years. A decision to target older children, rather than 6–7-year-olds, as for a TAS, is made to improve the chances of detecting infected individuals in the survey. In treatment-naive settings, older children have longer potential exposure to infection, and previous studies suggest that infection in older children represents infection in the population as a whole *(84, 85)*.

4.2.3 Survey sites

All public, private or religious primary schools are the main sampling units for confirmatory mapping surveys because of the logistical advantages of schools rather than communities.

In IUs with fewer than 40 primary schools, systematic sampling is recommended, in which all schools in the IU are visited and a set fraction of pupils in targeted grades are included, after adjustment for the expected non-response rate.

In districts with at least 40 schools, cluster sampling is recommended, whereby 30 schools are selected from a sampling frame that includes all primary schools in the district, by sampling with probability proportionate to the estimated size.

A tool has been developed, the Confirmatory Mapping Survey Sample Builder (SSB) *(86)*, for selecting primary schools to be included in the survey and for generating lists for selecting the pupils to be included in the survey. (To access the latest tool, please consult WHO.) To use the tool, the following information should be available:

- a list of all the primary schools in the IU;
- the estimated enrolment of pupils in the target population in each school; and
- the anticipated non-response rate (the proportion of enrolled pupils who are likely to be absent on any given day and those who do not consent to participation).

If sampling in schools is not possible, children may be sampled in the community. The same criteria as those for selecting schools should be used. In each selected community, children aged 9–14 years should be selected by random household sampling. Additional guidance is available from WHO upon request.

4.2.4 Selecting pupils

Systematic sampling of schools: The same sampling fraction (*f*) will be used in each school, resulting in an equal probability of selection of each pupil in the IU. This can be calculated manually from Equation 1 or automatically with the confirmatory mapping SSB tool *(41)*.

$$f = \frac{\text{target sample size}}{(\sum \text{children}_i)(1\text{-nonresponse rate'})} \quad (1)$$

Cluster-based sampling of schools: To ensure an equal probability of selection, an independent sampling fraction (f_i) is necessary for each selected school according to the expected enrolment of children in the targeted grades ($school_i$), the expected non-response rate and the target sample size per school (typically, 16 pupils per school). This can be calculated manually from equation 2 or automatically with the confirmatory mapping SSB *(86)*. A notable advantage of using school-specific sampling fractions to select pupils is that, on average, the number of pupils sampled per school will be relatively consistent. This is often beneficial for planning surveys, as the small sample size may allow survey teams to complete sampling in two schools per day.

$$f_i = \frac{\text{target school sample size}}{(\text{school}_{i^*})(1\text{-nonresponse})} \quad (2)$$

All pupils selected for the survey should be tested for Ag if *W. bancrofti* is suspected to be endemic or for Ab where *Brugia* spp. are suspected to be endemic.

4.2.5 Sample size

The sample size for a confirmatory mapping survey should be adequate to determine whether the prevalence of LF in older school children is ≥ 2% Ag or Ab. See Table 5 to determine the appropriate sample size for the target population and the number of schools in the IU.

4.2.6 Decision rule

To determine whether the target threshold has been reached, a critical cut-off value for the number of positive children has been established, such that, if the number of Ag- or Ab-positive children is at or below the critical cut-off value, the population prevalence is assumed to be below this threshold, and therefore LF transmission is considered unsustainable (see Table 5). IUs in which the number of children who test positive is less than or equal to the critical cut-off value, *d*, are considered to have "passed" the survey and are considered not to require MDA.

Conversely, IUs in which the number of positive children is greater than the critical cut-off value are considered endemic and require MDA. Additionally, the prevalence point estimate (no. of children who test positive / total no. of children tested) provides an estimate of the prevalence of LF infection in the target age group in the IU. For additional information on sample size determination and error rates, see Gass et al. *(80)*.

Table 5. Sample size and decision rules for confirmatory mapping surveys

Total population in the target age group in the IU (N)[a]	Systematic sample (IUs with < 40 schools)		Cluster survey (IUs with ≥ 40 schools)	
	Critical cut-off (d)	Sample size (n)	Critical cut-off (d)	Sample size (n)
≥ 2000	2	320	3	480
1000–1999	2	300	3	450
750–999	1	220	NA	NA
500–749	1	210	NA	NA
< 500	0.02 × N	Census (N)	NA	NA

IU, implementation unit; NA, not applicable.

d, the number of children allowed to test positive in order to "pass" below the threshold.

[a] Size of the entire population of children in the target age group living in the survey area.

5. Monitoring coverage of mass drug administration

Monitoring comprises routine collection and analysis of data on the delivery of services. It is an essential component of programme management. In LF programmes, monitoring provides important information to inform decisions about stopping MDA, but also on where and how work should be focused to improve access to and the reach of MDA (e.g. supply chain, human resources, messaging).

MDA coverage indicators allow programmes to monitor the number of people who have ingested the medicines and the geographical areas that have been treated. Indicators also show whether the population that requires preventive chemotherapy is being reached with MDA comprehensively.

5.1 Geographical area to be monitored

Most decisions on implementation and monitoring are made at the level of the IU, and it is this level of coverage that countries use to determine whether an MDA round was effective and, ultimately, whether the IU is eligible for an EMS. The number of people treated in each IU should be reported each year to WHO through the joint reporting form *(87)*. Programmes may also consider examination of MDA coverage at the sub-IU level, as such coverage data can be useful for identifying specific geographical areas or sub-populations with low coverage or no coverage (e.g. urban and hard-to-reach areas), which may be masked by high coverage at IU level.

5.1.1 Determining the population in the IU that requires preventive chemotherapy

Once an area that is endemic for LF has been identified by mapping, the total population in that IU is considered to be at risk of infection and requires preventive chemotherapy. All residents in an IU must be included, even those who are considered migratory populations, such as cattle herders, construction or seasonal workers and people living in refugee camps. A sub-set of the population that requires preventive chemotherapy will be eligible (targeted) for treatment according to the drug regimen used. Treatment eligibility and exclusion criteria are discussed further in section 5.1.3.

5.1.2 Determining the total population of the IU

Determination of the total population of an IU is important, as this number is not only the denominator used to monitor and evaluate MDA coverage but is also used to forecast the requirements for LF medicines and MDA planning. Possible sources of data for determining the total population are discussed below.

- ***Census***. Many countries conduct nationwide censuses, generally at 10-year intervals, and the data obtained are available for administrative units chosen as IUs. The total population in the

years between two censuses is commonly estimated by multiplying the population in the year of the census by the annual growth rate for each subsequent year (Table 6). Administrative units such as health districts have a unique annual growth rate that is provided in the census data. The most accurate estimates are obtained by using the unique annual growth rate for each IU. If this is not available, the growth rate at a higher administrative level can be used.

Table 6. Example calculation of population projections based on census data and annual growth rates

IU	2025 (year of census)	Annual growth rate[a] (%)	2026 calculation	2026 projected population	2027 calculation	2027 projected population	2028 calculation	2028 projected population
A	266 789	2.60	266 789 × 1.026	273 726	273 726 × 1.026	280 842	280 842 × 1.026	288 144
B	359 540	2.90	359 540 × 1.029	369 967	369 967 × 1.029	380 696	380 696 × 1.029	391 736
C	187 392	3.10	187 392 × 1.031	193 201	193 201 × 1.031	199 190	199 190 × 1.031	205 365

IU, implementation unit.

[a]A 2.60% annual growth rate equals a multiplication factor of 1.026 to determine the projected population each year.

- ***Special surveys***. In the absence of census data, surveys can be carried out under the auspices of the ministry of health, other disease programmes or other development sectors to estimate the population in different administrative units.
- ***Enumeration of household populations before MDA***. In many national disease programmes, household enumeration is conducted to record the target or eligible population. In LF programmes, this is often done by drug distributors, and the accuracy of enumeration depends on appropriate resource allocation for training and supervision. Enumeration need not be conducted annually but could be done once every few years, and the data could be used to make projections in the interim years (see Table 6). Data collected in an LF programme can also be used for other health activities, or the LF programme could benefit from enumeration of household populations performed in other health programmes.
- ***Microplanning***. Some LF programmes undergo rigorous microplanning before each MDA, with segmentation of the IU into smaller catchment areas with well-defined boundaries. Demographic data collected for each catchment area are used for population enumeration and are updated annually with each round of microplanning. The manual for NTD microplanning provides additional information on this activity *(88)*.

Each country will determine the most accurate source of data for determining the total population of an IU. In some countries, the source of population data may differ for different IUs. It is advisable to state the source of the data and to document why that data source was used in reporting to WHO.

5.1.3 Determining the target population in an IU

A certain section of the population that requires preventive chemotherapy will not be eligible for treatment and will therefore not be included in the population targeted for treatment. Ineligibility is determined according to the safety profile of the medicines used in MDA (Table 7). The population that is eligible for MDA is the population of the IU that requires preventive chemotherapy minus the ineligible population. The same data source should be used to calculate the total population and the eligible population in a given IU.

Table 7. Exclusion criteria[a] for LF MDA, by regimen, according to WHO guidance on LF MDA

Regimen	Exclusion criteria
Ivermectin, DEC, albendazole (IDA)	▪ Pregnant women ▪ Severely ill patients (including those with a history of neurocysticercosis, seizures or Stevens–Johnson syndrome) ▪ Children aged < 2 years – Children aged 2–4 years should be given DEC and albendazole – Children ≥ 90 cm in height (approximately equivalent to ≥ 15 kg body weight) should be given IDA ▪ Women breastfeeding infants aged < 1 week DEC is contraindicated in areas where onchocerciasis or loiasis are co-endemic. Ivermectin is contraindicated in areas where loiasis is co-endemic and is used restrictively for onchocerciasis, as it can cause serious adverse events in patients with loiasis.
DEC and albendazole	▪ Pregnant women ▪ Severely ill patients ▪ Children aged < 2 years DEC is contraindicated in areas where onchocerciasis or loiasis are co-endemic.
Ivermectin and albendazole	▪ Pregnant women ▪ Severely ill patients (including individuals with a history of neurocysticercosis, seizures or Stevens–Johnson syndrome) ▪ Children < 90 cm tall (approximately equivalent to < 15 kg body weight) ▪ Women breastfeeding infants aged < 1 week
Albendazole only (biannual, in areas co-endemic for LF and loiasis and not eligible for ivermectin or DEC)	▪ Pregnant women during the first trimester ▪ Severely ill patients (including individuals with a history of neurocysticercosis, seizures or Stevens–Johnson syndrome) ▪ Children aged < 2 years

DEC, diethylcarbamazine; IDA, ivermectin + diethylcarbamazine + albendazole; LF, lymphatic filariasis; MDA, mass drug administration; WHO, World Health Organization.

Sources: Lammie et al. *(17)*; WHO *(82, 89–91)*.

[a] People who have previously suffered one of the rare serious adverse events caused by a reaction to the medicines should be excluded from treatment *(92)*.

5.2 Monitoring indicators required

The objective of MDA is to administer antifilarial medicines to all eligible individuals in endemic IUs. For LF, MDA is typically administered once a year, although, in certain settings, such as where LF and loiasis are co-endemic, MDA is conducted twice a year *(4)*. For MDA to be effective, ≥ 65% coverage of the total population must be treated during each round of MDA. If MDAs do not reach this coverage, more rounds of MDA are likely to be required to reach below the elimination threshold *(93, 94)*. Furthermore, if evidence is found of people who did not ingest the medicines in any MDA round (never treated), reservoirs of infection may remain in the population, with an increased chance of continuing LF transmission, even if the IU reached effective coverage levels *(95–97)*.

Drug distributors should be trained and supervised to ensure that they use directly observed therapy when possible, to both maximize the impact of the programme and to ensure that the reported coverage reflects as closely as possible the number of people who ingested the medicines *(98–100)*. At the time of administration, drug distributors will record the following in their registers, according to the relevant distribution strategy:

- the number of individuals who ingested the medicines;
- those who were not eligible for treatment; and
- eligible people who did not ingest the medicines for various reasons.

These data are compiled by the drug distributor for the village, school or urban area and then typically sent to the health centre or health facility that oversees the catchment area. The IU authorities receive all the data from the health centres or facilities either directly or through an intermediate level. It is important that the data submitted to each IU are complete so that IU authorities have the most accurate information for compiling data and calculating coverage.

The following indicators are recommended for measuring the effectiveness of MDA.

The geographical coverage indicator is

the proportion of endemic IUs covered by MDA in a country.

The geographical coverage (country) is

the number of endemic IUs in which MDA is implemented / the total number of endemic IUs in which MDA is required × 100.

To determine MDA coverage in the IU, the geographical coverage (IU) indicator is used to better understand the situation. This indicator can help programmes detect if any part of the IU was missed during MDA. It allows flexibility for determining how a sub-IU should be defined (e.g. village, health area, defined urban area, defined rural area):

The geographical coverage (IU) is

the number of sub-IUs covered by MDA in an IU / total number of sub-IUs in an IU × 100.

The drug coverage indicator is the proportion of individuals who ingested the medicines. Data from the drug distributors in the IU are sent to the health centres or facilities and then compiled to indicate the drug coverage. For LF, drug coverage is calculated with the total population of the IU as the denominator. This is known as epidemiological coverage and reflects the proportion of the population that requires preventive chemotherapy that received MDA:

Epidemiological coverage is

number of people who were reported to have ingested the drugs / total population of IU × 100.

As noted above, the minimum effective epidemiological coverage is 65% of the total population in an IU. This is, however, only the minimum, and programmes are strongly encouraged to reach 100% of the eligible population and ensure that the entire eligible (target) population has an opportunity to take the medicines. Programme managers should use epidemiological coverage data to determine which, if any, IUs have low coverage, so that they then can investigate further and improve programme implementation, including with an immediate mop-up MDA.

In addition to the reported coverage of an entire IU, analysis of the data by age group (adults aged ≥ 20 years, preschool-aged children aged < 5 years, school children aged 5–14 years, and older children aged 15–19 years) and by gender is useful to determine any variation in coverage of different sub-populations *(5)*.

Calculation of the epidemiological coverage at sub-IU level (e.g. village, health area, health unit, town) is also useful for determining the coverage of smaller geographical units the coverage of which is masked by estimates of IU coverage. No coverage, low coverage or implausibly

high epidemiological coverage (e.g. 98% or 110%) warrants closer examination. If a sub-IU is missed or a sub-IU has low coverage, follow-up activities are warranted, such as a mop-up MDA, future investment in microplanning and social mobilization or use of the supervisor's coverage tool (SCT) *(5)*. The finding of a sub-IU with very high coverage suggests likely inaccuracies in the denominator. Sub-IU coverage can also inform selection of spot-check sites for EMS when choosing areas in which transmission is most likely.

5.2.1 Additional tools for monitoring coverage

WHO provides several tools for strengthening monitoring of coverage and for providing data in addition to those collected routinely to improve programme delivery (Table 8). The tools may be used in situations in which the reported epidemiological coverage does not reflect the actual coverage *(101, 102)* because, for instance:

- Drug distributors left behind medicines for household members who were absent during their visit but recorded them as having been taken as they presumed that the absentees would take the medicines on their return.
- In their enthusiasm to show good performance, drug distributors reported higher than actual coverage.
- The data on total population or target population were outdated or incorrect, resulting in an erroneous calculation of drug coverage. For example, drug distributors' lists of households did not represent a complete count, resulting in a too small denominator for calculating reported coverage.
- Miscalculations were made in the data for an IU, resulting in incorrect reported coverage.
- Data were missing from the calculation, resulting in incorrect reported coverage.

Table 8. Tools for improving the quality of reported data and information on preventive chemotherapy for NTDs

	Coverage evaluation survey	Supervisor's coverage tool	Data quality assessment
Purpose	To validate reported coverage (obtain a statistical point estimate)	To classify coverage as above or below a threshold	To verify reported data and assess the capacity of data management and reporting systems
Administrative level	IU	Sub-IU	National and/or IU
Sample size	> 500	20	Not applicable
Sites visited	30 villages	Context-specific (~ 20 villages)	12 service delivery points
Survey team	External to programme	Internal, self-assessment	Internal and external to programme
Timing	Within 3–6 months of MDA (ideal)	Towards the end of MDA or immediately afterwards	Every 3 years nationally, rotated every year in IUs
Duration	2–3 weeks	< 1 week	2 weeks

IU, implementation unit; MDA, mass drug administration; NTDs, neglected tropical diseases.

Coverage evaluation survey: The first of these tools is a coverage evaluation survey (CES), a population-based cluster survey designed to provide estimates of MDA coverage, which can be used to validate reported coverage. It is useful in IUs with known coverage challenges and in areas

that have had unsatisfactory results in previous epidemiological surveys, such as EMS and TAS, and further MDAs are required. It is recommended that a CES be conducted after the first round of IDA in an IU *(4)*. CES should be implemented ideally within 3–6 months of MDA to minimize recall bias and ensure that survey results will be available in time to inform the subsequent MDA. The CES should be carried out by an independent team not responsible for MDA implementation in the IU. For specific methods for designing, collecting and analysing CES data, see the WHO publication *(5)*.

Surveyed coverage indicator: A measure to complement and verify reported coverage with population-based cluster survey methods. Surveyed coverage is calculated as:

Number of "yes" responses on having ingested the medicine / Total number of people surveyed × 100

CES provide data for comparison with the reported epidemiological coverage, which can be used to assess the extent to which:

- treatment was directly observed;
- coverage of the eligible population was achieved;
- non-eligible people were treated;
- treatment frequency differed (e.g. never treated, treated once, treated two or more times);
- reasons were given for not ingesting the medicines; and
- drug coverage for other NTDs was achieved.

CES provide rich data for exploring the reasons for not participating in MDA, such as "fear of side-effects" and other barriers to inclusion, such as "drug distributor did not come." Data on proxy responses given by people in a household who respond on behalf of someone else who is not home at the time of the survey can indicate populations that might routinely miss both MDA and surveys because of their timing. Data from CES can be analysed by age and gender to inform social mobilization and strategies for subsequent MDAs for specific sub-populations.

Supervisor's coverage tool: With lot quality assurance sampling (LQAS), the SCT provides data for supervisors to identify issues of reach and access in a sub-IU. The SCT gives structure to supervision, providing information about high- and low-performing areas. The findings can be used to trigger actions to resolve issues in real time. For example, a mop-up campaign improves coverage in areas in which an SCT detected borderline or inadequate coverage. An SCT can be used for annual routine monitoring in the same geographical areas or in different areas either during MDA or immediately afterwards. Specific methods for designing an SCT and for collecting and analysing the data are described in a WHO publication *(5)*.

Data quality assessment: The Data Quality Assessment (DQA) tool for NTDs was developed to support national programmes in strengthening their health information monitoring and reporting systems. In the DQA, data from MDAs are used to assess the quality of reported data and the ability of NTD data management systems to collect, transmit, document and report high-quality, reliable data. DQAs rely on data compiled at all levels from the most recent MDA round. WHO recommends that DQAs be conducted by national programmes every 3–5 years or, in a typical LF programme, once during LF MDA. Specific methods for designing an SCT and for collecting and analysing the data are described in a WHO publication *(5)*.

5.3 Additional uses of data from coverage monitoring

Data from coverage monitoring can be used to evaluate the MDA, plan the next MDA, plan social mobilization strategies for future MDAs and determine eligibility for an EMS.

Evaluation meetings

District (IU), regional and national meetings should be held after an MDA to review data on drug coverage, to describe lessons learnt during implementation of the MDA and to determine that all the requisite information is available for finalizing and validating the MDA data. If the evaluation meeting is held in the IU, all sub-IUs will report their coverage data so that sub-IU level coverage data can be examined. Evaluation meetings also provide an opportunity to discuss the findings of supportive supervision, the SCT and the DQA. Recommendations can be made during such meetings for future MDA planning. A CES or an EMS planned after the most recent MDA can be discussed at the evaluation meeting.

Planning meetings

Planning meetings are also held at various levels, from national to sub-IU. Review of coverage data in previous MDAs and discussion of lessons learnt can improve future MDAs and drug coverage. Low drug coverage in a community (IU, sub-IU) can indicate issues for focused attention and the need for additional resources. Common lessons learnt concern the timing of MDA, its coordination with other public health programmes, the drug distribution strategy (e.g. house-to-house or at a post) and the supply chain. For example, a supply chain issue could delay an MDA to a time that is inconvenient for the community, such as harvest time or the rainy season, which can negatively impact drug coverage. Important lessons from use of CES, SCT and DQA and microplanning can also be shared during such meetings to help solve problems. Use of the WHO NTD Microplanning Manual *(88)* is recommended for planning at IU and sub-IU level.

Social mobilization strategies

The design and delivery of messages to LF–endemic communities can influence their perceptions about and willingness to participate in MDA and thus impact drug coverage. The messages should be clear, concise and unambiguous, tailored to the local context in local languages and address specific perceptions and misperceptions about MDA identified in the CES or by local research. The language should be simple, non-scientific and easily understood by people with primary school education. Ideally, messages should be reviewed annually and adjusted to reflect changes in the programme, evolving understanding by the community about MDA and events during the past year (e.g. rumours, serious adverse events). Delivery of messages is also important, and consideration should be given to the level of education or literacy in the community, accepted means of communication and mitigation of "message fatigue" through innovative strategies.

Low coverage in a sub-IU can indicate that the community is not responding well to the current strategy for social mobilization and that the messages and their delivery should be reviewed. The CES can provide coverage data by sub-population (e.g. age, gender) and information about the reasons for which certain parts of the population do not participate in MDAs. Both the CES and SCT can be used to collect data on people who are not treated during MDA or have never been treated, and these data can be used to strengthen future social mobilization and indicate aspects for further resource allocation, such as microplanning and specific changes in the social mobilization strategy.

Eligibility for EMS

As discussed in depth in section 6, IUs must have achieved ≥ 65% coverage of the total population for a requisite number of rounds – depending on the regimen – to be eligible for EMS. Tools such as the CES, SCT and sub-IU level coverage analysis can provide additional evidence of the true drug coverage. When there is concern about coverage, these tools can help national LF programmes to determine whether an IU is ready for an EMS or whether another round of high-coverage MDA is warranted so that they can place resources where they are needed most.

6. Epidemiological monitoring surveys (EMS)

In the first (2011) edition of this manual, sentinel and spot-check site assessments were recommended to collect reasonably accurate information on the trend of infection during the programme. Programme managers usually conducted baseline Mf surveys, followed by a mid-term impact assessment in sentinel and spot-check sites after three rounds of MDA. The mid-term results were used to provide concrete evidence for determining whether drug coverage in the first three rounds was adequate to decrease the prevalence of infection. The results were also used to provide data for advocacy for the endemic communities and to motivate staff.

Mid-term impact assessments, while important, are now considered optional for the two- and three-drug regimens, and national programmes are encouraged to use the various tools that have been developed to monitor coverage and to focus on reaching as many eligible people as possible during an MDA (section 5).

Sentinel and spot-check site assessments through the EMS are recommended to assess the impact of MDA on the prevalence of infection and whether an IU is eligible to conduct more rigorous surveys for deciding when to stop MDA (Table 9). EMS (formerly known as pre-TAS) are part of the stop-MDA strategy and should be conducted *(4)*:

- after at least five rounds of MDA with annual albendazole + ivermectin or annual albendazole + DEC, with "effective" defined as ≥ 65% coverage of the total population;
- after one or two effective rounds with IDA, depending on the use case; and
- after at least five effective rounds of MDA with biannual albendazole in areas co-endemic for *loiasis* as a mid-term assessment to monitor efficacy, and after at least 10 effective rounds of MDA with biannual albendazole.

Table 9. Characteristics of an EMS

Goal	▪ **Demonstrate that the prevalence in at least two high-risk sites in the EU is below the target threshold and that the EU is eligible for TAS or IIS**
Eligibility criteria	▪ At least five rounds of effective coverage (≥ 65% of total population) of a two-drug regimen ▪ At least one or two rounds of effective coverage with IDA, depending on the use case ▪ At least five rounds (mid-term) or 10 rounds (pre-stop) of effective coverage with biannual albendazole
EU size	▪ < 500 000 population ▪ Definition of "similar IUs" for grouping or splitting into EUs to include: contiguous, similar baseline prevalence, same number of MDA rounds, similar population density, similar elevation, similar coverage and compliance, similar characteristics of underserved areas
Sampling strategy	▪ Random sampling of households
Sample population	▪ Adults (males and females) aged ≥ 20 years
Indicators	▪ Mf among people who test positive by an RDT ▪ If Mf testing is not possible, Ag results can be used
Decision rule	▪ If Mf < 1% or Ag < 2% in each site individually in the EU, the EU is eligible for TAS or IIS

EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IIS, IDA impact survey; IU, implementation unit; MDA, mass drug administration; Mf, microfilariae; RDT, rapid diagnostic test; TAS, transmission assessment survey.

There are several key differences between the former pre-TAS and new EMS with the aim to improve the sensitivity of the survey to detect and respond to ongoing transmission. The EMS samples adults (≥ 20 years), and the threshold indicator in areas endemic for *W. bancrofti* is based on both Ag and Mf biomarkers. Random sampling is used in the EMS to generate a prevalence estimate. The timing of the EMS is no sooner than 9 months after the last MDA round with IDA and no sooner than 6 months after all other LF MDA regimens. The EU for an EMS consists of populations of < 500 000 people, and their formation is based on homogeneous risk.

The EMS determines whether an EU is eligible to undergo the TAS or IIS, both of which require significant resources to conduct. The results of an EMS conducted at a small number of sites, which costs far less than a TAS or IIS, are used to decide whether a full assessment (i.e. TAS) is warranted.

6.1 Geographical area to be surveyed

The study area selected for an EMS is designated an EU, which may comprise an IU, several IUs or part of an IU. The formation of EUs is an important programme decision that can affect detection of ongoing transmission. In general, LF surveys are a better tool for decisions in EUs in which the risk factors for LF transmission are homogeneous *(103, 104)*. Compared to larger EUs, smaller EUs are expected to be more homogeneous in terms of LF prevalence. The considerations for the formation of EUs for EMS described here are also relevant for TAS (section 7) and IIS (section 8).

6.1.1 Recommended criteria for formation of EUs

The following criteria should be considered when combining IUs. If any of the criteria recommended below are not met, consider forming separate EUs.

- IUs have received the minimum number of effective MDA rounds (see Table 9).
- IUs have received the same number of MDA rounds.

- IUs are contiguous.
- The baseline prevalence in the IUs was similar.
- The population density is similar (e.g. mainly rural or mainly urban).
- The elevation and vector abundance are similar.
- The population characteristics that may affect coverage or exposure are similar (e.g. socioeconomic status or ethnic group).
- The MDA coverage is similar.
- The total population of the EU is < 500 000, accounting for a projected population growth whereby the EU will maintain < 500 000 people through the TAS3/IIS3.

Some IU might have to be divided to form several EUs. An IU should be divided if it meets either of the following criteria:

- population > 500 000 (at the time of the EMS and projected through TAS3/IIS3) or
- the risk of transmission of LF varies widely within the IU.

Combination of IUs into a single EU may reduce overall survey costs but also has some risks. For example, if the threshold is exceeded, all the IUs that comprise the EU will have to continue MDA. Furthermore, the EU may pass even though the prevalence of infection in one or more IUs is above the threshold, which could allow transmission to recrudesce in those IUs. It may sometimes be more cost-effective to divide one IU into two or more EUs because of its size or heterogeneity of risk factors. Formation of smaller EUs may allow programmes to stop treatment in high-performing areas while targeting their remaining resources to the sites at which MDA is most needed.

6.2 When to conduct an EMS

In accordance with previous guidance, an EMS should be conducted at least 6 months after the latest MDA in areas in which one- and two-drug LF regimens were given. The time of detection of resurgence of Mf after treatment and operational feasibility for national programmes determine when surveys should be conducted, which should be at least 9 months after the latest MDA in areas in which IDA was used *(105)*.

An EU is eligible for EMS if at least five rounds of effective two-drug MDA, with ≥ 65% coverage of the total population, have been conducted; the rounds need not be consecutive (Table 10). If an EU fails an EMS, two effective annual two-drug MDA rounds should be conducted before the next EMS.

Where IDA is used, the EU must have conducted two IDA rounds of effective coverage before an EMS. Exceptionally, when IDA is introduced in an IU after three effective rounds of DEC and albendazole, the EU may proceed with EMS after at least one effective MDA round with IDA. This exception applies to IUs that have had no prior pre-TAS, EMS or TAS. If an EU that has received IDA is above the survey threshold for an EMS, two more effective annual IDA rounds should be conducted before the next EMS.

Programmes that provide biannual albendazole should conduct EMS as a mid-term assessment after five effective rounds and then again after 10 effective rounds. If the survey result for an EU is above the threshold, four more effective rounds should be implemented before an EMS is conducted again.

Table 10. Timing of and types of biomarkers used in EMS

MDA regimen	MDA eligibility criteria	Biomarkers	Timing
Annual ivermectin and albendazole or annual DEC and albendazole	After five effective rounds or after two effective rounds when previous survey results were above the threshold	Ag where *W. bancrofti* is endemic or anti-*Brugia* Ab seroprevalence where *Brugia* spp. are endemic, followed by Mf in people positive for Ag or Ab	At least 6 months after last LF MDA
Annual IDA	After one effective round when there were three previous effective rounds of DEC and albendazole or after two effective rounds when there were zero to two previous effective rounds of DEC and albendazole or after two effective rounds when previous survey results after IDA were above the threshold	Ag where *W. bancrofti* is endemic or anti-*Brugia* Ab seroprevalence where *Brugia* spp. are endemic, followed by Mf in people positive for Ag or Ab	At least 9 months after last LF MDA *(105)*
Biannual albendazole (only in areas co-endemic for *LF* and *loiasis*).	After five effective rounds at mid-term or after 10 effective rounds before stopping or After four effective rounds when previous survey results were above the threshold	Ag followed by Mf in people positive for Ag	At least 6 months after last LF MDA

Ab, antibody; Ag, antigen; DEC, diethylcarbamazine; EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IU, implementation unit; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae.

6.3 Implementation of an EMS

National programmes are encouraged to adapt and use the EMS preparation checklist (Annex 8) while planning an EMS.

6.3.1 Target population

To increase the sensitivity of an EMS to detect ongoing transmission, the survey should address Mf in adults (≥ 20 years), because adults have a higher prevalence of Mf than children *(106–109)*. Some studies have identified infections and ongoing transmission among adults when infection in children is below the threshold *(104, 110)*. In most areas, decision criteria based on infection in adults can be considered conservative.

The survey population should be similar to that of the EU (e.g. farmers, fishermen or urban, peri-urban or rural). All members of the population at the site should be included; if the population is large, sub-unit(s) of the site can be chosen randomly through segmentation. A hamlet, village or segment of a sub-district can be chosen in rural areas, and a small community or segment of a borough or ward can be chosen in a city or town. All adults (≥ 20 years of age) who live in the

area are eligible for testing. Pregnant and lactating women should not be excluded from the assessment.

6.3.2 Selection of survey sites

A survey site is defined as the lowest-level administrative structure in the country on which the LF programme has data. It could be a village, block or street, depending on the local setting. In many cases, the LF programme identified a sentinel site for each IU before the first round of MDA. This site was often that found to have the highest prevalence during mapping or in a separate baseline survey before MDA. Sentinel site surveys were historically conducted to assess Ag or Mf, or both. In some cases, such as when resources were scarce or when an IU was changed to another district, the sentinel site represented more than one district or IU.

Spot-check sites are additional sites in an EU that are assessed during an EMS at the same time as the sentinel site(s). Both sentinel and spot-check sites should be communities expected to have the highest prevalence in the EU. Spot-check sites should be chosen according to factors such as low MDA coverage, high baseline prevalence and high vector density. At least one sentinel and one spot-check site should be selected per EU.

If there has never been a sentinel site in an EU, at least two spot-check sites should be selected. When a sentinel site reaches the criterion of < 2% Ag or < 1% Mf, it is not surveyed in subsequent EMS, and a new spot-check site is chosen to replace it.

The choice of sentinel and spot-check sites depends on the country situation. While general guidance is given here, it is recommended that programme managers discuss and seek advice from WHO on the approach that is appropriate for a given setting.

Characteristics of sentinel sites

A sentinel site should:

- be in an area of known high risk of transmission (high parasite prevalence, vector abundance or clinical disease), which are likely to require the longest time and the largest number of MDA rounds to achieve interruption of transmission. If specific data on transmission risk are not available, the site should be chosen on the basis of the best information available;
- have received no prior or ongoing MDA for onchocerciasis, when possible;
- have a stable population that is not affected by migration; and
- have similar demographic characteristics as the whole IU.

If it is a small site that cannot realistically yield a survey sample of 300 adults because of absence or non-response, a "related" neighbouring community should also be selected as part of the same sentinel site to enable testing of at least 300 people.

Sites found to have a high prevalence during mapping or baseline surveys should be designated sentinel sites. Once chosen, the same site should be used throughout the programme to assess the impact of MDA. A sentinel site that meets the criteria of < 2% Ag or < 1% Mf is not surveyed in subsequent EMS, and a new spot-check site is chosen to replace it. (See section 9 on responding to survey outcomes that are above the threshold.)

Characteristics of spot-check sites

Spot-check sites have the same characteristics as sentinel sites. They provide additional information on the prevalence of Ag or Mf in the EU and can be used to counteract any potential bias at sentinel sites *(111, 112)*. They should be in an area considered at high risk for continued

transmission. Analysis of MDA data by sub-IU may help to identify areas of relative low coverage for selection of spot-check sites. At least one spot-check site should be chosen per EU; more such sites could be selected when necessary or resources permit. A spot-check site that records outcomes above the threshold criteria must be included in subsequent repeat EMS in the EU until the site reaches the threshold criteria for passing (section 9).

6.3.3 Sample size

Each site should collect data on at least 300 individuals aged ≥ 20 years.

6.3.4 Selection of households

If the population of adults in the selected site is < 400, every adult should be tested (census). Random sampling of adults in selected sentinel and spot-check sites is recommended for sites in which the population of adults is > 400. When random sampling is used, an estimate of prevalence can be generated, which is better than a convenience sample, as it can eliminate types of sampling bias that could result in an incorrect decision about whether criteria have been met. Two methods can be used for random selection of adults.

Systematic sampling of households. A unique sampling interval is calculated for the community. From a listing or numbering of households, teams pick a random number between 0 and the sampling interval and then add the sampling interval repeatedly to the random starting number to generate a list of the households that should be selected. All adults in each selected household should be tested.

$$\text{Household sampling interval} = (n') * (1-r) / (q),$$

where

n' = estimated population of adults at the site,

r = the expected non-response rate and

q = the desired sample size per site.

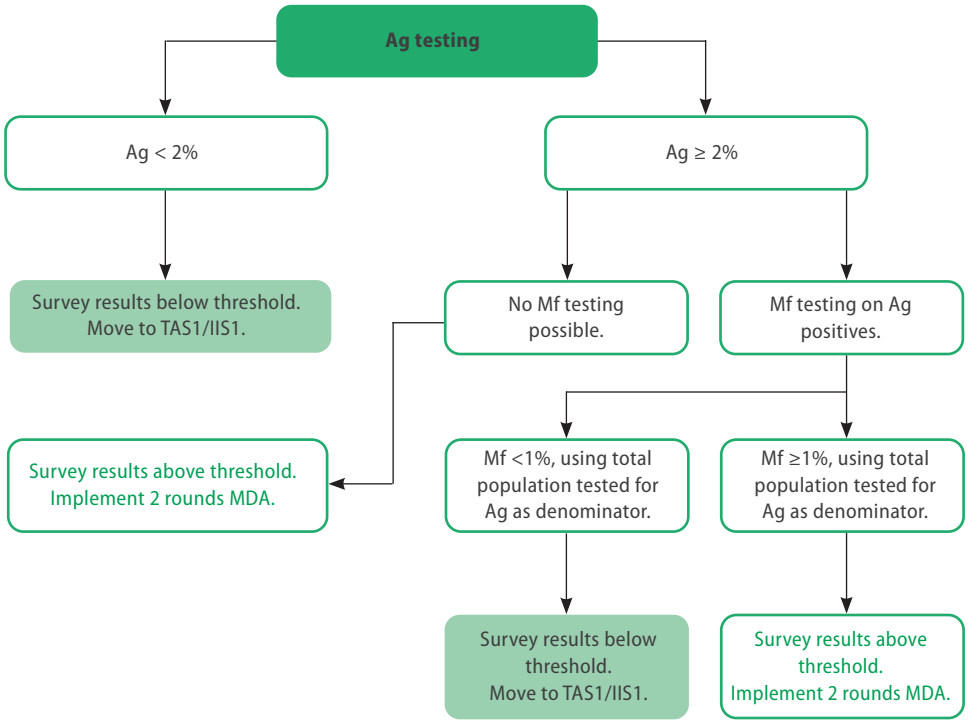
Segmentation. The community is split roughly into equal segments of 100 households, and two or three segments are randomly selected according to the number of households necessary to reach the target sample size of adults. All households in the selected segment are visited, and all adults in each household are eligible for testing. If random sampling is not possible, it is important to ensure (i) equal geographical representation of the site in the sample and (ii) inclusion of groups at highest risk in the sample.

6.3.5 Survey results and decision

The EU is considered to have passed if each surveyed site in the EU is below the required threshold. A site is considered to have passed when the Ag prevalence is < 2.0% or the Mf prevalence is < 1.0% (Fig. 5).

When Mf is tested in Ag-positive people, the denominator for calculating Mf prevalence should comprise the total population tested for Ag using a rapid test, and the numerator should comprise all people who tested positive for Mf in blood smear microscopy. In this calculation, all Ag-negative people are counted as if they were Mf-negative. If people who are Ag-positive cannot be tested for Mf, they should be counted as Mf-positive in the numerator.

Fig. 5. Determination results and actions for an EMS



Ag, antigen; EMS, epidemiological monitoring survey; IIS, IDA impact survey; MDA, mass drug administration; Mf, microfilariae; TAS, transmission assessment survey.

If one or more sites record outcomes above the threshold, the EU has not passed the EMS. When an EU passes, a stop-MDA survey (TAS or IIS) is recommended as soon as possible (section 9).

When an IU or EU is split into smaller units for any reason (e.g. re-districting, to obtain homogenous EUs), the original IU or EU results and decisions (passed or above the threshold) apply to all the divided units, irrespective of location and the results of sentinel or spot-check sites included in the surveys.

Individuals found to have Mf or Ag in the surveys should be treated according to national guidelines. Eligible people should be treated with the IDA regimen *(4)*. It is recommended that all family members of positive individuals also be treated *(113, 114)*. If people who test positive are planned to be followed-up with blood films for Mf testing, they should not be treated until an additional blood specimen has been collected during the hours of peak Mf circulation.

6.4 Diagnostics

Programmes should use RDTs followed by Mf testing by blood smear microscopy for all people who test positive in the RDT. If rapid tests are not available, programmes can conduct Mf testing only (section 3). As Mf prevalence decreases dramatically after MDA, measurement of its prevalence provides evidence of the effectiveness of the MDA *(32)*. Ag rates decrease more slowly than those of Mf and therefore provide underestimates of the effects of MDA, particularly after the first few rounds *(69, 115, 116)*.

If Mf is difficult to measure, e.g. because insecurity prevents collection of night blood samples and cannot be evaluated, Ag can be used to make a decision. Meeting the Ag criteria for EMS is considered to be a more conservative approach. Programmes should continue MDA if the prevalence of Ag is ≥ 2% if no Mf results are available.

6.5 Data collection and use

Programmes should ensure collection of complete, high-quality data during EMS. Demographic data should be linked to the results of both RDTs and Mf testing. Electronic data collection can provide data monitoring and updates in real time and georeferenced data points for creation of maps. National programmes are also encouraged to adapt and use the EMS supervision checklist (Annex 9).

Programme managers should collect not only data on diagnostic test results but also simple information from participants on their age, gender, history of having ever been treated in an MDA, number of previous treatments received and clinical manifestations of LF. To identify people who have never been treated, the following question should be posed: "Including this year, how many times have you taken pills for LF?" with response categories of "never", "once" and "two or more times." Consult WHO for access to tools intended to help programmes reach "never treated" populations.

6.6 Integration of this approach with other NTDs

In areas where LF and other NTDs are endemic, the prevalence of other diseases can also be assessed at sentinel and spot-check sites, for example, by collecting stool samples from the population to detect soil-transmitted helminthiases (STH) and/or schistosomiasis. Indicators of cross-cutting impact, such as for anaemia, disability and blindness, could also be included in data collection at sentinel and spot-check sites, when appropriate *(117)*. Information such as the prevalence of clinical manifestations of LF, previous participation in MDA could be collected. Collection of data on bed net usage during an EMS would be valuable in areas where malaria is co-endemic.

6.7 Reporting EMS to WHO

Countries should report their plans to conduct EMS to WHO. If diagnostic tests are being requested through WHO, communication with WHO is required at least 6 months before the EMS. After the surveys have been completed, the results should be reported to WHO, at least annually, through the Epidemiological Data Reporting Form (EPIRF). Programmes are also encouraged to submit any narrative report summarizing survey results.

7. Transmission assessment surveys

Evaluation is necessary to determine whether programmes have achieved their objective of reducing LF transmission in endemic populations to a level at which it is probably no longer sustainable and recrudescence is unlikely to occur. TAS are designed to help programme managers to determine whether an area is below this threshold of infection *(62)*. In this edition of the manual, several changes have been made to the TAS, outlined in detail in this section, to improve the sensitivity of the surveys to detect and respond to ongoing transmission *(28)*. The prevalence target threshold is now < 1% Ag (*W. bancrofti*) and Ab (*Brugia* spp.) for all vector and parasite species. The critical cut-off value for all vector species is lower. As for the EMS, the EU for the TAS will consist of populations < 500 000 and will be derived according to homogeneous risk. Actions are provided on following-up positive individuals and clusters with targeted treatment.

This section also identifies the TAS as the survey to be used after an EMS that is below threshold in any of the following scenarios:

- MDA was delivered as a one-drug regimen (biannual albendazole), and the total number of MDA rounds with ≥ 65% coverage was at least 10.
- MDA was delivered as a two-drug regimen (ivermectin + albendazole; DEC + albendazole), and the total number of MDA rounds with ≥ 65% coverage of the total population was at least 5.
- One round of IDA was delivered after > 3 two-drug rounds, with ≥ 65% coverage of the total population in at least 4 rounds, and no prior pre-TAS, EMS or TAS has been above threshold.
- Two rounds of a two-drug regimen with ≥ 65% coverage of the total population were delivered in response to a survey above threshold in an EU.

Section 8 provides information on use of the IDA impact survey after delivery of more than one round of IDA.

The TAS SSB tool *(118)* can be used to automate calculations for determining the appropriate survey strategy. The design of the TAS is flexible and can therefore be adapted to best fit the local situation, as it depends on factors such as the net primary-school enrolment ratio, the population size, the number of schools or EAs and the feasibility of survey methods.

7.1 Geographical area to be surveyed

The TAS should be conducted at EU level and use the same definitions of an EU created for the EMS (see section 6.1).

7.2 When to conduct a TAS

A TAS should be conducted when all IUs in the EU have met the recommended criteria for achieving the number of MDA rounds with ≥ 65% coverage of the total population and have passed the EMS (section 6). The TAS may be conducted as soon as possible after passing EMS. In a few exceptional circumstances, epidemiological data support proceeding to a TAS before the recommended number of effective MDA rounds has been achieved. Consult WHO in such situations for expert review and support in deciding whether to proceed to a TAS.

Given the lead times required to ensure that medicines are available and to prepare for an MDA, programmes might plan an additional round of MDA, regardless of the results of the EMS or TAS. Planning of an additional round should take into account the resources and medicines available. If an additional round is conducted after a passed EMS, a TAS can be implemented any time after the MDA.

7.3 Implementation of a TAS

7.3.1 Target population

Children aged 6–7 years are recommended as the target population for a TAS, as they are a target age group that should be protected from LF infection in settings in which five or more rounds of MDA have successfully interrupted transmission. Infected children represent incident infections and indicate recent transmission.

In school-based surveys, first- and second-year primary-school children approximate the study population, although a few children may be outside of those ages. Household surveys should focus on children aged 6–7 years in the selected households. Migrant children in the target age group who currently reside in the EU should be included in the TAS *(119, 120)*.

7.3.2 Survey design

The survey designs summarized below are intended for implementation in EUs known to have been previously endemic for either *W. bancrofti* only or *Brugia* spp. only. Fig. 6 illustrates the steps in conducting a TAS. For countries or EUs with small populations, the survey design might have to be modified. In these cases, WHO should be consulted.

School-based survey. If the net primary-school enrolment ratio[1] in the EU is ≥ 75%, schools will be the survey sites, and first- and second-year primary school pupils will be the survey population. All children enrolled in the first or second year of primary school should be considered eligible for the survey sample. Although a small number of this survey population may fall outside the intended target age of 6–7 years, the group still represents incident infection.

Data on school enrolment (the numbers of first- and second-year primary-school children and a list of all primary schools in the EU) and the average absentee rate for this group should be obtained with assistance from the ministry of education. When this number is not available, it can be estimated from census data and the expected rate of primary school enrolment. When there is evidence of high rates of school absenteeism in communities considered to be at high-risk for LF, a community-based survey should be considered.

[1] Net primary-school enrolment ratio is the number of children enrolled in primary school who are in the age group that officially corresponds to primary schooling, divided by the total population of the same age group. In some countries, the admission ratio, that is, the net first-year enrolment ratio, may be available. If so, this is a more useful indicator for decision-making.

Community-based survey. In areas in which the rate of school enrolment is < 75%, census EAs are recommended as the clusters if cluster sampling is used. EAs are usually the smallest area for which census population results are available. Although a community might be designated as an individual EA, the definitions are not interchangeable, as one EA may include more than one small community, and larger communities may be divided into more than one EA. Survey teams should obtain EA maps from the census office, and the maps should be used during the survey to ensure that the survey teams include all households within the boundaries of the EA and only the households within the boundaries of the EA in selecting households.

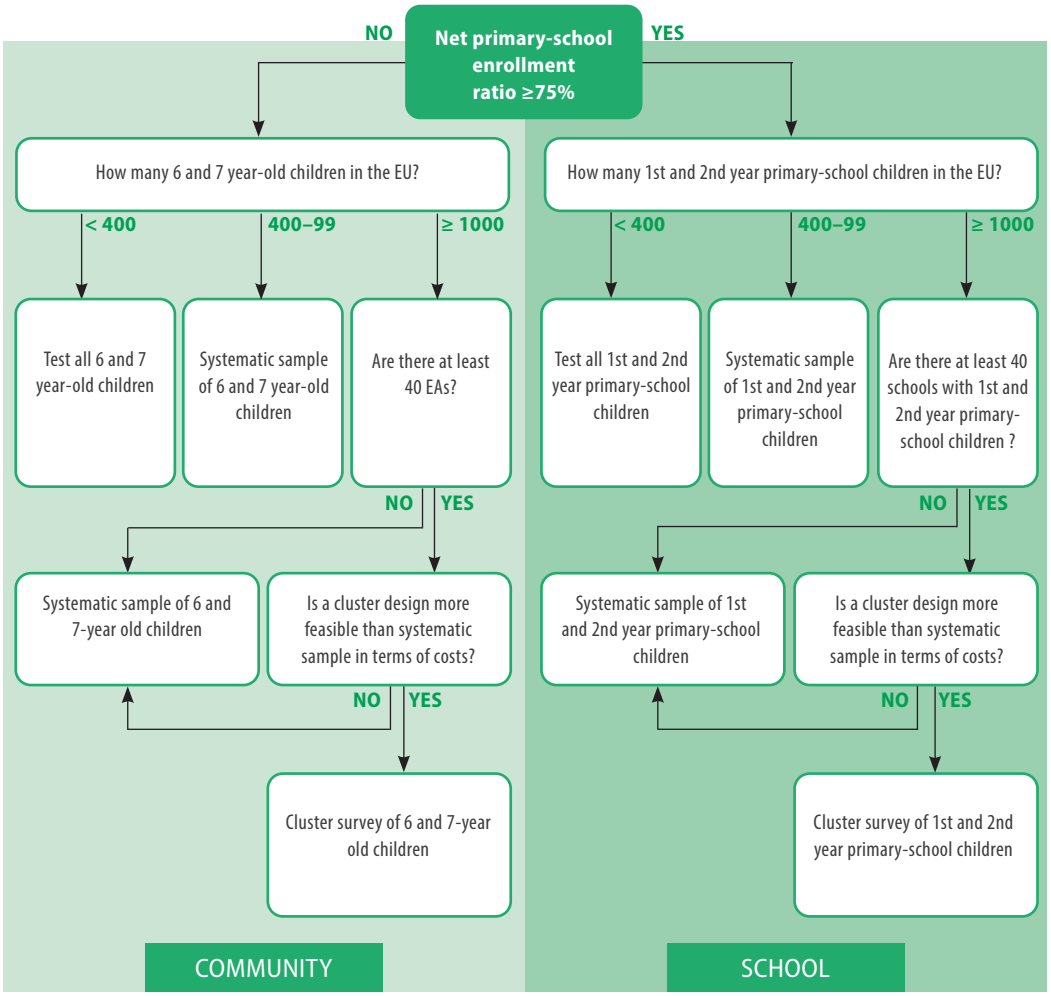
Community-based household surveys are more expensive and time-consuming than school-based surveys; however, if less than 75% of children are enrolled in schools, school-based surveys could potentially introduce significant selection bias, which could lead to statistically significant differences in the rates of infection between children attending school and those who do not.

In community household surveys, all children aged 6–7 years in the EU (data from the national census bureau) are eligible for inclusion. If there are census data only for 5–9-year-olds, it is reasonable to approximate 40% for the proportion of 6–7-year-olds. Data projected from the most recent census should factor in the average projected annual population growth rate.

Census. In EUs in which the total number of children aged 6–7 years is < 400, the TAS should be a census, such that all children aged 6–7 years or all first- and second-year primary-school children should be tested.

For both community-based household surveys and school-based surveys, children should be selected using a cluster-sample design or directly by systematic sampling. The choice between these sampling methods depends on the number of 6–7-year-olds and the number of clusters (schools or EAs) in the EU. Sample sizes are smaller for systematic sampling; however, survey teams will have to visit all EAs or schools in the EU. Sample sizes for cluster-based surveys are larger, but only a subset of schools or EAs in the EU must be visited. In both sampling methods, a recommendation to stop or continue MDA will be based on whether the number of Ag-positive or Ab-positive children identified in the sample exceeds the critical cut-off value in Table 11. This survey approach is an example of cluster-based LQAS. The TAS SSB tool *(118)* automates calculations for determining the appropriate survey strategy and is the tool recommended for planning surveys. To access the latest tool, please consult WHO.

Fig. 6. Algorithm for choosing the TAS design for all EUs, regardless of vector species



Ag, antigen; EMS, epidemiological monitoring survey; IIS, IDA impact survey; MDA, mass drug administration; Mf, microfilariae; TAS, transmission assessment survey.

7.3.3 Selecting survey sites

A numbered list of all primary schools for school-based surveys, or EAs for community-based surveys, in the EU should be prepared in advance by the country programme manager. To achieve better geographical distribution, the school or EA list should be numbered by geographical proximity rather than in alphabetical order. The TAS SSB tool should then be used to generate random numbers that correspond to the schools or EAs in the list to be selected for surveying. For systematic sampling, all schools and EAs on the list will be selected. For cluster-sample surveys, a minimum of 30 schools or EAs will be selected.

7.3.4 Sample size calculations

The sample sizes required for TAS are listed in Table 11. The TAS SSB tool can also be used to calculate sample sizes automatically. The target threshold to be measured in the TAS is < 1% Ag prevalence (where *W. bancrofti* is endemic) or < 1% Ab prevalence (where *Brugia* spp. are endemic). The sample sizes and critical cut-off values were chosen so that an EU has:

- at least a 75% chance of passing if the true prevalence of Ag (or Ab) is 0.25%; and
- no more than about a 5% chance of passing (incorrectly) if the true prevalence of Ag (or Ab) is ≥ 1%.

Table 11. Sample size and critical cut-off values for TAS for either systematic or cluster sampling

Target population size (total number of children aged 6–7 years)[a]	Systematic sampling design		Cluster sampling design		
	Sample size (n)	Critical cut-off value	Sample size (n)[b]	No. of clusters	Critical cut-off value
399	Census	< 0.01*n[c]	Cluster sampling is not recommended; use systematic sampling.		
400	284	1			
600	365	1			
800	438	1			
1000	506	1	759	Divide the sample size for a cluster survey by the average number of target-age children per school/EA and round up to the nearest integer. If this integer is < 30, then the number of clusters is 30.	1
1200	520	1	780		1
1400	530	2	795		3
1600	594	2	891		3
2000	606	2	909		3
2400	614	2	1228		4
2800	678	2	1356		4
3200	684	2	1368		4
3600	688	2	1376		4
4000	690	2	1380		4
5000	696	2	1392		4
6000	762	3	1524		6
8000	766	3	1532		6
10 000	770	3	1540		6
14 000	774	3	1548		6
18 000	776	3	1552		6
24 000	778	3	1556		6
30 000	778	3	1556		6
40 000	842	3	1684		6
49 999	842	3	1684		6
>50 000	846	3	1692		6

EA, enumeration area; TAS, transmission assessment survey.

[a] Refers to the population being surveyed, such as first- and second-year primary-school children or children aged 6–7 years in the community. For a population size between two adjacent Ns in the table, the lower N should be used.

[b] For the cluster design, the assumed design effects are 1.5 if the population size is < 2400 and 2.0 if the population size is ≥ 2400.

[c] For example, if there is a total of 300 first- and second-year primary-school children in the EU, all are tested and three are antigenaemic. The EU would fail the TAS, because the proportion of children tested who are antigenaemic is 1.0%, not < 1.0%. In this case, 0.01 × N = 0.01 × 300 = 3. The critical cut-off value, d, would be the first integer < 3, which is 2.

Box 2. Details of sample size calculations

For decision-making, the TAS algorithm provides a situation-specific decision rule (sample size *n* and critical cut-off value *d*). Decision rules are based on the probability, calculated with the cumulative hypergeometric distribution function, of finding no more than d children positive for the marker being used (Ag or Ab) in a sample of n target-age or target-grade children drawn from a total survey population of *N* such children. The cut-off *d* is determined to limit the maximum type 1 error (alpha; the risk of falsely concluding that an EU is below the TAS threshold) to ≤ 5% under the null hypothesis (H0) that the prevalence of the marker in the population *N* is at or above the threshold level (1%) and to maintain the power of the test ≥ 75% under the alternative hypothesis (H1) that the true prevalence is below 25% of the null threshold level (0.25%).

The power of a statistical test is the probability that the null hypothesis is rejected, and the alternative is accepted when the alternative is true. The power requirement in the TAS decision rules resulted from the aim that EUs in which the prevalence of Ag or Ab has been lowered below the alternative threshold by a comfortable margin have a strong chance of concluding correctly that MDA can be stopped. There is a trade-off between the power of the TAS and the sample size requirements. The current parameters of "> 75% power when the true prevalence is 0.25%" were determined to appropriately balance cost against programme needs.

The decision rules selected in Table 11 were the values closest to those that provide alpha error < 5% and power > 75% for a given value of N, with the smallest sample size. When cluster sampling is used, in place of systematic sampling, *n* and *d* must be multiplied by the expected design effect (alpha error and power remain unchanged). A design effect of 1.5 was assumed for cluster-sample designs when *N* is < 2400, and 2.0 was assumed when *N* is ≥ 2400.

Rationale for the change to a < 1% TAS threshold for all vector and parasite species

The threshold of < 1% Ag or Ab for passing the TAS and the associated sample sizes and critical cut-off values represent a departure from the previous guidance on TAS. In this latest edition, the sample size and critical cut-off values for TAS are the same for all vector species. The < 1% Ag or Ab threshold will apply to all LF settings (*Aedes, Anopheles, Culex* and *Mansonia*) and should be applied in all future TAS1, TAS2 and TAS3. The threshold need not be applied retrospectively to TAS that have already been conducted.

The rationale for reducing the TAS threshold from < 2% to < 1% antigenaemia in areas endemic for *Anopheles*, *Culex* and *Mansonia* to match that of *Aedes* is based on observations from over 1000 TAS that have already been reported to WHO *(1, 121)* and from models for predicting LF elimination. Observations that support this change include the following.

- Settings in which *Culex* are found have the highest rate of failure in TAS2 and TAS3, suggesting that settings passed TAS1 without having interrupted transmission *(122)*. Reducing the threshold to <1% will lower the critical cut-off value, making it more difficult for settings with a significant number of positive cases to pass the TAS. The change is intended to help programmes identify problem areas sooner so that the MDA can continue while the necessary logistics are in place and programme momentum is established.
- Several reports of modelling suggested that passing a TAS (at the previous <2% Ag threshold) does not always lead to sustained elimination and that a lower TAS threshold would increase the probability that the transmission breakpoint has been reached *(123–126)*.
- Empirical data also suggest that the previous TAS threshold (< 2% Ag) was not sensitive enough to detect ongoing transmission in some settings *(108, 110, 127)*. In the study in Sri Lanka, if the new < 1% antigenaemia threshold had been applied, the IU with ongoing transmission would have been identified in the TAS.

- In areas with *Aedes,* while the threshold of <1% remains unchanged *(127, 128)*, the sample size per cluster and the critical cut-off values are significantly reduced. This change is warranted, as there are diminishing returns to increasing the number of children sampled per cluster for estimating the average EU prevalence of LF. The reduction in sample size facilitates surveys in *Aedes* areas without sacrificing the risk of falsely passing the TAS. (The risk of type 1 error remains < 5%.)

The following box provides examples of survey design and critical cut-off values for school-based and community-based surveys.

Box 3. Examples of survey design and critical cut-off values

Example 1: School-based survey, cluster sampling

- 20 000 first- and second-year primary-school children enrolled in the EU = target population size
- 400 primary schools
- From Table 11, population = 18 000
  - Cluster design preferred (because > 40 schools in the EU)
  - Sample size = 1552 first- and second-year primary-school children
  - Number of clusters in the survey sample = 32
  - All first- and second-year primary-school children included in the survey sample in each of the 32 selected schools
  - Critical cut-off = 6

Example 2: School survey, systematic sampling

- 1250 first- and second-year primary-school children enrolled in the EU = target population size
- 35 primary schools
- From Table 11, population = 1200
  - Systematic sampling (not cluster sampling) survey design
  - Sample size = 520 first- and second-year primary-school children
  - Critical cut-off = 1

Example 3: Community-based survey, cluster sampling

- 25 150 6–7-year-olds in the EU = target population size
- 325 EAs
- From Table 11, population = 24 000
  - Cluster design preferred (because > 40 EAs in the EU)
  - Sample size = 1556 6–7-year-old children
  - 30 clusters required for the sample size
  - Critical cut-off = 6

7.3.5 Common challenges in sample size

Absenteeism and non-response: To account for absentees in selected schools and households or refusal to participate, the TAS SSB tool allows input of an expected absentee rate. The rate differs by country, the demography of the EU and the timing of the survey. For school surveys, programme managers are advised to consult teachers and the ministry of education to estimate the expected absentee rate, apart from children who are not enrolled. If the absentee rate is not known, it could be estimated by visiting a few schools and consulting teachers. It is recommended that the survey be conducted when the absentee rate is projected to be the lowest.

Once the expected absentee rate has been entered, the TAS SSB tool will add additional clusters (schools or EAs) to compensate and recalculate the sampling interval if necessary. The clusters and individuals selected originally should be sampled even if the target sample size has been met.

Exceeding the target sample size: If the sample size is exceeded before all the selected clusters have been sampled, enumeration should continue until all the clusters have been surveyed. It is important, from a statistical and representative point of view, to complete sampling in all the planned clusters before concluding the survey; the team should not stop the survey prematurely if the sample size is met before the last cluster is complete. When preparing for a survey, therefore, programmes should be sure to have "buffer" stocks of RDTs and other supplies.

Unable to reach the target sample size: The TAS SSB tool allows for selection of five "extra" clusters to be visited only if the target sample size is not reached after the original clusters have been surveyed. The extra clusters should be visited in the order in which they are listed in the TAS SSB, which is the order of random selection. There is no need to sample any extra clusters once the target sample size has been achieved or exceeded; the survey team can stop upon completion of the respective cluster.

If the target sample size is not met after sampling the extra clusters, the programme should consult WHO on how to proceed. If the shortfall in sample size is due to inaccurate estimates of school attendance (e.g. children have migrated to urban cores and are no longer attending school in rural areas), it may be appropriate to use a new critical cut-off value. This is done by consulting Table 11 and selecting the row that is closest to, without exceeding, the actual sample size and applying the new corresponding critical cut-off value. A sample size shortfall due to a larger-than-expected non-response or absenteeism rate introduces greater potential bias. In such instances, "mop-up" sampling could be conducted in the selected clusters to reach populations that were previously missed.

To avoid sampling shortfalls, the best practice is to review the actual non-response rate after the first two or three clusters have been surveyed. If the non-response rate differs significantly from that anticipated or if actual school attendance differs significantly from that entered into the TAS SSB, the programme manager is strongly advised to update the estimates of non-response rate and/or population in the TAS SSB. This will result in new sampling lists, which should be more accurate. This may avert additional activities to reach the target sample size at the end of the survey.

7.3.6 Randomized selection of school children and households

The TAS SSB tool will calculate a sampling fraction, which is the proportion of children to be surveyed per school for school surveys and the number of households to be surveyed per EA for community surveys. The TAS SSB tool will also calculate the sampling interval (inverse of the sampling fraction) and a random starting point within the sampling interval for generating two numbered lists (A and B) to facilitate selection of school children and households. After deciding on the order in which school children or households will be selected in each school or EA, the

survey teams randomly select list A or list B. This process should be repeated at each new cluster visited, with list A or list B randomly selected each time.

To understand how list A and B are calculated, if the random starting point on a list is 2.2 and the sampling interval is 2.5, the first child or house selected would be #3, immediately followed by #5 (2.2 + [1 × 2.5]), #8 (2.2 + [2 × 2.5]), #10 (2.2 + [3 × 2.5]) and #13 (2.2 + [4 × 2.5]). Note that all selections are rounded up to the nearest integer, but the calculation includes decimals. If the sampling interval is 1, all children or households in the selected schools and communities will be surveyed, and list A and B will not be required.

The starting number in list B is equal to the sampling interval minus the starting number in list A. Therefore, use of both lists controls the sample size, as the starting number used for schools or EAs will not be consistently high or low within the sampling interval.

7.3.7 Cut-off criteria

The TAS is designed to give programme managers a critical cut-off value. If the number of Ag- or Ab-positive results found is no higher than this number, the EU "passes", and it is assumed that transmission can no longer be sustained, even after MDA has been stopped.

In areas endemic for *W. bancrofti*, if the number of Ag-positive children tested is less than or equal to the critical cut-off value in Table 11, it is likely that transmission can no longer be sustained. In such cases, the programme can decide to stop MDA in the EU. If the number of Ag-positive children is greater than the critical cut-off value, MDA should continue in the EU for two more rounds.

In areas in which *Brugia* spp. are endemic, the same critical cut-off value for the number of Ab-positive children will be used as in *W. bancrofti* areas. While it is recognized that Ab levels will probably be higher than Ag levels *(64, 129, 130)* and the threshold may therefore be conservative, it has been reported that the BmR1 recombinant Ab response in humans clears rapidly with clearance of infection and is therefore considered to be a good indicator of current infection status *(131, 132)*.

7.4 Diagnostics

Where *W. bancrofti* is endemic, rapid Ag tests should be administered to all surveyed individuals to measure levels of antigenaemia. These tests require no laboratory equipment, and the results can be processed quickly. A positive result indicates the presence of adult worms and is therefore a measure of the potential for ongoing transmission. LF rapid Ag tests are available for use in TAS through WHO (see section 3).

There is currently no Ag test for use in areas in which *Brugia* spp. are endemic. Countries should consult WHO to obtain rapid Ab tests for detecting the presence of antifilarial Ab. Rapid Ab tests should be administered to all individuals in a survey to detect Ab (section 3). If the Ab test is positive, programme managers could conduct follow-up testing for Mf at night, during the hours of peak Mf circulation. These data will help better define the relation between Ab and Mf positivity. If such tests are not available, the programme can collect blood films for Mf and serum samples for testing by enzyme-linked immunosorbent assay in a laboratory.

In areas endemic for both *W. bancrofti* and *Brugia* spp., if RDTs are available for both parasites, both should be used. Positive results should be evaluated separately against the critical cut-off values. For example, if the critical cut-off value for an EU is six, and the survey results yield four positive rapid Ag tests and three positive rapid Ab tests, the EU would pass the TAS, as each positive value

is less than six. If either diagnostic test is not available, Mf is the best indicator and can be collected with the survey methods introduced in section 8.

Even if programmes follow the manufacturer protocols for use of rapid Ag and Ab tests, irregularities may be observed (e.g. invalid tests or defective kits). A survey respondent who is tested with an invalid rapid test should be tested again, if possible. If neither a positive nor a negative result is obtained in the second test or a second test cannot be done, the respondent should be excluded from the total sample (Table 12). Programmes should record any irregularities, with photographs of irregular tests when possible, and report the irregularities to WHO. To access the latest diagnostic feedback form, please consult WHO. Feedback is critical to ensure continuous improvements of the quality of tests.

Table 12. Algorithm for interpretation of rapid Ag and Ab test results, and actions

First test result	Second test result	Result interpretation	Action or treatment required
Negative	No further testing required	Negative	–
Positive	No further testing required	Positive	Provide treatment
Invalid	Positive	Positive	Provide treatment
Invalid	Negative	Negative	–
Invalid	Invalid	Invalid	Exclude from sample
Invalid	Refused or testing not done	Invalid	Exclude from sample

Ab, antibody; Ag, antigen.

7.5 Team composition and workflow

7.5.1 Team composition

Each survey field team should consist of at least three members, one responsible for registering children and managing supplies, one phlebotomist and test preparer, and one test reader to record and report results. A minimum of three or four field teams is recommended, but the ideal number will depend on the size of the EU and the number of clusters to be covered. Additionally, if survey data are collected electronically, one member of each team should be responsible for collecting and charging the equipment each day. One individual should be selected from the entire group (i.e. not from each team) as the systems administrator, whose responsibilities are to synchronize and distribute the data collected by each field team.

It is important for programme managers to organize field teams and designate and define their roles before actual field work. A training session over several days on the survey design, electronic data capture method, blood sampling procedures and diagnostic test reading is recommended for new teams. For experienced teams, a 1-day refresher course may be sufficient. Bench aids for conducting the appropriate diagnostic tests are available for distribution and should be included with the survey preparation materials (Annexes 3–7).

7.5.2 Specimen collection and testing

The following protocol can be used to organize schools and communities for collection of demographic information and blood specimens and for conducting diagnostic testing. Each country programme should, however, decide on the most appropriate method in accordance with their local setting without disrupting the statistical integrity of the survey design. The chosen method should be used in all clusters in the EU.

School-based surveys

When the field team arrives at a designated primary school, they should work with teachers, the headmaster or school officials to gather all the children in first and second years. If not all children are to be surveyed (i.e. sampling interval > 1.0), the first- and second-year students should be lined up so they can be counted.

The team should keep a record of the total number of first- and second-year school children attending and absent from each school on the day of the survey. The numbers should be compared with the expected enrolled number and the predetermined absentee rate to decide whether additional clusters are necessary as the survey progresses.

The team leader then flips a coin to decide whether list A or list B will be used.

Children in line are selected according to the number on the chosen list. Selection of children should continue until the next number on the list is higher than the total number of first- and second-year children lined up at the school.

The team should then collect demographic data and blood specimens from the selected children. For school surveys, RDTs can be used and read in the field. If RDTs are used in the evening or at night, adequate lighting is essential for reading and recording an accurate result.

All positive cases should be treated with the treatment regimen used in the country. Status of residency should be checked for all positive cases to detect any significant migration in the area that could affect the impact of MDA rounds; a non-resident could be defined as someone who has lived in the area for < 1 year.

The steps should be repeated for each selected school, and additional schools if necessary, to meet the target sample size. Even if the number of positive results exceeds the critical cut-off value, the survey team should continue to collect information on all children sampled in the school.

Community-based (household) surveys

At each selected census EA or community, team leaders should work with village officials or community health workers to verify the estimated number of households in the EA and plan a walking route that will take them by every household. Sketch maps of the EA may be acquired from the census department. The community should be sensitized well in advance of the sample collection date.

A designated "mapping team" can be used to enumerate and mark the selected households before the field team begins. The team will then walk the chosen route to enumerate each household. From the list selected by the coin toss (list A or B), the team will sample all 6–7-year-old children in each selected household. If there are no 6–7-year-old children in the selected house, the team proceeds to the next house on the list. Selection and sampling are continued until the next number on the list exceeds the total number of households in the EA.

The team should keep a record of children who are absent from each household at the time of collection, and all efforts should be made to follow up the absentees later but within a reasonable time to complete the survey. The number of absentees and the total number of children surveyed per EA should be recorded and compared with the predetermined absentee rate and the expected population of children aged 6–7 years to determine whether additional clusters might be required as the survey progresses.

An alternative to house-to-house visits is preparation by village leaders of a list of 6–7-year-olds in the EA and arrangement for them to gather at a central location at a given time. The field team would select children for sampling from the local list of all 6–7-year-olds, as in school surveys.

The team should proceed to collect demographic data and blood specimens from all 6–7-year-old children in each selected household. For community surveys, it is recommended that blood samples be collected in heparin tubes before later testing in a laboratory or other controlled environment. This reduces the time between sample collection when moving from house to house and reduces the risk of test reader error due to coagulation of blood.

All positive cases should be treated with the treatment regimen used in the country. Residency status should be checked to detect any significant migration in the area that could affect the impact of MDA rounds; a non-resident could be defined as someone who has lived in the area for < 1 year.

The steps for each chosen EA should be repeated and additional EAs added if necessary to achieve the target sample size.

Even if the number of positive results exceeds the critical cut-off value, the survey team should continue to collect information on everyone in the sampled households in the EA.

7.6 Data collection and use

Programmes should create a system to ensure collection of complete, high-quality data during TAS, including linking of demographic data to the results of rapid tests to ensure correct attribution of test results. When available, barcodes with unique identifiers are efficient means in field surveys for matching demographic data with test results. Although programmes can use either paper or electronic systems for collecting data, electronic data collection has several advantages *(133)*. Electronic data collection systems can include checks during data collection to reduce errors or missing values and facilitate collection of georeferenced data points. Further, electronic data collection allows programmes to create data dashboards to track the progress of TAS activities in real time to ensure that surveyors are meeting sample size targets. Nevertheless, programme managers should consider the local context when determining the most appropriate strategy for data collection, such as computer literacy and the availability of electricity at survey sites. For data collection in countries in the African Region, standardized TAS electronic data collection tools are available through ESPEN (the Expanded Special Project for Elimination of Neglected Tropical Diseases) on the ESPEN Collect platform *(134)*. Programmes or regional tools may be available for other WHO regions.

In all TAS, the GPS coordinates at the sampling sites should be collected and stored, as they can be used to determine the spatial distribution of positive cases found during the TAS and displayed on maps for visual interpretation, as illustrated by Hast et al. *(135)*. Programmes are required to review cluster-level results after TAS, as both the concentration and location of positive cases should be used to inform programmatic decisions. For example, if positive cases are concentrated in a specific geographical area, targeted MDA may be considered, in addition to subdivision of the EU for future surveys (see sections 7.7 and 9 for greater detail).

7.7 Handling positive cases found during TAS

All people who test positive with an RDT during any survey should be treated. It is often best to treat such individuals immediately, to avoid loss during follow-up. If blood will be collected to assess for Mf, treatment should only be delayed until blood has been collected. Survey teams should carry a stock of the LF medicines used in the country to treat people who test positive. Studies have shown that clusters of infected children are associated with a higher likelihood of ongoing community transmission *(136, 137)*. Because LF infection clusters spatially, treatment should also be provided to household members of positive children in EUs meeting criteria to stop MDA *(138, 139)*. In settings where onchocerciasis is not endemic, eligible people should be treated with the IDA regimen *(4)*. Table 13 lists proposed programmatic actions in response to positive tests in EUs where criteria for stopping MDA was met i.e. passed TAS1, TAS2 and TAS3.

People who test positive should not only be treated, but their history of exposure should be investigated, particularly whether the individual migrated from an endemic area. Significant migration from endemic areas can reduce the effectiveness of local MDA rounds, especially if those who have migrated are untreated *(140, 141)*. If a non-resident (defined as someone who has lived in an area for < 1 year) is found to be positive, the area from which he or she migrated should be recorded, so that the area can be prioritized for ongoing surveillance.

Table 13. Recommended actions to be taken when positive cases are found in EUs that have passed a TAS

TAS outcome	Recommended action: the programme should determine which action in the outcome category is most appropriate in the local context		
	TAS1	TAS2	TAS3
Any positive children during TAS	▪ Treat positive child and any household members. ▪ Proceed to TAS2 as scheduled.	▪ Treat positive child and any household members; if resources allow, treat neighbours and the community around the household of the positive child. ▪ Proceed to TAS3 as scheduled.	▪ Treat positive child and any household members; if resources allow, treat neighbours and the community around the household of the positive child.
One cluster of ≥ 2 positive children in the cluster[a]	▪ Provide two additional rounds of targeted treatment in the community(s) represented by the schools/EA. ▪ Proceed to TAS2 as scheduled.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by the schools/EA. ▪ Proceed to TAS3 as scheduled.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA. ▪ Conduct EMS in targeted communities 6 months after the second round of targeted treatment to determine whether the prevalence of Ag or Mf is below the threshold.
Two or more clusters of ≥ 2 positive children in each cluster that appear to be grouped geographically[a]	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA. ▪ Consider dividing the EU into two smaller EUs for the next TAS, so that the positive clusters are together in one of the smaller EUs. ▪ Proceed to TAS2 as scheduled considering the 2 smaller areas as separate EUs.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA. ▪ Consider dividing the EU into two smaller EUs for the next TAS, so that the positive clusters are together in one of the smaller EUs. ▪ Proceed to TAS3 as scheduled considering the 2 smaller areas as separate EUs.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA.[b] ▪ Conduct EMS in targeted communities 6 months after the second round of targeted treatment to determine whether the prevalence of Ag or Mf is below the threshold.
Two or more clusters with ≥ 2 positive children in each cluster, and the clusters do not appear to be grouped geographically[a]	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA. ▪ Proceed to TAS2 as scheduled.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA.[b] ▪ Proceed to TAS3 as scheduled.	▪ Provide two additional rounds of targeted treatment in the community(s) represented by schools/EA.[b,c] ▪ Conduct EMS in targeted communities 6 months after the second round of targeted treatment to determine whether the prevalence of Ag or Mf is below the threshold.

Ag, antigen; EA, enumeration area; EMS, epidemiological monitoring survey; EU, evaluation unit; Mf, microfilariae; TAS, transmission assessment survey.

[a] Notify and seek advice from WHO in such instances.

[b] (Optional): Programmes may decide to conduct additional sampling in communities near the clusters that exceeded the cluster-level cut-off to determine whether the targeted treatment should be extended beyond the single communities included in the TAS. If available, geostatistical tools may be used to predict communities at high risk for additional targeted sampling. If further investigation identifies signs of more widespread transmission, the programme may decide to "fail" some or all of the EU.

[c] (Optional): The most conservative decision after identification of several positive cases during a TAS3 is to conduct two additional rounds of MDA in the entire EU and then repeat TAS3.

7.7.1 Observation of positive clusters over time

After MDA stops in the EU, programmes should consider including the schools or communities in which positive children were found as "purposeful sites" (schools or communities suspected of being at greater risk of ongoing transmission) in future surveillance activities (see section 9).

7.8 Integration of this approach with other NTDs

TAS may be used as a platform for integrated NTD surveys. WHO recommends that assessment of STH infections be integrated into a TAS to establish a new baseline for STH prevalence when MDA for LF has stopped *(142)*, and an SSB has been developed for the integrated survey *(143)*. The results for STH can be used to determine future deworming frequency. Timor-Leste has used TAS as the platform for school surveys for other diseases such as scrub typhus, leptospirosis, scabies, yaws, taeniasis and STH, which has enabled programme decisions for some of these NTDs *(144)*.

In countries co-endemic for onchocerciasis and LF, an integrated TAS (iTAS) can be used to assess the seroprevalence of onchocerciasis and to determine where ivermectin should be maintained for eliminating the disease. A manual to support NTD programmes in conducting iTAS will soon be made available by WHO.

7.9 Reporting TAS to WHO

Countries should report their plans to conduct a TAS to WHO through the TAS eligibility and planning form *(145)*, with any request for diagnostic tests through WHO. After the surveys are completed, the results should be reported to WHO at least annually through the EPIRF. Programmes are also encouraged to submit any narrative report summarizing the survey results.

8. IDA impact survey

To accelerate the global elimination of LF, in 2017, the WHO recommended use of IDA, a triple drug regimen *(4)*. IDA is recommended for use in settings in which onchocerciasis is not endemic and districts have either not yet started MDA, have conducted fewer than four effective rounds of MDA or in which the MDA results were suboptimal. One current challenge in implementing the IDA regimen is knowing when treatment can be stopped, i.e. when transmission has been reduced to a level at which infection is no longer sustainable in the absence of additional treatment. While IDA is very efficient in clearing Mf, CFA persists long after adult worm death or sterilization *(60)*. Consequently, when Ag is the indicator in a survey for decision-making, areas in which IDA MDA has been effective could still fail the surveys due to Ag prevalence *(28)*. B*m*R1 recombinant Abs, where *Brugia* spp. is the parasite, are also expected to persist after IDA MDA *(146)*. Furthermore, in areas that receive only two annual rounds of IDA, it can no longer be assumed that any Ag- or Ab-positive signal in 6–7-year-old children is a sign of incident exposure.

This section outlines the methods used in an IDA Impact Survey (IIS) *(147)*, which differs from a TAS. To increase confidence that the IDA regimen has successfully stopped transmission, it is necessary to demonstrate that Mf levels in adults in the EU are below a 1% threshold (< 0.5% when *Aedes* is the vector). Programmes are encouraged to review cluster-level results and to take appropriate action if one or more clusters has an Mf prevalence above the cluster-level threshold *(148)*. This section describes selection of community clusters for inclusion in the IIS, random sampling of adults in each selected cluster with a segmentation approach, the diagnostic tests to be performed, how to interpret the findings, and how to follow up positive individuals and clusters with targeted treatment. Table 14 summarizes the characteristics of the IIS, which are discussed in detail below.

Table 14. Characteristics of an IDA impact survey

Goal	**Demonstrate that the average prevalence in the EU is probably below the target threshold and that few, if any, hotspots of transmission remain**
Eligibility criteria	▪ EMS sentinel and spot-check sites < 1% Mf (*Anopheles, Culex, Mansonia*) or < 0.5% *Aedes*
EU size	▪ < 500 000 population
Sampling strategy	▪ 30-cluster sampling with probability proportional to estimated size ▪ Random systematic sampling of households used to select individuals in each cluster
Sample population	▪ Adults (males and females) aged ≥ 20 years
Indicators	▪ Mf among people who test positive by RDTs
Decision rule	▪ Average Mf in the EU < 1% (*Anopheles, Culex, Mansonia*) or < 0.5% (*Aedes*) and additional cluster follow-up as warranted in Table 21 (see section 8.3.6)

EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IU, implementation unit; MDA, mass drug administration; Mf, microfilariae; RDT, rapid diagnostic test.

8.1 Geographical area to be surveyed

The study area selected for an IIS is also the EU. See section 6 for criteria for forming an EU.

8.2 When to conduct an IIS

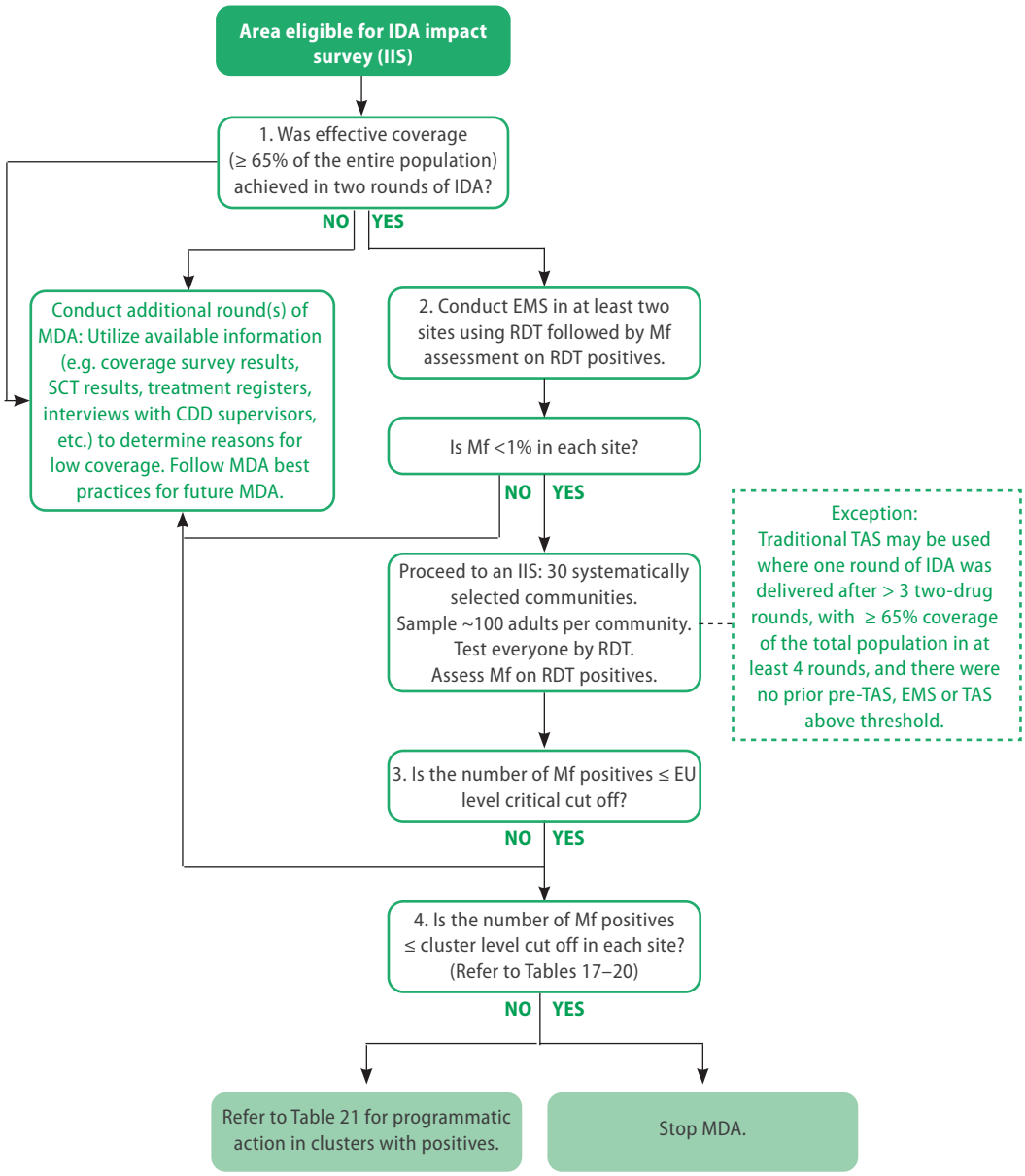
IIS is appropriate and necessary for deciding whether to stop treatment after an EMS that is below threshold in either of the following scenarios:

- two rounds of IDA with ≥ 65% coverage of the total population have been used to accelerate the LF elimination timeline and decrease the number of MDA rounds.
- two rounds of IDA with ≥ 65% coverage of the total population were delivered in response to a survey above threshold in an EU.

Section 7 provides information on use of the TAS among children in all other scenarios.

IIS should be conducted when all the IUs in the EU have met the recommended criteria for achievement of the number of MDA rounds with ≥ 65% coverage of the total population and the criteria in the EMS (section 6). An EMS should be conducted at least 9 months after an MDA in areas treated with IDA. If the EMS results are < 1% Mf in all sites, an IIS can be conducted as soon as possible after the EMS. Because of the timing of the EMS and the fact that the IIS will include Mf collection, the IIS should be conducted no sooner than 9 months after the last round of IDA MDA. Fig. 7 presents a flow chart for determining when after IDA MDA an IIS should be conducted in an EU.

Fig.7. Algorithm for implementing IIS



CDD, community drug distributor; DA, diethylcarbamazine + albendazole; EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IIS, IDA impact survey; MDA, mass drug administration; Mf, microfilariae; pre-TAS, pre-Transmission Assessment Survey; RDT, rapid diagnostic test; SCT, supervisor's coverage tool; TAS, transmission assessment survey.

8.3 Implementation of an IIS

An IIS requires community-based sampling and testing of adults. The definition of what constitutes a community should be in accordance with the local context (e.g. village, hamlet, census EA) and should represent the smallest administrative unit in the EU for which a list of all units can be obtained, with its estimated population.

8.3.1 Target population

The target population for an IIS is adults aged ≥ 20 years. This intentional difference from the TAS is due to the greater efficacy of IDA than of the standard two-drug regimen in reducing the concentration of Mf in a person's blood *(59, 149)*. This greater efficacy suggests that IDA has the potential to reduce the total number of MDA rounds required to interrupt transmission. Given the reduced number of MDA rounds recommended before an impact survey and the fact that IDA has limited impact on reducing Ag, both children and adults may still test Ag positive after IDA, even if transmission has been interrupted. Mf should therefore be used as the indicator to assess the impact of IDA. In LF-endemic communities, Mf prevalence is lowest in children compared to other age groups and is highest in adults, who carry the highest Mf burdens and represent the greatest risk for propagating LF in the community. The absence of Mf in adults is a good indicator that there is no longer ongoing transmission of LF in the community. Therefore, Mf is best measured in the adult population.

8.3.2 Survey design

The appropriate sampling design depends on the number of communities in the EU. If the EU has fewer than 40 communities, systematic sampling is required; if the EU has ≥ 40 communities, cluster sampling is preferred. See below for instructions on conducting systematic vs cluster sampling for an IIS.

Geostatistics is a branch of statistics that can be used to make predictions for diseases that have spatial patterns (e.g. clustering of LF cases or the association between LF risk and elevation). Recent geostatistical studies have shown that the same predictive performance can be attained as in a TAS or IIS with sampling in fewer sites *(150)*. Programmes may use geostatistical methods to design more efficient IIS, as long as the predictive performance for measuring the IIS threshold (< 1% Mf where *Anopheles, Culex* or *Mansonia* are the vector; < 0.5% Mf where *Aedes* is the vector) is the same as or better than that of the IIS (see section 8.3.4) *(151)*.

8.3.3 Selecting survey sites

To select communities as clusters for an IIS, a list of all communities in the EU should be obtained, with their respective estimated populations, preferably listed in geographical order, such as from northwest to southeast. From this list, 30 clusters will be selected according to probability proportionate to estimated size sampling. The IDA Impact Survey Sample Builder *(152)* has been developed to assist survey teams in selecting sites. To access the latest tool, please consult WHO. If systematic sampling is to be used (for EUs with < 40 communities), it is unnecessary to select clusters for the survey, as every community in the EU will be included.

To select clusters manually:

1. Create a spreadsheet containing a list of all communities in the EU and their estimated populations, listed according to approximate geographical proximity. For example, start in the northwest part of the EU and list each community, moving southeast until every community has been listed.

2. Create a column with the expected number of adults aged ≥ 20 years in each community by multiplying the estimated population of the community by the proportion of people aged ≥ 20 years in the country, which can be obtained from either census data or Population Pyramids *(153)*.

3. Calculate the expected total number of adults aged ≥ 20 in the EU by adding all values in this column, and then refer to Table 15 (*Anopheles, Culex, or Mansonia*) or Table 16 (*Aedes*) to determine the appropriate sample size and target cluster size for the survey.

4. Communities in which the expected number of adults is below the target cluster size (according to the values in tables 15 and 16) should be merged for sampling purposes with the next community on the list, such that the estimated population for the new "combined community" is the sum of the two individual populations.

5. Create a column with the running total for the cumulative population in the EU by adding the target populations from the previous rows to the current row.

6. Calculate the sampling interval as: [total EU population] / [30].

7. Choose a random number (*r*) between 1 and the sampling interval. The community that contains the rth person (according to the column with the cumulative population) corresponds to the first cluster selected from the list. For example, if the sampling interval is 6877 and the random number is 2003, the selected cluster is the first community for which the cumulative population contains the 2003rd person.

8. Next, add the sampling interval to the random number to obtain the second selected cluster. For example, 2003 + 6877 = 8880. Thus, the second cluster corresponds to the first community in which the cumulative population exceeds 8880.

9. Continue adding the sampling interval and selecting the first community for which the cumulative population contains the new sum until the end of the list is reached and 30 clusters have been selected.

Some larger communities may be selected as a cluster more than once. Therefore, the sample size in these large clusters will be two or three times greater than that of the other clusters (if the large cluster was selected two or three times).

If one or more of the "combined communities" is selected as a cluster, both communities that make up the "combined community" will be visited during the survey, and the same sampling interval (calculated below) will be applied in the two communities.

8.3.4 Sample size calculations

The sample size is powered to determine if the average prevalence of Mf in the EU is < 1% when the vector is *Culex* spp., *Anopheles* spp. or *Mansonia* spp. and < 0.5% in areas in which the vector is *Aedes* spp. The sample size is based on the assumption of a type 1 error rate of $a = 0.05$ (i.e. the likelihood of a false conclusion that an EU with a prevalence that exceeds the threshold will be classified as being below the threshold) and a type 2 error rate of $\beta = 0.25$ (i.e. the likelihood that an EU with a true prevalence that is half the threshold will be classified as exceeding the threshold). These error rates are similar to those applied in the TAS (see section 7), and therefore the decision-making power is comparable. See Tables 15 and 16 for additional details on sample size calculations.

Table 15. Sample sizes and critical cut-off values by population size for areas in which the principal vectors are *Anopheles*, *Culex* and *Mansonia* to detect a 1% Mf threshold in adults

Target population size in EU (adults aged ≥ 20 years)	Systematic sampling		Cluster sampling		
	Sample size[a]	Critical cut-off value[b]	Sample size[c]	Average sample size per cluster[d]	Critical cut-off value[b]
5 000–9 999	1515	9	3030	101	18
10 000–23 999	1545	9	3090	103	18
24 000–74 999	1560	9	3120	104	18
≥ 75 000	1575	9	3150	105	18

[a] Based on detecting a threshold of <1% with 5% chance of type-1 error and ~75% power (when the true prevalence is 0.5%).

[b] If the number of Mf-positive individuals in the survey is equal to or lower than the critical cut-off value, the average prevalence in the EU is probably <1%; the survey manager should examine the cluster level results in tables 17 and 19 below to confirm that there are no clusters that exceed the critical cut-off value.

[c] Based on a threshold of <1% with 5% chance of type-1 error, ~75% power (when the true prevalence is 0.5%) and a design effect of 2.0.

[d] A unique sampling fraction will be calculated for each selected cluster, such that the average number of people sampled per cluster and per age group is constant.

Table 16. Sample sizes and critical cut-off values by population size for areas in which the principal vector is *Aedes* to detect a 0.5% Mf threshold in adults

Target population size in EU (adults aged ≥ 20 years)	Systematic sampling		Cluster sampling		
	Sample size[a]	Critical cut-off value[b]	Sample size[c]	Average sample size per cluster[d]	Critical cut-off value[b]
5 000–5 999	2380	7	3570	119	11
6 000–6999	2400	7	3600	120	11
7000–9999	2500	7	3750	125	11
10 000–14 999	2760	8	4140	138	12
15 000–29 999	2820	8	4230	141	12
30 000–54 999	3100	9	4650	155	14
55 000–109 999	3120	9	4680	156	14
> 110 000	3140	9	4710	157	14

EU, evaluation unit; Mf, microfilariae.

[a] Based on detecting a threshold of < 0.5% with 5% chance of type-1 error and ~75% power (when the true prevalence is 0.25%).

[b] If the number of Mf-positive individuals in the survey is less than or equal to the critical cut-off value, the average prevalence in the EU is likely to be < 0.5%; the survey manager should examine the cluster-level results in tables 18 and 20, below, to confirm that there are no clusters that exceed the critical cut-off value.

[c] Based on detecting a threshold of < 0.5% with 5% chance of type-1 error and ~75% power (when the true prevalence is 0.25%) and a design effect of 1.5.

[d] A unique sampling fraction will be calculated for each selected cluster, such that the average number of people sampled per cluster and per age group is constant.

8.3.5 Selection of households and testing adults

Cluster sampling

Calculating the cluster-specific household sampling interval

A unique sampling interval will be calculated for each cluster to determine the households to be selected for inclusion. Unlike in the TAS, probability proportionate to estimated size is used to select the clusters, and a sampling interval is required that is based on the estimated size of the cluster to maintain an equal probability sample in the EU. This has the desirable effect of a consistent sample size in each cluster and enables assessment of the target threshold at cluster level. The cluster-specific household sampling interval is calculated automatically in the IIS SSB tool or can be calculated as follows:

$$\text{household sampling interval for cluster i} = (n_i') * (1\text{-}r) / (q) \text{ where,}$$

n_i' = estimated population of adults in cluster i

r = the expected non-response rate, and

q = desired sample size per cluster.

The survey planning team at central level should generate a sampling list for each cluster according to the cluster-specific sampling interval. This is done by choosing a random starting number between 0 and the sampling interval and then adding the sampling interval repeatedly to the random start to generate a list of households that should be selected. (Note: the IIS SSB will make these calculations automatically).

Selecting households and enrolling individuals

Upon arrival in the selected cluster, the team should meet with local leaders to explain the purpose of the survey and to solicit a local volunteer, such as a community health worker, to be a community guide. The guide will help the team to identify a route through the community that will pass by every household. Starting with the first house identified by the guide, the survey team should number each house (preferably with chalk, if acceptable). For each numbered house that corresponds to a number on the cluster-specific sampling list, the survey team should stop, enrol and test all adults aged ≥ 20 years living in the household.

Sampling should continue until every household in the cluster has been enumerated, and all adults living in households on the sampling list have been enrolled and tested or their refusal or absence documented. Sampling is not stopped once the average sample size per cluster has been achieved, nor are replacement households included if the average sample size per cluster is not reached. Rarely will the actual sample size achieved in each cluster match perfectly with the average cluster sample size; however, if the population estimates and absentee rates are reasonably accurate, small fluctuations do not matter. If the survey team observes large differences between the expected and actual sample sizes, the population estimate or absentee rate should be corrected early in the survey.

Systematic sampling

Calculating the EU sampling interval

In systematic sampling, a single EU sampling interval is calculated, which is applied to each community in the EU to determine which households to survey. Unlike in cluster-based sampling, described above, in which a unique sampling interval is calculated for each cluster, use of a single sampling interval for the EU results in variation in the number of adults sampled per community in proportion to the size of the community. The sampling interval is calculated automatically in the IIS SSB or can be calculated as follows:

$$\text{EU sampling interval} = (N') * (1-r) / m, \text{ where,}$$

N' = estimated population of adults in the EU

r = the expected non-response rate and

m = target sample size.

The IIS SSB generates two lists (A and B) from the EU sampling interval, and the numbers in these lists correspond to the household numbers that should be selected for the survey. Upon arrival in each community, the team should meet with local leaders to explain the purpose of the survey and solicit a local volunteer, such as a community health worker, to be a community guide. The team should then flip a coin to determine whether list A or list B will be used. Starting with the first house identified by the guide, the survey team should walk a route through the community that passes by each household and number the households (preferably with chalk, if acceptable). For each numbered house that corresponds to a number on the selected list (A or B), the survey team should stop and enrol and test all adults aged ≥ 20 years who live in the household. Sampling should continue until every household in the community has been enumerated, and all adults living in households on the sampling list have been enrolled and tested or their refusal or absence documented.

8.3.6 Cut-off criteria and interpretation

The critical cut-off value is designed for rapid interpretation of data from an IIS to determine whether the prevalence is above or below the threshold for decision-making. The IIS differs from the standard TAS in that two critical cut-off values are assessed: one to assess prevalence in the EU and one to assess prevalence in the cluster. In both instances, it is the number of individuals who test positive for Mf, and not the number of those who test positive in an RDT, that should be compared with the corresponding critical cut-off value.

Step 1: Assess the critical cut-off for EU-level decisions

After completion of an IIS, the number of individuals who test Mf positive in the entire sample should be compared with the critical cut-off value in Table 15 (for *Anopheles*, *Culex* or *Mansonia*) or Table 16 (for *Aedes*). This value is designed to measure whether the upper bound of the one-sided 95% CI exceeds the target threshold (< 1% for areas with *W. bancrofti* and < 0.5% for those with *Brugia* spp.). If the number of Mf positives exceeds the critical cut-off value in the table, the EU requires additional rounds of IDA. If the number of Mf positives is less than or equal to the critical cut-off value in Table 15 or 16, it can be concluded that the average Mf prevalence in the EU is below the target threshold, and the programme manager should proceed to step 2 to assess the threshold at cluster level.

Step 2: Assess the critical cut-off for cluster-level decisions

For each cluster (community) in the survey, the programme manager should compare the number of Mf-positive individuals with the critical cut-off values shown in Table 17 (for *Anopheles*, *Culex* or *Mansonia* when cluster-based sampling is used), Table 18 (for *Aedes* when cluster-based sampling is used), Table 19 (for *Anopheles, Culex* or *Mansonia* when systematic sampling is used) or Table 20 (for *Aedes* when systematic sampling is used). As the population size of communities can vary widely, it is important to use the critical cut-off value that corresponds to the estimated total target population of adults in that community.

The cluster-level critical cut-off value is designed to measure whether the lower bound of the one-sided 95% CI exceeds the target threshold (< 1% for *Anopheles, Culex, Mansonia* or < 0.5% for *Aedes*). Note that, unlike in the EU-level assessment, the cluster-level critical cut-off value is used to identify clusters that definitely exceed the target threshold (at > 95% likelihood), as the small sample size in each cluster makes it impossible to classify areas as below the target threshold. If the number of Mf positives in each cluster surveyed is less than or equal to the appropriate critical cut-off value for that cluster size, the entire EU is said to "pass", and it can be assumed that transmission has been interrupted and MDA can be stopped. If, however, the number of Mf-positive adults in one or more clusters exceeds the appropriate cluster critical cut-off value, the programme manager should refer to Table 21 to find the most appropriate decision for the local context. Programmes may consider targeted treatment of clusters where several Ag positive adults are identified, even if the number of Mf positive adults is below the critical cut-off value.

Table 17. Critical cut-off values for community-level decisions in areas with *Anopheles, Culex* or *Mansonia* when cluster sampling is used

Total population of adults (aged ≥ 20 years) in the cluster	Critical cut-off value[a]
≤ 200	1
201–499	2
≥ 500	3

The goal is to identify any clusters in which the Mf prevalence is likely to be >1%.

[a] If the number of Mf positives in a single cluster is greater than the critical cut-off value, the cluster prevalence likely exceeds 1% (at the lower bound of the one-sided 95% CI).

Table 18. Critical cut-off values for community-level decisions in areas with *Aedes* when cluster sampling is used

Total population of adults (aged ≥ 20 years) in the cluster	Critical cut-off value[a]
≤ 200	0
201–399	1
≥ 400	2

The goal is to identify any clusters in which the Mf prevalence is likely to be > 0.5%.

[a] If the number of Mf positives in a single cluster is > critical cut-off value then cluster prevalence likely exceeds 0.5% (at the lower bound of the one-sided 95% CI).

Table 19. Critical cut-off values for community-level decisions in areas with *Anopheles, Culex* or *Mansonia* when systematic sampling is used

Total population of adults (aged ≥ 20 years) in the community	Critical cut-off value with < 40 in sample	Critical cut-off value with 40–89 in sample	Critical cut-off value with ≥ 90 in sample
≤ 150	1	1	1
151–250	2	2	2
251–550	2	2	3
551–650	2	3	3
≥ 651	2	3	4

The goal is to identify any clusters in which the Mf prevalence is likely to be > 1.0%.

[a] If the number of Mf positives in a single cluster is greater than the critical cut-off value, the cluster prevalence is likely to exceed 1% (at the lower bound of the one-sided 95% CI).

Table 20. Critical cut-off values for community-level decisions in areas with *Aedes* when systematic sampling is used

Total number of adults (aged ≥ 20 years) in the community	Critical cut-off value with < 80 in sample	Critical cut-off value with ≥ 80 in sample
≤ 300	1	1
301–500	2	2
≥ 501	2	3

The goal is to identify any clusters in which the Mf prevalence is likely to be > 0.5%.

[a] If the number of Mf positives in a single cluster is greater than the critical cut-off value, the cluster prevalence is likely to exceed 0.5% (at the approximate lower bound of the one-sided 95% CI).

Table 21. Recommended actions to be taken when the number of Mf positives is less than critical cut-off value for the overall EU but one or more clusters exceeds the cluster-level critical cut-off value

IIS outcome	Recommended action: The programme should determine which action in the outcome category is most appropriate in the local context.		
	IIS1	IIS2	IIS3
Any RDT-positive adult found during IIS	▪ Treat positive individuals and any household members with IDA. ▪ Proceed to IIS2 as scheduled.	▪ Treat positive individuals and any household members with IDA; if resources allow, treat neighbours and the community around the household of the positive individual. ▪ Proceed to IIS3 as scheduled.	▪ Treat positive individuals and any household members with IDA; if resources allow, treat neighbours and the community around the household of the positive individual.
One cluster exceeds the cluster-level critical cut-off value for Mf-positive adults.[a]	▪ Provide two additional rounds of targeted IDA in the cluster in which the threshold was exceeded. ▪ Proceed to IIS2 as scheduled.	▪ Provide two additional rounds of targeted IDA in the cluster in which the threshold was exceeded. ▪ Proceed to IIS3 as scheduled.	▪ Provide two additional rounds of targeted IDA in the cluster in which the threshold was exceeded. ▪ Conduct an EMS in the cluster at least 9 months after the second round of targeted IDA to determine whether the prevalence of Mf is below the threshold.
Two or more clusters exceed the critical cut-off value for Mf-positive adults and appear to be grouped geographically.[a]	▪ Provide two additional rounds of targeted IDA in the clusters in which the threshold was exceeded. ▪ Consider dividing the EU into two smaller EUs for the next IIS, such that the positive clusters are together in one of the smaller EUs; the new, smaller EUs will remain in place for IIS2 and IIS3. ▪ Proceed to IIS2 as scheduled.	▪ Provide two additional rounds of targeted IDA in the clusters in which the threshold was exceeded. ▪ Consider dividing the EU into two smaller EUs for the next IIS, such that the positive clusters are together in one of the smaller EUs.[b] ▪ Proceed to IIS3 as scheduled.	▪ Provide two additional rounds of targeted IDA in the clusters in which the threshold was exceeded.[b,c] ▪ Conduct an EMS in the clusters at least 9 months after the second round of targeted IDA to determine whether the prevalence of Mf is below the threshold.
Two or more clusters exceed the critical cut-off value for Mf-positive adults but *do not* appear to be grouped geographically.[a]	▪ Provide two additional rounds of targeted IDA in the clusters in which the threshold was exceeded. ▪ Proceed to IIS2 as scheduled.	▪ Provide two additional rounds of targeted IDA in the clusters in which the threshold was exceeded.[b] ▪ Proceed to IIS3 as scheduled.	▪ Provide two additional rounds of targeted IDA in the community(s).[b,c] ▪ Conduct EMS in targeted communities 9 months after the second round of targeted treatment to determine whether the prevalence of Ag or Mf is below the threshold.

Ag, antigen; EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IIS, IDA impact survey; Mf, microfilariae; RDT, rapid diagnostic test.

[a] Notify and seek advice from WHO in such instances.

[b] (Optional): Programmes may decide to conduct additional sampling in communities near the clusters that exceeded the cluster-level cut-off to determine whether the targeted treatment should be extended beyond the single communities included in the TAS. If available, geostatistical tools may be used to predict communities at high risk for targeted sampling. If further investigation identifies signs of more widespread transmission, the programme may decide to "fail" some or all of the EU.

[c] (Optional): The most conservative decision after identification of several positive cases during a TAS3 is to conduct two additional rounds of MDA in the entire EU and then repeat TAS3.

The following boxes provide examples of survey design and cut-off levels for IIS.

Box 4. Example of IIS results in an area in which *Anopheles*, *Culex* or *Mansonia* is the primary vector and cluster-sampling is used

Principal vector: *Anopheles, Culex* or *Mansonia*

63 000 adults aged ≥ 20 years are estimated to live in the EU

287 communities in the EU

Survey design: cluster survey

From Table 15, sample size = 3120

IIS results:

3093 adults surveyed, 6 Mf-positive individuals identified

4 clusters had Mf-positive individuals

Cluster A had 2 Mf-positive individuals (estimated adult population = 279)

Cluster B had 1 Mf-positive individual (estimated adult population = 205)

Cluster C had 2 Mf-positive individuals (estimated adult population = 621)

Cluster D had 1 Mf-positive individual (estimated adult population = 182)

Critical cut-off interpretation:

Step 1. EU-level assessment: Number of Mf positives in survey (6) is less than or equal to the critical cut-off value (18); proceed to Step 2.

Step 2. Cluster-level assessment (see Table 17):

Cluster A: number of Mf positives (2) is less than or equal to the critical cut-off value (2)

Cluster B: number of Mf positives (1) is less than or equal to the critical cut-off value (2)

Cluster C: number of Mf positives (2) is less than or equal to the critical cut-off value (3)

Cluster D: number of Mf positives (1) is less than or equal to the critical cut-off value (1)

Programme conclusion: "Passes" IIS; transmission is likely interrupted, and the EU can proceed to post-MDA surveillance. Treat the RDT-positive individuals detected in the survey and their household members with IDA.

Box 5. Example of IIS results in an area in which *Aedes* is the primary vector and cluster-sampling is used

Principal vector: *Aedes*

23 000 adults aged ≥ 20 years are estimated to live in the EU.

91 communities in the EU

Survey design: cluster survey

From Table 16, sample size = 4230

IIS results:

4251 adults surveyed, 5 Mf-positive individuals

3 clusters had Mf-positive individuals

Cluster A had 1 Mf-positive individual (estimated adult population = 190)

Cluster B had 1 Mf-positive individual (estimated adult population = 355)

Cluster C had 3 Mf-positive individuals (estimated adult population = 488)

Critical cut-off interpretation:

Step 1. EU-level assessment: The number of Mf positives in the survey (5) is less than or equal to the critical cut-off (12). Proceed to Step 2.

Step 2. Cluster-level assessment (see Table 18):

Cluster A: The number of Mf positives (1) is greater than the critical cut-off value (0)

Cluster B: The number of Mf positives (1) is less than or equal to the critical cut-off value (1)

Cluster C: The number of Mf positives (3) is greater than the critical cut-off value (2)

Programme conclusion: Two clusters exceeded the critical cut-off value. The programme should consult Table 21 and conduct two additional targeted rounds of IDA in the two clusters. Determine whether the 2 clusters exceeding the cut-off value are grouped geographically and, if yes, consider dividing the EU for the next IIS. Treat the Mf- and RDT-positive individuals detected in the survey and their household members with IDA.

Box 6. Example IIS results in an area in which *Anopheles, Culex* or *Masonia* is the primary vector and systematic sampling is used

Principal vector: *Anopheles, Culex* or *Mansonia*

10 850 adults aged ≥ 20 years estimated to live in the EU

37 communities in the EU

Survey design: systematic sampling

From Table 15: sample size = 1545

IIS results:

1601 adults surveyed, 7 Mf-positive individuals

4 clusters had Mf-positive individuals

Cluster A had 1 positive out of 36 tested (estimated adult population = 80)

Cluster B had 2 positives out of 48 tested (estimated adult population = 112)

Cluster C had 2 positives out of 83 tested (estimated adult population = 148)

Cluster D had 4 positives out of 56 tested (estimated adult population = 260)

Critical cut-off interpretation:

Step 1 EU-level assessment: The number of Mf positives in the survey (7) is less than or equal to the critical cut-off value (9). Proceed to Step 2.

Step 2. Cluster-level assessment (refer to Table 19):

Cluster A: The number of Mf positives (1) is less than or equal to the critical cut-off value (1)

Cluster B: The number of Mf positives (2) is greater than the critical cut-off value (1)

Cluster C: The number of Mf positives (2) is greater than the critical cut-off value (1)

Cluster D: The number of Mf positives (4) is greater than the critical cut-off value (2)

After investigation, the programme finds that all four clusters are located in the northern, mountainous region of the EU.

Programme conclusion: Three clusters exceeded the critical cut-off value. The programme should consult Table 21 and conduct two additional targeted rounds of IDA in each of the three clusters. For all future IIS, the EU will be divided into two smaller EUs, such that the northern region (where all the positive clusters were found) constitutes one EU and the southern region is a separate EU. Treat the Mf- and RDT-positive individuals detected in the survey and their household members with IDA.

8.3.7 Addressing common challenges in sample size

Absenteeism and non-response: To account for absentees in selected households or refusal to participate, the IIS SSB tool allows users to input an expected non-response rate. The rate will vary by country, the demography of the EU and the timing of the survey. Programme managers are advised to consult local officials during social mobilization to determine the time of day and year when people are most likely to be at home. If the expected non-response rate is not known at the time the survey is designed, 2–3 days of training can be used to pilot-test the sampling method at several sites (not among those selected for the survey) to make a reasonable estimate of the non-response rate. Entry of this estimate into the IIS SSB tool will result in automatic adjustment of the sampling interval. If a selected household is abandoned or no one is home at the time of the visit, the survey team should proceed to the next household on the list; a replacement household is not necessary. Households in which an eligible adult is absent but expected to return later the same day should be noted by the survey team and revisited on the same or a later day if more than one day is necessary to complete the sample in a given community.

Exceeding the target sample size: If the sample size is exceeded before all the original clusters have been sampled, teams should continue until all the original clusters have been surveyed. When preparing for the survey, therefore, programmes should be sure to have "buffer" stocks of RDTs and other supplies. The team should not stop the survey prematurely if the sample size is met before the last cluster is complete; it is important, from a statistical and representative point of view to complete sampling in all the planned sites before concluding the survey.

Unable to reach target sample size: If the target sample size is not met after completing the sampling interval in all selected clusters, the programme should consult WHO to discuss how to proceed. If the sample size shortfall is due to inaccurate census estimates (e.g. the actual population in the communities is less than the projections used to determine the sampling intervals), it may be appropriate to use a new critical cut-off value. This is done by consulting Table 15 or 16 and selecting the row that is closest to (without exceeding) the actual sample size and applying the new corresponding critical cut-off value. If the sample size shortfall is due to a larger-than-expected rate of non-response or absenteeism, the potential bias is greater. In such instances, the ideal solution is to conduct "mop-up" sampling in the selected clusters to reach populations that were previously missed. If this is not feasible, additional clusters could be added to increase the sample size.

To avoid sampling shortfalls, the best practice is to review the actual non-response rate after the first two or three clusters have been completed. If the non-response rate differs significantly from that which was anticipated or if the actual community populations differ significantly from those reported in the census, the programme manager is strongly advised to update the non-response rate and/or population estimates in the IDA SSB. By doing so, the programme manager may avoid addition of additional activities to reach the target sample size at the end of the survey.

8.4 Diagnostics

In areas endemic for *W. bancrofti*, all enrolled adults should be tested with a rapid Ag test that has been validated by WHO (section 3). Where *Brugia* spp. are endemic, all adults should be tested with a rapid Ab test that has been validated by WHO. In all settings, as it is not possible to determine whether a positive Ag or Ab test in an adult indicates the presence of live adult worms, Mf testing by thick blood smear microscopy is required for all individuals who test positive by RDT. Individuals who tested positive by an Ag or Ab test should be visited during the hours of peak Mf presence (e.g. 22:00–02:00 h for nocturnally periodic settings) and blood samples should be collected for Mf microscopy. Blood samples for Mf testing should not be collected before 21:00 h, with the exception of *Aedes* areas where Mf are diurnally periodic.

8.5 Data collection and use

Programmes should create a system to ensure collection of complete, high-quality data during IIS and to link demographic data to the results of rapid tests to ensure correct attribution of test results. When available, barcodes with unique identifiers are a useful means for linking demographic data to test results in the field. While programmes can use either paper or electronic systems for collecting IIS data, there are several advantages to using electronic data collection *(133).* Such systems can provide data checks during data collection and thus reduce errors or missing values and facilitate collection of georeferenced data. Further, electronic data collection allows programmes to create data dashboards to track the progress of IIS activities in real time to ensure that surveyors meet sample size targets. Despite these advantages, programmes should consider the local context in determining the most appropriate strategy for data collection (e.g. computer literacy, availability of electricity at survey sites).

It is important that all IIS collect and store the GPS coordinates at the survey sites, as the coordinates are useful for determining the spatial distribution of positive cases during IIS. Programmes should review cluster-level results after an IIS, and both the concentration and location of positive cases should be considered in programme decision-making. For example, if positive cases are concentrated in a specific geographical area, targeted MDA may be considered, in addition to subdividing EUs in future surveys (see Table 21 above and section 9 for more detail).

8.6 Reporting IIS to WHO

Countries should report their plans to conduct an IIS to WHO through the TAS eligibility and planning form *(145),* with any request for diagnostic tests through WHO. After surveys have been concluded, the results should be reported to WHO at least annually through the EPIRF. Programmes are encouraged also to submit any narrative report of the survey results.

9. Responding to survey results that are above the threshold

Since publication of the WHO TAS manual in 2011, 20 countries have reported TAS results above the threshold, i.e. have "failed", in at least one IU. While the rate differs by country, globally, approximately 6% of all TAS results were above the threshold *(154)*. Recent modelling has identified predictors of TAS results above the threshold at EU level, including a high baseline prevalence, high population density and low elevation *(155)*.

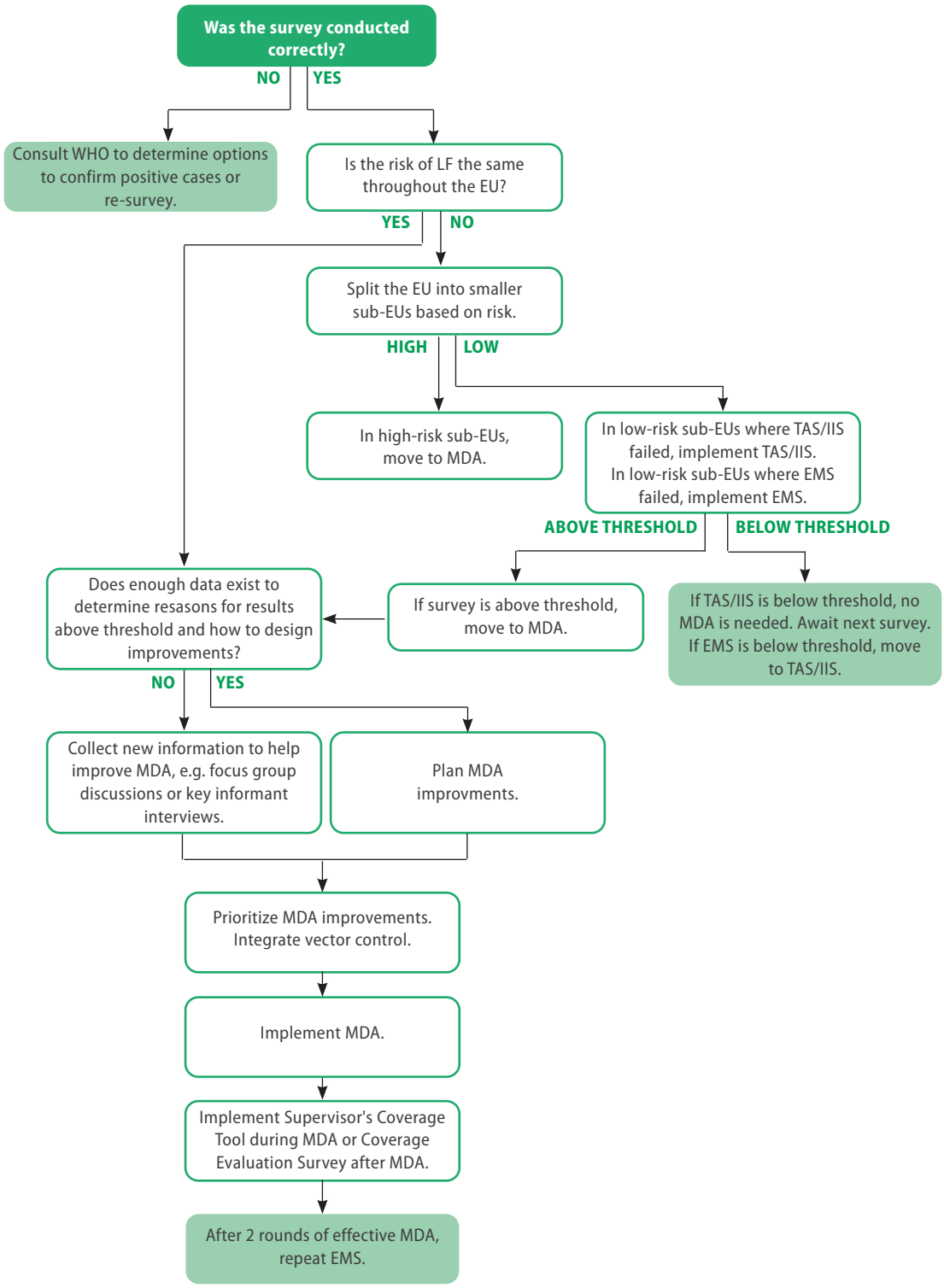
Thus far, approximately 13–27% of EMS (previously called pre-TAS) have shown results above the threshold *(156)*. EMS are designed to determine whether an EU should progress to TAS or IIS, and results above the threshold suggest that the surveys are achieving the intended outcomes. Sentinel and spot-check sites that are above the threshold may reveal programmatic issues that could be addressed in subsequent, repeated MDA.

In 2016, in response to requests from LF-endemic countries, WHO developed standard operating procedures for investigating and responding to survey results above the threshold *(2)*. These procedures included using checklists for planning TAS, supervising survey implementation, investigating results and planning repeated surveys after further MDA. The aim of this section is to consolidate best practices on preventing survey results above the threshold, on investigating those surveys and on corrective action. All LF surveys (EMS, TAS, IIS), including those with results above the threshold, should be reported to WHO using the EPIRF form.

9.1 Why national programmes should investigate survey results above the threshold

Once an EMS, TAS1 or IIS1 shows results above the threshold, WHO recommends two further rounds of MDA before reassessment. EUs that receive albendazole monotherapy twice a year should receive four more biannual rounds before reassessment. To ensure that the additional rounds of MDA are effective in reducing infection prevalence to a level at which MDA can be stopped, the programmes should investigate why the results were above the threshold (Fig. 8) by further review and analysis of available data and, if possible, collection of new quantitative and qualitative information.

Fig. 8. Investigation and response to EMS, TAS and IIS results above the threshold



EMS, epidemiological monitoring survey; EU, evaluation unit; IIS, IDA impact survey; LF, lymphatic filariasis; MDA, mass drug administration; TAS, transmission assessment survey; WHO, World Health Organization.

The first step in investigating survey results above the threshold is to determine whether the survey was conducted correctly, specifically:

- Were the IUs eligible?
- Were any issues found through the survey supervision checklists?
- Was the protocol followed, e.g. was the sample size met?

Countries can use several tools to determine whether a survey was conducted correctly. Annexes 8 and 10 provide checklists for preparing EMS and TAS or IIS, and annexes 9 and 11 provide supervision checklists for EMS and TAS or IIS that can be used by national programmes and implementing partners. The supervision checklists can be adapted for various levels of supervision, depending on staff roles and responsibilities. If these tools indicate that a survey was not conducted correctly, discussions should be held with WHO to determine whether it should be conducted again and how it should be improved. The tools should be used during implementation of all surveys to ensure quality.

The second step is to determine whether the risk of ongoing transmission is homogenous throughout the EU. In some cases, most of the positive cases found in a TAS or IIS may be clustered in one geographical area of the original EU. In other cases, the EU might be at heterogeneous risk of ongoing transmission, due to differences in elevation, a rural–urban divide, population demographics or MDA coverage. In these situations, the original EU could be divided into several sub-EUs. A follow-up TAS or IIS could be conducted to rule out sub-EUs at low risk that which might not require MDA, such as areas in which no or few positive cases were found in the original survey. Alternatively, after two rounds of MDA in the entire EU, the EU could be divided into two EUs for surveys.

Box 7. Step two examples

Example 1. An EU is composed of three districts; however, all the positives in TAS1 were found in two of the three districts. The third district could be surveyed again as a separate sub-EU to determine whether it could be excluded from receiving MDA, and the other two districts could progress directly to design and implementation of two rounds of MDA. This option is, however, resource intensive as it involves more surveys, different approaches within the EU and potential issues of the feasibility of treating only part of an EU.

Example 2. A TAS1 in an EU consisting of one district records transmission above the threshold. The EU was largely rural when MDA was begun over 5 years previously; however, a section of the district has become urbanized, with high migration and temporary residents. After two subsequent rounds of MDA, the district could be divided into two EUs: urban and rural. An EMS could be conducted and two new spot-check sites formed in each new EU.

The third step is to analyse data from surveys and on MDA coverage to determine why MDA does not appear to have succeeded. The following questions could be answered (Box 8):

Box 8. Step three example questions

- Were there differences in infection rates between males and females?
- Did certain geographical areas in the EU have low coverage? Were certain communities in the EU never treated or under-treated (e.g. missed in one or more rounds)?
- Did certain population groups in the EU have low coverage or were never treated or under-treated?
- Why were some people not treated in a previous MDA?

Annexes 12 (EMS) and 13 (TAS/IIS) contain checklists with longer lists of questions for investigating survey results above the threshold. Data from multi-year sub-district MDA coverage, coverage evaluation surveys, data quality assessments and the supervisor's coverage tool can all be used to answer the questions *(5)*.

The fourth step, if necessary, is to collect new information to answer the questions in annexes 12 (EMS) and 13 (TAS/IIS) to determine how a new MDA could be improved, such as:

- What are the barriers to taking part in MDA?
- What are the most effective messages and channels for conveying information?
- What are the most effective distribution strategies for MDA?

The data collected should often be both quantitative and qualitative. GPELF partners have developed tools for collecting such information, such as the *Guide to improving MDA using qualitative methods (157)*. If the NTD programme team does not have the capacity to collect qualitative data, further training and/or hiring of a consultant should be considered.

If TAS2 or TAS3 shows results above the threshold, the approach to investigation and the next steps should be more contextualized. The following steps should guide an appropriate response:

1. Report the results, and consult WHO.
2. Use the investigation tools in annexes 12 and 13 to prepare a report that includes previous TAS or other survey results, an analysis of the geographical clustering of people who have tested positive, past MDA coverage and any information on vector control.
3. Convene an expert review meeting, with support from WHO, to discuss the report and determine the options.
4. Prioritize improvement to MDA, and closely monitor implementation of MDA (section 5, section 9.4).

9.2 Where national programmes should investigate survey results above the threshold

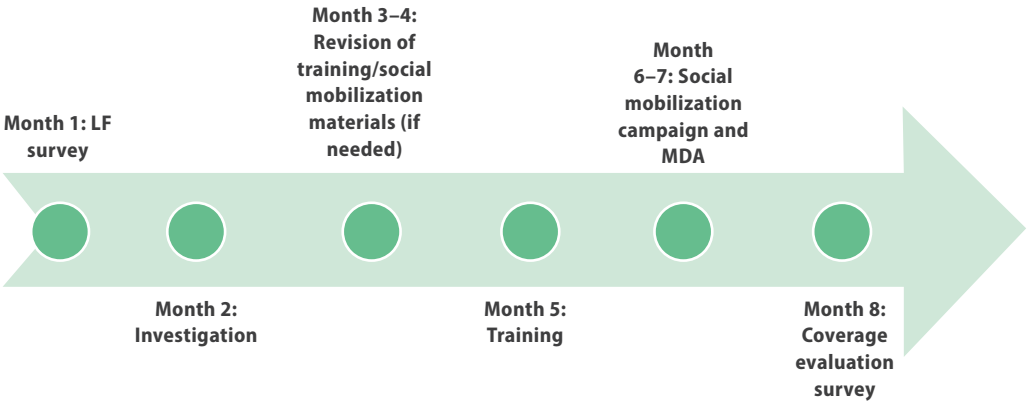
Quantitative information on previous MDA coverage should be compiled at sub-district level, if possible. Other data from coverage evaluation surveys, data quality assessments, baseline and mid-term sentinel and spot-check sites should be compiled and plotted on maps, if possible. Collection of qualitative data should be prioritized in sub-districts that are known to have low coverage and/or Ab-, Ag- or Mf-positive results in previous surveys.

If the reasons for survey results above the threshold are not apparent after analysis of the available information, the national programme might have to arrange visits to EUs, especially those with clusters of positives, to collect more data, interview stakeholders and/or hold focus group discussions with community members or community drug distributors.

9.3 When national programmes should investigate survey results above the threshold

LF surveys are usually conducted at least 6–9 months after the latest MDA. National programmes therefore have at least 6 months to collect information and make changes to improve the next MDA. Data collection must therefore be efficient and focused, with minimal time for analysis, so that changes can be made rapidly. Fig. 9 provides an illustrative timeline for investigation.

Fig. 9. Sample timeline for investigation of survey results above the threshold before an MDA



LF, lymphatic filariasis; MDA, mass drug administration.

Ideally before implementing a survey, past information should be checked to guide formation of EUs and to flag areas at greater risk of ongoing transmission and therefore potential results above the threshold. When feasible within budget cycles, programmes should set aside contingency funds for investigating and improving MDA when the results are above the threshold. Reports indicate that planning for investigation and MDA of about 15% of EUs surveyed is reasonable.

For eligible countries that are considering introduction of IDA after the failure of a previous survey, as recommended by WHO, the timeline becomes more complicated. Programmes are requested to submit applications for donations of ivermectin for IDA through the Mectizan Donation Program 9 months before an MDA. The application must include a specific plan for ensuring the quality of the MDA with IDA; the plan may not be ready until investigations are complete, making it difficult to maintain the annual treatment cycle. Contingency planning before results above the threshold are found may therefore save time and reduce delays in conducting MDA.

9.4 Planning and conduct of MDA

After a survey yields results above the threshold, ensuring the quality of subsequent MDA requires a review of previous strategies and modifications to the programme, such as microplanning, including use of the SCT and CES (section 5). Other resources that can be used to improve MDA planning and implementation, include the *Microplanning manual to guide implementation of preventive chemotherapy to control and eliminate neglected tropical diseases (88)*, *Safety in administering medicines for neglected tropical diseases (90)*, *Eliminating neglected tropical diseases in urban settings (158)* and *MDA preferred practices (159)*.

9.5 Other measures available to support MDA

National programmes should also explore the addition of or an increase in vector control activities in the EU when possible. For example, in areas with *Anopheles* vectors, LF programmes could collaborate with national malaria control programmes to target or enhance vector control interventions in EUs with results above the threshold. National LF programmes could include vector control messages citing use of bed nets and indoor residual spraying in messages about MDA. The WHO manual *Lymphatic filariasis: a handbook of practical entomology for national lymphatic filariasis elimination programmes (29)* describes development of a control plan and outlines vector-specific entomological control procedures.

DEC-medicated salt has been effective in reducing Mf prevalence and interrupting transmission in some settings *(18, 160, 161)*. DEC salt can be used as an adjunct measure only in countries that are not co-endemic for onchocerciasis or loiasis. As with MDA, the effectiveness of DEC salt administration depends on coverage of the total population.

Countries may also consider a test-and-treat strategy in small populations in which MDA alone has not achieved ≥ 65% coverage of the total population. To implement this strategy, programmes should prepare for the additional costs of RDTs and achieve high compliance with testing.

9.6 Conducting EMS after MDA

If the results of an EMS are above the threshold, any site at which values ≥ 2% Ag or ≥ 1% Mf were found should be sampled again in a repeat survey. Sites that were below the threshold should be replaced by new spot-check sites of expected high risk. If both sites have results above the threshold, an additional spot-check site may be surveyed to provide more information about the EU and inform MDA strengthening efforts if the survey fails.

If TAS1 or IIS1 have results above the threshold, two new spot-check sites should be selected for the next EMS. The sites should be those at the expected highest risk, which are often those with the highest proportion of positives in TAS or IIS. There is no need to include the sentinel site, as it showed < 2% Ag or < 1% Mf in the first EMS and would therefore presumably pass again.

If TAS2 or IIS2 or TAS3 or IIS3 provides results above the threshold, the next steps depend on the guidance of WHO. If two rounds of MDA are recommended, an EMS would then be conducted in the EU, and, if the EU passes that survey, TAS1 or IIS1 would be applied. Before conducting an EMS, programmes should consider dividing the EU into sub-EUs, if they did not do so during the investigation stage described above in Step 2 of section 9.1.

9.7 Conducting TAS or IIS after MDA

When planning a TAS or IIS, national programmes should consider whether the previous EU could be divided into smaller units and whether that would facilitate programmatic decisions. It may be useful if the previous EU consisted of multiple IUs, had a total population of > 500 000 or had clusters of children with positive results. If so, the newly formed EUs should be retained throughout subsequent surveys.

10. Surveillance

LF elimination activities will continue to be required even after MDA has stopped or validation has been attained. The continuing work of national programmes should include provision of the essential package of care for people affected by lymphoedema and hydrocoele and surveillance to detect recrudescence *(23, 31)*. Surveillance consists of two phases: shorter-term surveillance in the years following cessation of MDA (post-treatment surveillance) and longer-term surveillance once validation criteria have been met (post-validation surveillance).

10.1 Post-treatment surveillance

Post-treatment surveillance is conducted in each EU after MDA has been stopped to ensure that the rate of infection is still below the target threshold. Modelling simulations have suggested that, if recrudescence occurs, it is most likely within the first 5 years of stopping MDA *(124)*. As noted earlier, TAS and IIS are the tools currently used to determine whether MDA can be stopped. These surveys are then repeated twice at 2-year intervals as post-treatment surveillance. For example, if TAS1 is passed in 2025 and MDA stops, the TAS should be repeated in 2027 (TAS2) and 2029 (TAS3).

Depending on the level of Ag, Ab or Mf detected during these surveys and the clustering of people who test positive, additional rounds of MDA, targeted treatment or reconstitution of EUs might be necessary for the next survey. Surveys are continued to compare the numbers of people who are Ag, Ab or Mf positive with the critical cut-off value; they are not designed to compare differences among repeated surveys. As infected children represent new infections, fewer and fewer positive children should be observed in each successive survey if transmission has been interrupted. When adults are surveyed, the Mf prevalence should remain below the critical cut-off value. The results of a post-treatment surveillance survey that are higher than the critical cut-off value could indicate that transmission is ongoing. It is important to report such results and to consult WHO on the next steps (see section 9). Even positive results in areas in which the overall results are below the critical cut-off value should be investigated and responded to with targeted treatment (sections 7 and 8).

Before conducting a repeat survey, programmes should consider whether the EUs should be reformed. Consult the checklist in section 6.1 to determine whether EUs should be divided to meet new criteria.

10.2 Post-validation surveillance

PVS is a longer-term activity conducted any time after TAS3 or the IIS3 and required after validation of elimination as a public health problem has been achieved. Although validation is conferred only at national level, countries are encouraged to start PVS in EUs once they pass TAS3 or IIS3.

PVS has several aims *(31)*. The primary and minimum aim is to ensure that recrudescence has not occurred and infection in EUs is still below target thresholds. The secondary, advanced aim is to

verify elimination of transmission, the criteria for which are yet to be defined. The primary clinical aim is to detect and provide the essential package of care for people affected by lymphoedema and hydrocoele.

As LF infection is predominantly asymptomatic during the infective stage, PVS should consist of active surveillance. In order to improve the sustainability and long-term feasibility of surveillance, it should ideally be integrated with surveillance strategies for other conditions, or existing surveillance platforms should be used. Surveillance should be prioritized in areas that were previously under MDA and are considered to be at greatest risk of recrudescence. Surveillance should include reporting of affected people, who should be maintained in health information systems to ensure that care is provided. PVS strategies should ensure that appropriate, adequate response measures are available.

The extent of risk of transmission depends on various epidemiological, programmatic, environmental, socioeconomic and demographic factors, which differ according to the country setting, vector and parasite species. Examples of risk factors are:

- epidemiological *(162, 163)*: highest baseline endemicity, cluster(s) of positives in previous surveys, and zoonotic potential;
- programmatic *(15, 163)*: lowest MDA coverage, higher prevalence of never-treated population, missed or interrupted MDA rounds, previous epidemiological surveys above the threshold (e.g. pre-TAS/EMS, TAS, IIS), the largest EUs and lowest bed net coverage or use;
- environmental *(127, 164–166)*: high elevation, high mosquito density, abundance of vector larval habitat, temperature and rainfall patterns that support vector breeding; and
- socioeconomic or demographic *(155, 164, 165)*: poor living conditions, migration from endemic countries and population density.

To assist programmes in prioritizing areas to be considered for PVS, they can use the *Post-validation surveillance district prioritization tool (167)* to generate a priority ranking of IUs that could be considered for PVS activities. This tool provides a quantitative assessment of risk based on factors that are hypothesized to be associated with ongoing or recrudescent transmission.

The secondary and longer-term aims of post-validation surveillance are to verify elimination of transmission. WHO has not defined the parameters to be measured or the criteria that would be required to demonstrate zero transmission.

10.3 Implementation of post-validation surveillance

Surveillance is a critical component of ensuring the success of global elimination and eradication programmes *(168, 169)*, including lymphatic filariasis *(107, 170)*. The types of post-validation surveillance activities to be implemented and the platforms available depend on the country situation. Preferably, a combination of at least two of the following four platforms should be used:

- health facility screening
- standardized surveys
- Mx
- surveys targeted to high-risk areas or high-risk groups.

Ongoing surveillance activities include health facility or routine screening of high-risk populations. Mx may be considered ongoing if conducted routinely. Inclusion of LF testing in standardized surveys and surveys targeted to high-risk areas are examples of periodic surveys.

10.3.1 Health facility screening

Clinical laboratories in hospitals or health centres where routine blood collection occurs could be asked to test a certain number of blood samples a month for the presence of Mf, Ag or Ab *(171, 172)*. Collection of data on LF through mechanisms available at health facilities may be the most sustainable method, as they would be integrated into the health care system. For example, data on biomarkers for LF in children born after MDA could be assessed from periodic processing of dried blood spot collections. Women being screened during antenatal testing could also be tested for LF antigenaemia. The information from health facility screening could be reported to the national programme and other disease control programmes. Any LF infections identified could be treated directly and also investigated by staff of the national programme to determine an appropriate response.

Box 9. Togo surveillance case study

Togo was the first country in sub-Saharan Africa to eliminate LF, in 2017. To detect and respond to any recrudescence of LF infection, Togo, with the support of partners, launched surveillance in 2006 with several modalities.

Health facility-based surveillance (2006–2015): The programme recruited staff from 47 hospital laboratories throughout the country to examine nocturnal malarial thick blood smears for the presence of Mf collected from emergency room or hospitalized patients *(172)*. All positive and 10% of negative slides were re-read at a national reference laboratory. Togo developed an algorithm for addressing positive cases in the surveillance network, whereby any person who was Mf or Ag positive was followed-up with Mf testing as confirmation, and confirmed cases were investigated by testing the 500 nearest people to the individual for Mf to determine whether targeted treatment should be initiated.

This system achieved good geographical coverage, with at least one health facility in 97% of national districts submitting samples *(171)*. Within the first 2 years of surveillance, 30% of the 3777 villages in Togo were represented in the sample *(172)*. Between 2006 and 2011, only three positive cases of Mf were detected in the laboratory network, all of which were detected in districts that were initially mapped as non-endemic. Follow-up of these cases did not find evidence of ongoing LF transmission *(171, 172)*.

Dispensary extension (2010–2015): Despite the good geographical representation of the laboratory network, 20 areas were identified that were under-sampled in the hospital-based model *(171)*. Thus, surveillance was extended by training one nurse in a dispensary in an area not covered by the laboratory network to collect filter-paper blood spots from 20 people presenting at the dispensary each quarter. The samples were shipped periodically to a reference laboratory in the capital for Og4c3 testing. Positive samples were re-tested for Mf and cases were investigated as described above. Between 2010 and 2015, 6788 blood spots were collected, of which 19 were positive by Og4c3 but all were negative for Mf *(173, 174)*.

Mx (2016–2017): To further support the claim that Togo had interrupted transmission of LF, Mx was conducted in three districts in northern Togo in which Mf-positive people had been identified in other post-treatment surveillance activities *(174)*. In each district, 30 villages were selected, with probability proportionate to size. Mosquitoes were collected by pyrethrum spray catch, human landing catches and exit traps in some locations, identified morphologically and screened for the presence of *W. bancrofti* DNA by pool screening with a LAMP assay. A total of 15 539 mosquitoes were collected, 72.6% of which were the primary LF vector, *An. gambiae*. None of the mosquito pools was positive for *W. bancrofti* DNA.

Migrant populations survey (2018): As the three countries surrounding Togo (Benin, Burkina Faso and Ghana) remain endemic for LF, the programme conducted a survey of several migrant populations to determine the risk of re-introduction of LF into Togo *(140)*. A cross-sectional survey was conducted in northern Togo in three migrant populations: nomadic pastoralists, Togolese citizens who migrate to neighbouring countries for seasonal labour and refugees from Ghana displaced by communal conflict. All the participants were tested for Ag, and those who were positive were tested for Mf. An overall prevalence of 4.2% Mf was found, with pastoralists representing the highest proportion of positive individuals (11.9%).

10.3.2 Standardized surveys

In some settings, integration of the collection of LF biomarkers into other standardized surveys in endemic countries is an opportunistic approach for generating useful signals for the LF programme. Examples include Demographic and Health Surveys, malaria indicator surveys, UNICEF multiple indicator cluster surveys and other population-based seroprevalence surveys (e.g. for trachoma and vaccine-preventable diseases) *(175)*. In these situations, LF testing would be integrated into an existing sampling frame and strategy, which may or may not involve the optimal sampling population and require adjustments *(176)*. Nevertheless, these surveys can provide useful signals that can be followed by LF-specific surveys. Leveraging such surveys may be particularly useful for monitoring in "low-risk" settings, where high-risk areas for targeted surveillance had not been identified.

10.3.3 Molecular xenomonitoring

Molecular xenomonitoring (Mx) is a non-invasive and sensitive strategy for detecting LF in communities. It has been shown that a strong linear relationship exists with human microfilariae prevalence *(75)*. Thus Mx has been deployed in many post-MDA contexts *(177–179)*. Mx, which consists of direct assessment of parasites in vector mosquitoes by PCR techniques *(41, 73, 74)*, could be used to detect signals and determine whether the prevalence of infection in vectors is above or below a threshold that would trigger a targeted response. Mx could also be used with another post-validation surveillance method to build evidence of elimination of transmission *(174, 177)*. Mx could be integrated with other disease elimination programmes, by use of traps to collect several vector species or in places in which the same mosquito species is a vector for several diseases *(180)*. While Mx can detect the presence of Mf in a community, research should be conducted to develop more feasible methods for sampling and testing. Performance of Mx requires:

- trapping sufficient numbers of mosquitoes, which may be difficult due to differences in the behaviour of species;
- an appropriate sampling strategy, trap placement and site selection in the EU to provide meaningful estimates of the prevalence of infection in the vectors; and
- laboratory capacity and resources to collect and process mosquitoes and conduct appropriate PCR.

10.3.4 Targeted surveys

Targeted surveys should be considered in two settings: where there are high-risk areas and where there are high-risk populations. In high-risk areas (according to criteria in section 10.2), surveys can be implemented at EU or sub-EU level to determine whether the prevalence is above or below a threshold that will trigger a programme response. In this case, determination of whether a targeted survey is required would be based on a review of available data and a clear geographical delineation. In high-risk populations, such as mobile populations, refugees, migrant workers from endemic countries, and socially excluded ethnic and linguistic groups, the goals of a targeted survey would be to identify focal transmission and to determine whether the prevalence is above or below a threshold that would trigger a response and ensure treatment to all populations *(140)*. Targeted surveys for LF can be integrated to collect data for other diseases to improve the service to the communities assessed and increase the value of the investment by informing multiple public health programmes *(181, 182)*.

Box 10. Thailand post-validation case study

After validation of the elimination of LF in Thailand in 2017, the Ministry of Public Health developed guidelines for post-validation surveillance to ensure that Thailand maintained an LF infection rate < 1% Mf *(120)*. Various surveillance methods are used, including:

- human blood surveys: annual surveys in 10% of previously endemic IUs by testing for antigenaemia or Mf;
- vector surveys: surveys in 1% of previously endemic IUs in each province;
- surveys among registered and unregistered migrants to test for Ag in five provinces with the largest migrant populations; testing unregistered migrants in locations where they can be accessed for health screening (e.g. construction sites, plantations); and surveillance of registered migrants through routine health screening conducted by various agencies; and
- targeted surveys in areas with animal reservoirs: surveys in both humans and cats in Narathiwat Province where zoophilic *B. malayi* infections have been found.

Confirmatory mapping surveys, EMS, TAS and IIS are acceptable methods for targeted surveys during PVS with the currently available biomarkers. Table 2 (in section 3) lists the available biomarkers, with a description of how they can best be used during post-validation surveillance.

Targeted surveys may also be used to follow up any signal of infection or transmission identified in one of the previous three platforms. For example, if infected individuals in a particular community are detected during health facility screening, an EMS could be undertaken to investigate whether the infection is more widespread. Similarly, if a national serosurvey detects a signal of infection in a district that was never classified as endemic, a confirmatory mapping survey could be conducted to determine whether targeted treatment is warranted.

10.4 Timing and duration of post-validation surveillance

PVS activities should be established once national validation has been achieved *(31)*; however, PVS can be started as soon as possible after TAS3 or IIS3. As IUs commonly progress at different rates in implementing MDA and surveys, especially in large countries, PVS activities should be pilot-tested in eligible areas to develop a feasible approach to PVS that could be scaled up by the time the country is validated.

Additional evidence is required to define the optimal duration of surveillance activities after validation, and the guidelines outlined here will be reviewed as new evidence emerges. Surveillance activities, ideally integrated into the health system, should continue for as long as resources allow but for no less than 10 years after validation. As the lifespan of an adult worm exceeds 5 years and may exceed 10 years in some settings, any residual infections at the time of stopping MDA should be decreasing during the post-validation phase *(183, 184)*. The criteria and process of validation were established for GPELF in 2017 *(31)*. WHO is aware of PVS activities in 8 of the 19 countries that have officially been validated as having eliminated LF as a public health problem *(154)*. In recent reports to WHO from a few such countries, Ag have been found in individuals more than 13 years after MDA was stopped. Modelling simulations show that prevalence can be maintained below elimination as a public health problem levels for over 10 years but not eliminated *(124)*. Long-term follow-up studies in India showed persistence of residual infections in the adult population 20 years after interventions had been stopped *(185)*. Detection of incident infections during surveillance thus indicates that PVS should be continued.

10.5 Use of surveillance data

10.5.1 Response

Responding to surveillance signals in an appropriate, timely manner is critical to ensuring that recrudescence does not occur in areas under surveillance and to supporting future claims of elimination of transmission of LF. Countries should review their surveillance data periodically to identify any signals and to determine if any further action is warranted.

Surveillance signals

A signal is defined as detection of a LF biomarker that alerts the programme that transmission may be continuing in a community. Countries should triage and verify signals that are received through various surveillance modalities to evaluate the likelihood that a signal represents ongoing transmission. Interpretation of a signal depends on the surveillance modality and diagnostic method used in the surveillance system(s). Countries may use Mf, Ag, antifilarial Ab or filarial DNA in vectors (Mx). See section 3 for more information on selecting and using LF diagnostic tests.

An Mf-positive individual can be considered a source of transmission if they reside in an area in which mosquito vectors are also present. Individuals in whom Ag is detected can be assumed to be currently or recently infected and a potential source of transmission. When possible, individuals who are Ag positive should be tested for Mf. It is important to collect samples for Mf testing before providing anti-filarial treatment. Individuals with positive antifilarial Ab tests can be assumed to be either exposed, infected or previously infected; however, this does not necessarily indicate that transmission is ongoing, especially in older individuals. An antifilarial Ab signal in young children, however, represents recent exposure to LF and suspected recent transmission. Detection of filarial DNA in mosquito vectors indicates that mosquitoes are ingesting blood from infected individuals and may spread the infection to other people. This represents potential transmission. Table 22 outlines the interpretation of various signals.

Table 22. Interpretation of LF biomarker signals

Signal	Interpretation
Mf-positive person	Source of transmission
Ag-positive person	Infected, potential source of transmission
Antifilarial Ab-positive person	Exposed, infected, previously infected; in young children, a sign of recent exposure and suspected recent transmission
Pools of mosquito vectors positive for filarial DNA	Potential transmission

Ab, antibody; Ag, antigen; LF, lymphatic filariasis; Mf, microfilariae.

Further investigation is warranted in communities in which a signal is detected to determine whether the signal represents ongoing transmission. This depends on the diagnostic method used, the surveyed population and surveillance platform.

Countries should collect information on individuals who test positive, including their residency history, age, gender, other demographic factors and history of MDA. This information can indicate who in an EU is at greatest risk for infection and therefore the targeted treatment strategies. Information on where the positive individuals work or attend school may indicate focal areas for transmission and targeted treatment.

The response to signals depends on the surveillance platform used and the type of signal identified. A signal generally warrants a follow-up targeted survey or treatment. Targeted

treatment of communities may be necessary to stop any resurgence of transmission or residual infections. See section 9 for responses to results above the threshold in LF surveys.

Screening in health facilities

Table 23 lists the results of screening in health facilities and the necessary responses. If no-one in the health facility tests positive, no response is required. Any individual who has an LF infection and their family members should be offered treatment. Programmes should consult WHO about whether a targeted survey in the health facility catchment area is warranted to determine whether targeted treatment is required.

Table 23. Findings of and responses to screening in health facilities

Finding	Response
No positive cases	No response required
Positive cases	Collect additional information about the individual and perform an Mf test if not already done. Offer treatment to people with positive results and their household members. Consider whether a targeted survey in the health facility catchment area is warranted.

Mf, microfilariae.

Standardized surveys

Programmes should analyse survey results to identify any LF signals. If LF signals are present, the programme should analyse the distribution of positive signals and determine whether they are geographically or demographically related. These data can be used to determine whether targeted follow-up surveys are necessary, including any additional sampling in the EU or sub-EU(s) in which a positive signal was observed. The targeted survey should be designed to test whether the prevalence in the EU is above the defined threshold for that survey (e.g. Mf > 1% in adults).

Table 24 lists standardized survey findings and the responses required. If a signal is detected in many communities in an EU, programmes may consider directly providing targeted treatment rather than conducting additional targeted LF surveys. Where eligible, IDA should be provided according to WHO recommendations *(4)*. Targeted treatment should emphasize reaching people who have never been treated, and a test-and-treat strategy may be considered for people who hesitate to receive LF medication. Depending on the size of the EU, an EMS, TAS or IIS should be conducted after two effective rounds of targeted treatment.

Table 24. Standardized survey findings and responses

Finding	Response
No positive cases	No response required
Positive cases	Consult WHO for additional guidance. Collect additional information about individuals who test positive and perform an Mf test if not already done. Offer treatment to people with positive results and to their household members. Analyse the distribution of positive results. Determine where follow-up targeted LF surveys are required. Conduct targeted LF surveys.

LF, lymphatic filariasis; Mf, microfilariae; WHO, World Health Organization.

Targeted periodic surveys

Targeted periodic surveys are recommended when there are areas or populations that are suspected to be at high-risk of recrudescence of transmission. They should also be conducted in response to a signal from another surveillance modality (e.g. health facility assessment, TAS signal, standardized survey signal) or among high-risk areas or populations. Any of the recommended GPELF surveys can be used (confirmatory mapping, EMS, TAS or IIS), with their corresponding thresholds for action (Table 25). Ideally, the same method should be used over time.

Table 25. Determination of ongoing transmission according to diagnostic method, survey population and mosquito vector

Diagnostic method	Survey population group	Protocol	Recommended threshold(s)	Reference
Blood film, microscopy for Mf	Community (aged ≥ 20 years)	EMS, IIS	1.0% (*Anopheles*, *Culex* or *Mansonia*), or 0.5% (*Aedes*)	section 6 (EMS); section 8 (IIS)
Blood sample	Community (aged ≥ 20 years)	EMS	2.0%	section 6 (EMS)
Rapid test to detect Ag (CFA)	Children (aged 9–15 years)	Confirmatory mapping	2.0%	section 4 (confirmatory mapping)
Blood sample, Rapid test to detect anti-filarial Ab	1st- and 2nd-grade pupils	TAS	Upper bound of CI < 5%	section 7 (TAS)

Ab, antibody; Ag, antigen; CFA, circulating filarial antigen; CI, confidence interval; EMS, epidemiological monitoring survey; IIS, IDA impact survey; Mf, microfilariae; TAS, transmission assessment survey.

Table 26 outlines targeted periodic survey findings and the responses required. If the results of the given survey are above the respective threshold (Table 25), programmes should conduct two rounds of targeted treatment, preferably with IDA where eligible, according to WHO recommendations *(4)*. The treatment should emphasize reaching people who have never been treated. When feasible, a test-and-treat strategy may be considered for people who hesitate to receive treatment. The impact is measured after two targeted treatment rounds with ≥ 65% coverage of the total population.

Table 26. Targeted periodic survey, findings and responses

Finding	Response
No positives cases	No response required
Positive results below the threshold	Collect additional information about individuals who test positive, and perform Mf test if not already done. Offer treatment to people with positive results and to their household members. Analyse the results by cluster or community, if applicable. If any cluster exceeds the threshold, two rounds of targeted treatment should be provided.
Positive results above the threshold	Two rounds of targeted treatment. Target those who have never been treated; offer a test before treatment to anyone who refuses treatment (test-and-treat). Repeat the targeted survey after two rounds of targeted treatment with ≥ 65% coverage of the total population.

Mf, microfilariae.

Molecular xenomonitoring

Table 27 outlines the findings of Mx surveys and the responses required. If no positive vector pools are detected, no further response is required. If positive pools are detected but are below the threshold, programmes can consider implementing a targeted LF survey in communities with positive pools (Table 28). If the number of positive pools exceeds the mosquito species-specific threshold, programmes may either conduct a targeted LF survey or proceed directly to two rounds of targeted treatment. In eligible areas, IDA should be used according to WHO recommendations *(4)*. The targeted treatment should emphasize reaching people who have never been treated, and a test-and-treat strategy may be considered for people who hesitate to receive MDA medication.

Table 27. Mx survey findings and responses

Finding	Response
No positive pools	No response required
Positive pools but below the threshold	Implement targeted LF surveys in communities with positive pools.
Surveys with positive pools above the threshold	Implement targeted LF surveys in the EU or conduct two rounds of targeted treatment in the entire survey area. Target those who have never been treated; those who refuse treatment are offered a test before treatment (test-and-treat). Reassess in an EMS, IIS or TAS after two rounds of targeted treatment with ≥ 65% coverage of the total population.

EMS, epidemiological monitoring survey; EU, evaluation unit; IIS, IDA impact survey; LF, lymphatic filariasis; Mx, molecular xenomonitoring; TAS, transmission assessment survey.

Table 28. Determination of ongoing transmission by Mx

Diagnostic method	Survey population	Protocol	Provisional thresholds (%)	Reference
Mx of pools of collected mosquitoes	*Culex quinquefasciatus*	Not standardized	0.25	*(73, 74, 110, 174, 186)*
	An. gambiae		1.0	
	Ae. polynesiensis		0.10	
	Mansonia[a]		0.5	

Mx, molecular xenomonitoring.

[a] Provisional threshold to be revised as new data are available.

10.5.2 Reporting

Countries should analyse their surveillance data at least annually, by site or IU, and report to WHO on the EPIRF. To report surveillance results, select an appropriate survey type in the EPIRF LF sheet. WHO will append surveillance reports to country dossiers which, in the future, may strengthen the evidence that elimination of transmission has been achieved.

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Annexes

Annex 1. Methodology for the development of this second edition

The first edition of this manual was published in 2011. This second edition was developed through a global consultative process involving experts from all regions of the World Health Organization (WHO) in which lymphatic filariasis (LF) is endemic to ensure its suitability to all settings.

1. WHO formed a steering group (Annex 2) to review the first edition, establish the scope of the second edition and identify where updates were needed. The approval of this WHO technical product was assessed against the document *WHO public health goods technical products on norms/standards, data and research (TPs) quality assurance companion: guidance for TP development*.[1] The process of development is outlined below. Evidence for updates is cited directly in the manual itself in the relevant sections where changes were made between the 2011 and 2025 editions. As much of the development of the document occurred during the pandemic, the group met mostly through virtual meetings to develop an outline and drafting plan and review progress of the manual development.

2. WHO convened a series of virtual technical consultations (Annex 2) in 2020 and 2021 to review the outline and discuss needed changes according to the following specific programmatic steps: mapping, monitoring, stopping MDA by regimen, post-MDA surveillance and post-validation surveillance. WHO convened follow-up meetings to finalize updates on the above topics.

3. A Core Drafting Group (Annex 2) was formed from a subset of the steering group to draft sections of the manual. The manual was updated by the Core Drafting Group through in person and virtual meetings and discussions in 2021. WHO oversaw updates to each section of the manual and provided final review of content.

4. WHO assigned a first round of peer reviewers (Annex 2) to each section based on their expertise in the subject area. Peer reviewers provided feedback from January to April 2022.

5. WHO convened an in-person technical consultation (Annex 2) in April 2022 to review the feedback from peer reviewers and propose revisions. As revisions were made, WHO convened a series of virtual technical consultations with the same technical experts (Annex 2) in 2023 to review proposed revisions according to the programmatic steps (listed above in 2.). Consensus on the proposed changes was developed using an informal approach that stipulated *a priori* that judgements for each change would be made with complete consensus achieved through group discussions. Should complete consensus fail to be reached, judgements would be considered final with more than two thirds votes of participants. Meeting participants were actively asked for dissenting views, which were discussed. During actual deliberations, group discussions helped to reach full consensus.

6. To determine the acceptability of the proposed new guidance, WHO initiated a stakeholder engagement process in 2023, whereby an open call was made to complete a survey, available in English and French, which assessed the agreement of the proposed changes among survey respondents. Feedback shared by respondents was considered by WHO, discussed in technical meetings. The proportion of respondents that selected agree or strongly agree ranged from 77% to 96% for each proposed change.

[1] World Health Organization. (2022a). Technical products on norms/standards, data and research (TPs). Quality assurance companion: guidance for TP development: quality assurance of TPs for 2022–2023 – Principle, criteria, process and checklists, March 2022. Geneva: World Health Organization [WHO public health goods].

7. WHO assigned a second round of peer reviewers (Annex 2) to provide feedback on the final document.

8. WHO coordinated a final technical review to discuss feedback from the second peer reviewers and finalize the document.

Diagnostic test validation

In 2019, WHO launched the Diagnostic Technical Advisory Group for Neglected Tropical Diseases (DTAG) to advise WHO on priority diagnostic needs, conduct landscape analyses of diagnostics and develop target product profiles (TPPs) in addition to establishing a standardized approach to the validation of new NTD diagnostic tools. A DTAG subgroup on LF was established as a priority which, in addition to developing two TPPs, advised WHO on the standardized validation of two new LF tests in both laboratory and field settings where programmes deploy the tests when conducting the EMS, TAS and IIS. In addition, the DTAG in collaboration with WHO Prequalification initiated an independent WHO Expert Review Panel for NTD diagnostics to advise WHO on procurement of diagnostic tests. Through these mechanisms, WHO is able to advise countries on tests acceptable for use in the Global Programme to Eliminate Lymphatic Filariasis.

Declarations of interests and their management

The "Declaration of interests for WHO experts" form was completed by all technical meeting participants, peer reviewers and core drafting group members and assessed by WHO. Any reported interests of concern were reported at the beginning of meetings. All external experts, in accordance with WHO policy, disclosed any potential conflicts of interest that might affect, or might reasonably be perceived to affect, their objectivity and independence in relation to the subject matter of the meetings. WHO reviewed each of the declarations and concluded that none could give rise to a potential or reasonably perceived conflict of interest related to the subjects discussed at the meeting or covered by the manual.

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Annex 3. Recommended procedures for the detection and identification of microfilariae in blood

The filarial parasites *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori* are the three species that cause lymphatic filariasis (LF). These parasites live in the lymphatic vessels of humans and have unique characteristics. Microfilariae of all three species can be detected in the blood of infected humans. This annex provides descriptive information to aid in the detection and identification of microfilariae of these parasites. .

Table A3.1. Periodicity, distribution and recommended times for collection of blood specimens for testing for microfilariae

Species	Periodicity	Distribution region, sub-region or country	Recommended blood collection time	Main vector
Wuchereria bancrofti	Nocturnal periodic	Africa, Americas, Eastern Mediterranean, South-East Asia, Melanesia, Micronesia	22:00–01:00 (peak 24:00)	*Anopheles, Culex*
	Nocturnal sub-periodic	South-East Asia	20:00–22:00 (peak 21:00)	*Aedes*
	Diurnal sub-periodic	Polynesia	15:00–17:00 (peak 16:00)	*Aedes*
Brugia malayi	Nocturnal periodic	South-East Asia	22:00–01:00 (peak 24:00)	*Anopheles, Mansonia*
	Nocturnal sub-periodic	South-East Asia	20:00–22:00 (peak 21:00)	*Mansonia*
Brugia timori	Nocturnal periodic	Indonesia, Timor-Leste	22:00–01:00 (peak 24:00)	*Anopheles*

Source: World Health Organization. (2013). *Lymphatic filariasis: a handbook of practical entomology for national lymphatic filariasis elimination programmes*. (https://iris.who.int/handle/10665/87989).

Blood collection

Microfilariae appear in the blood, with a marked nocturnal periodicity in most settings. Some species and strains, however, are nocturnally subperiodic or diurnally subperiodic (Table A3.1). The times for collection of blood specimens should be selected in accordance with the expected periodicity of the parasite.

Fingerstick blood collected at the recommended time is an appropriate sample for assessing microfilaraemia in the EMS and IIS. Annex 4 is a job aid, demonstrating the proper technique for collecting fingerstick blood.

Preparation of blood smears

Preparation of blood smears is the recommended method for quantitative detection of microfilariae in human blood samples collected by fingerstick. Annex 5 describes how to prepare a blood smear.

Examination of blood smears for microfilariae

Systematic examination of the entire prepared blood smear under a microscope is important. Using the x 10 objective, start at one end of the prepared slide and carefully examine each field of view by moving

in a serpentine manner. Distinguishing details of microfilariae can be confirmed under the x 40 objective. Descriptive characteristics of microfilariae are used to identify the filarial species (Table A3.2).

Table A3.2. Characteristics of the microfilariae of human lymphatic filarial parasites

Characteristics	*B. malayi*	*B. timori*	*W. bancrofti*
Sheath	Present	Present	Present
Length (µm)	175–230	265–325	240–300
Width (µm)	5.0–6.0	4.4–6.8	7.5–10.0
Tail	Tapered; subterminal and terminal nuclei widely separated	Tapered; subterminal and terminal nuclei widely separated	Tapered; anucleate
Key features	Long head space, sheath stains pink in Giemsa; terminal and subterminal nuclei	Long head space; sheath unstained in Giemsa; terminal and subterminal nuclei	Short head space; sheath unstained in Giemsa; body in smooth curves; dispersed nuclei

Under a light microscope, microfilariae appear (after appropriate staining) as primitive organisms, serpentine in shape, enclosed in a sheath and filled with the nuclei of many cells. Not all filarial species have a sheath. In the three parasites that cause LF, the sheath may extend a short or long distance beyond either extremity. In some species, depending on the stain used, the sheath displays a unique staining quality which aids in species identification.

The nuclei of the cells that fill the body are usually darkly stained and may be crowded together or dispersed. The anterior extremity is characteristically devoid of nuclei and is called the cephalic or head space; it may be short or long. As you look from the anterior to the posterior end of the body, you will see additional spaces and cells that serve as anatomical landmarks. These include the nerve ring, excretory pore, excretory cell and anal pore. In some species, an amorphous mass called the inner body and four small cells (known as rectal cells) can be seen. Some of these structures and their positions are useful in identifying the species. Other useful features include the shape of the tail and the presence or absence of nuclei within it.

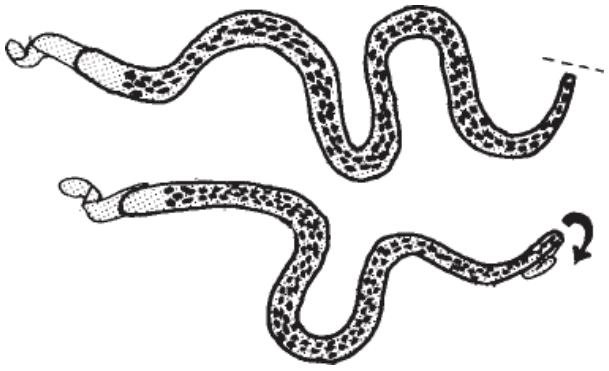
Colour images of stained microfilariae and their characteristics can be found in the WHO Bench Aids for the diagnosis of filarial infections and available online (https://www.cdc.gov/dpdx/lymphaticfilariasis/index.html).

Identification of species can be difficult and, without proper training, mistakes can be made. Systematic study of all the characteristics described above should make it possible to identify the species with certainty. Identification must not be based on a single characteristic but on all the features together.

Possible causes of misidentification

- ***Broken or folded tail.*** If the tail of *W. bancrofti* is broken or folded over (Fig. A3.1), it appears to have nuclei extending to the tip, as in *Loa loa*.
- ***Torn or colourless sheath***. The sheath is sometimes torn or almost colourless. In *Loa loa*, for example, the sheath appears as a colourless space between the tail and the blood cells.
- ***Unusually large or small microfilariae***. Some *Mansonella perstans* are very long (e.g. 200 µm), and some *W. bancrofti* and *Loa loa* are small (e.g. 250 µm).
- ***Badly prepared smears (or films)***. If *W. bancrofti* is damaged when the smear (or film) is being made, it may appear twisted, and *Loa loa* may show a few curves.
- ***Examination of thin films.*** Identification of microfilariae on stained thin films is not recommended, as the microfilariae are shrunken, distorted and difficult to recognize.

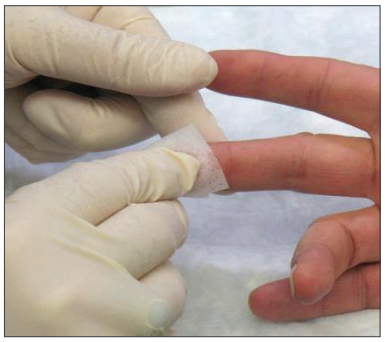
Fig. A3.1. Possible cause of misidentification of *W. bancrofti*: broken (top) or folded (bottom) tail



Annex 4. Fingerstick blood collection technique

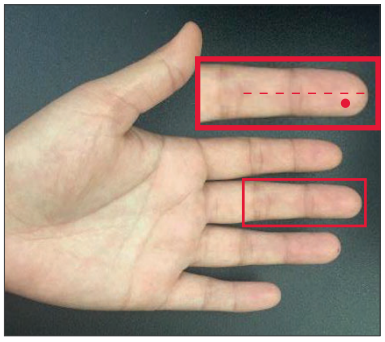
Clean the finger to be pricked with an alcohol swab, and allow the finger to dry completely.

1



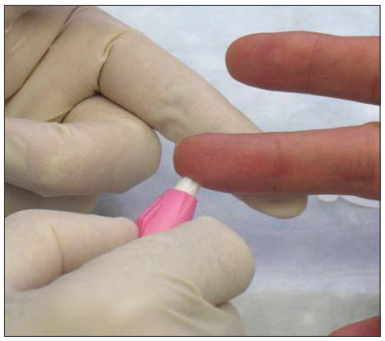
The lancet should be placed off centre from the middle of the fingerpad.

2



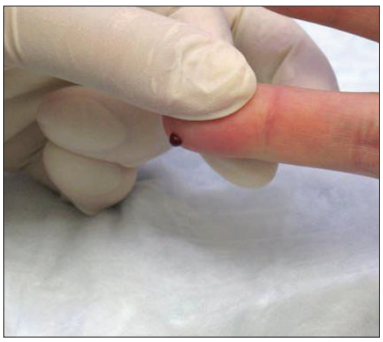
Using a sterile lancet, puncture the internal side of the finger with one quick, deliberate stroke to achieve good blood flow; immediately discard the lancet.

3



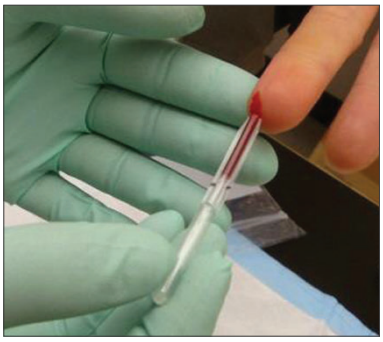
Collect the blood into a sample collection device (4a), a microtainer tube coated with an anticoagulant (4b), or onto filter paper (4c) according to the use.

4

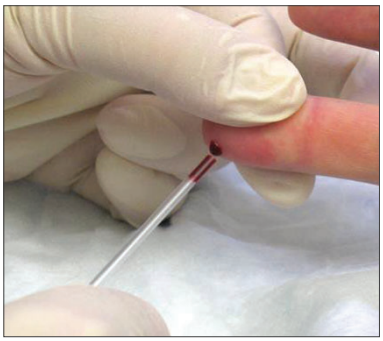


4a

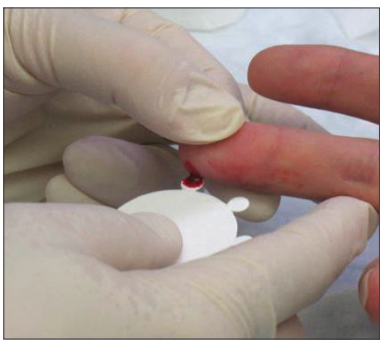
Note: When collecting into tubes, it is advisable to collect slightly more than the necessary volume of blood to ensure that an adequate volume of blood is available in case of clotting or spillage.



4b



4c



Annex 5. Preparing blood smears for detecting microfilariae of *Wuchereria bancrofti* and *Brugia* spp.

This annex describes how to prepare a blood smear. Although the procedure is relatively simple, adequate training is necessary to ensure that slides are prepared properly and consistently.

Basic guidelines

i. Always use universal safety precautions when handling blood.

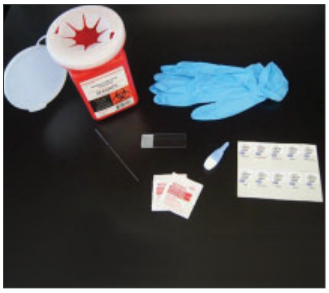
ii. Blood must be collected between **22:00 and 02:00 h**, except in locations with diurnal periodicity, such as the South Pacific.

iii. This is a 2-day procedure. Before beginning, ensure enough time to complete the entire process.

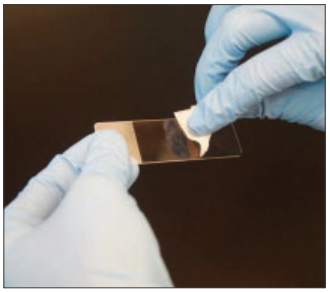
Test procedure – Day 1; estimated time: 10 min

Organize supplies

√ Gloves
√ Capillary tube
√ Pipette & tips
√ Slide
√ Barcode label or pencil
√ Alcohol swab
√ Waste container

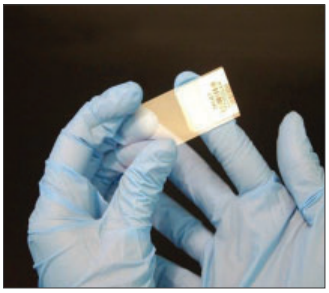


1 **Clean microscope slides with alcohol so that they are free of dust and oil residue. Allow the slides todry completely.**

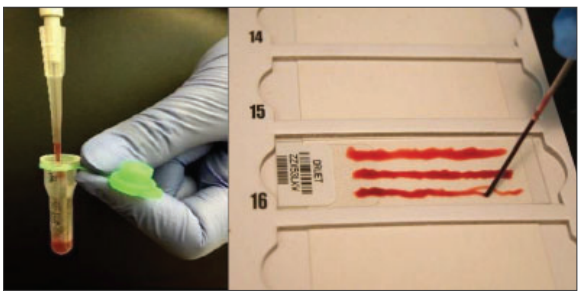


2 **Label the slides with unique IDs.**

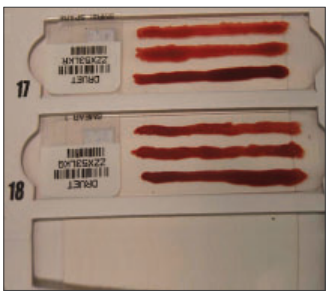
***Note*: if pre-printed labels are not available, use a pencil to write the ID on the slides.**



3 **Pipette three parallel lines of 20 µL of blood along the length of the slide, or use a capillary tube to prepare three parallel lines of 20 µL each.**



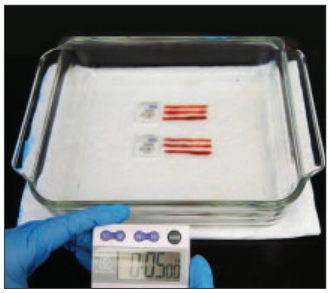
4 **Allow the slide to dry thoroughly (24–72 h) in air undisturbed**



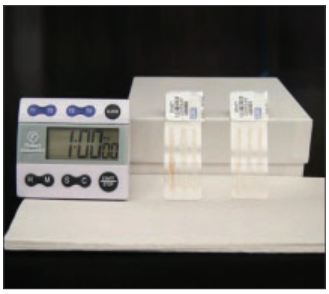
***Note*: Air bubbles may form if blood is not expelled smoothly from the pipette. Gently drag the pipette tip through bubbles to remove them.**

Test procedure – day 2; estimated time: 4.5 h

5 Place the slides in distilled water (preferred) or tap water for approximately **5 min** to de-haemoglobinize the blood.

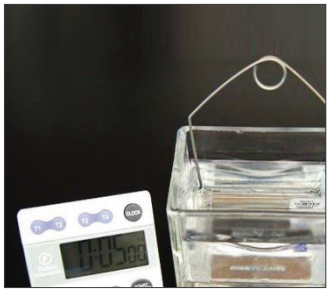


6 Air dry the slides for **1 h** or until dry. This can be done on paper towels or a staining rack.



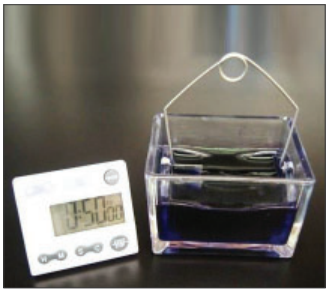
7 Fix the slides in methanol for 5 min. Allow to dry in air.

***Note*: methanol is hazardous.**

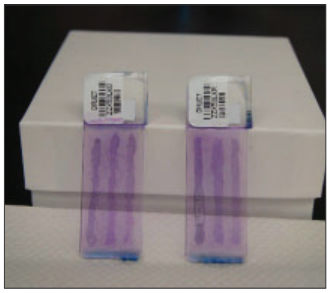


8 Stain the slides in a 1:50 dilution of Giemsa stock for 50 min.

***Note*: 1 mL Giemsa stock + 49 mL distilled water.**



9 Allow slides to dry in air completely. This can be done on paper towels.



10 Store slides in a slide container.

De-haemoglobinization is necessary to clear the red blood cells so that the microfilariae can be more easily seen. It is complete when the smear turns an opaque greyish-white. This may take more than 5 min. Caution must be exercised at this time because the smear is fragile, and rough washing or agitation can result in it floating off the slide.

In Giemsa staining, the general rule is to stain for a time equivalent to the concentration of the stain. Routinely, we use a 1:50 dilution of stock Giemsa and stain for 50 min. The final volume of working stain should be based on the amount necessary to submerge the slides completely. In general, if the white blood cell nuclei are properly stained, the microfilariae should also be adequately stained. Note that the pH of the staining solution is not critical for Giemsa staining of films to be examined for lymphatic filariasis microfilariae. The overall colour of the smear may range from pink to purple to blue, depending on the pH, but the microfilariae will be stained adequately regardless of colour.

Note: Giemsa stain should be prepared fresh from stock daily.

Annex 6. Bioline™ Filariasis Test Strip

The Bioline™ Filariasis Test Strip is a rapid diagnostic test used for qualitative detection of *Wuchereria bancrofti* antigen in human blood samples collected by fingerstick. Although the test is relatively simple to use, adequate training is necessary to reduce inter-observer variation and misreading of strips.

Basic guidelines

i. Kits should be stored at 2–37 °C. Test strips should **not** be frozen. The kit is stable until the expiration date marked on its outer packaging when stored as specified. Kits should **not** be used past the expiration date.

ii. Before beginning field surveys, two test strips from each lot of kits should be tested with a positive control, which can be obtained from WHO. **Do not** use test strips that give negative results when tested with the control.

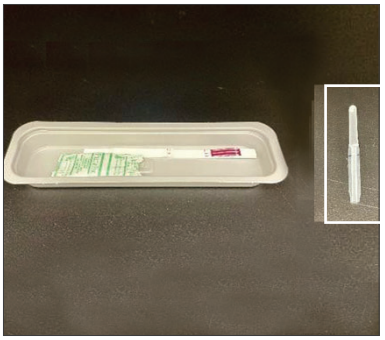
iii. A cool box is not required when transporting test strips for use in the field; however, care should be taken not to expose test strips to extreme heat for prolonged periods.

iv. Test strips must be read under bright, unfiltered light. Faint lines can be difficult to see when lighting is not adequate. This is especially important when reading test strips at night.

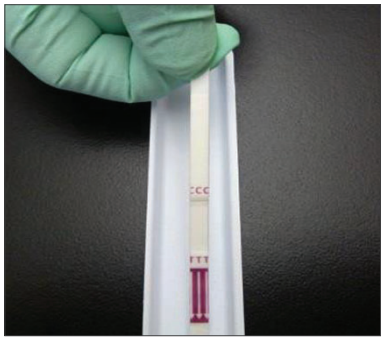
Test procedure

1

Allow all kit components to equilibrate to ambient temperature (15–37 °C) before testing.
Remove contents from the foil pouch just before use. The materials provided include one test strip, plastic work tray and a fixed-volume (75 µL) micropipette.



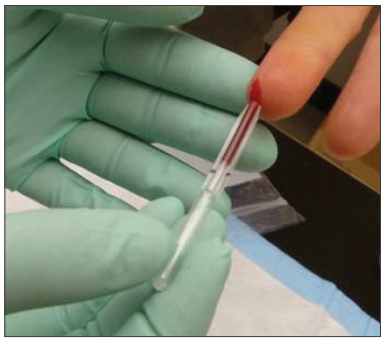
2



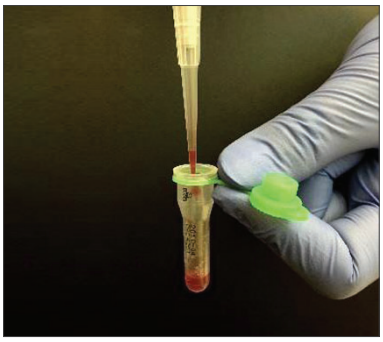
Test strips should be handled carefully and held only at the end without the arrows. Do not apply pressure to the sample pad at the bottom of the strip. Strips should be labelled with appropriate patient identifiers and placed on the plastic work tray before adding the sample.

Note: **It is advisable to secure the test strip to the work tray with a sticker-type patient identifier label or tape.**

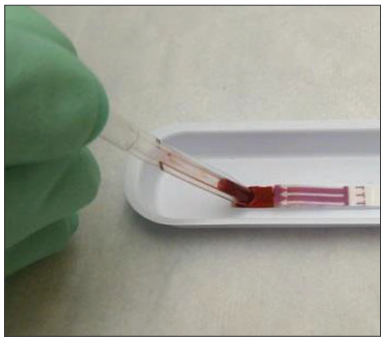
3



Collect 75 µL of fingerstick blood by holding the micropipette supplied slightly below the horizontal plane. **Do not** squeeze the bulb end of the micropipette when collecting the sample. Alternatively, measure 75 µL of anti-coagulated blood (**heparin only**) from a microcentrifuge tube with a calibrated micropipettor. **Do not** add blood directly from the finger to the strip.



4

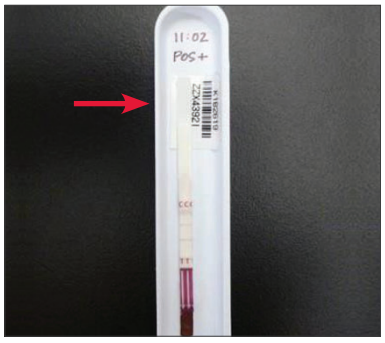


Slowly add the blood sample to the lower half of the sample pad by gently squeezing the bulb.

Set a timer for 10 min.

Note: **It is helpful to record the reading time on the work tray.**

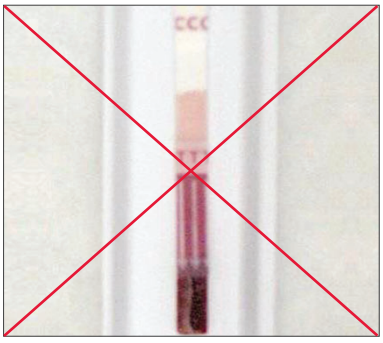
5



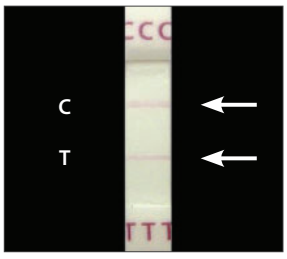
Read test results exactly 10 min. after the sample has been added.

Note: **Record the appropriate result on the plastic work tray**

DO NOT read tests if the sample has not migrated **ALL** the way up the test strip

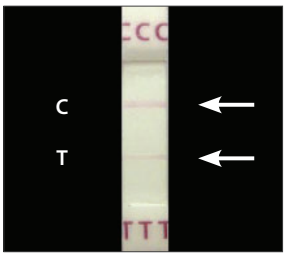


Test interpretation

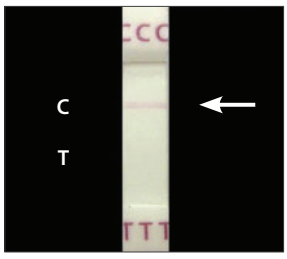


POSITIVE

Any visible pink line in the test area should be interpreted as a positive result



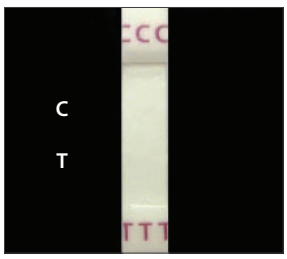
POSITIVE (weak)



NEGATIVE

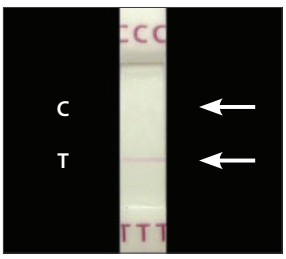
Control line only

C = control
T = test



INVALID

No lines appear



INVALID

Test line only

Annex 7. STANDARD™ Q Filariasis Ag Test

The SD Biosensor STANDARD™ Q Filariasis Ag Test (QFAT) is a rapid diagnostic test used for qualitative detection of *Wuchereria bancrofti* antigen in human serum, plasma or whole blood samples. Whole blood collected by fingerstick is the most common sample type used in the Global Programme to Eliminate Lymphatic Filariasis. Although the test is relatively simple to use, adequate training is necessary to reduce interobserver variation and to ensure accurate reading of results.

Basic guidelines

i. Kits should be stored at 2–40 °C. Cassettes should **not** be frozen. QFAT kits are stable until the expiration date marked on the outer box when stored as specified. Kits should **not** be used past the expiration date. **Note that cassettes and buffer may have a different expiration date than that on the outer box; however, it is the expiration date on the outer box that should be used.**

ii. Before beginning field surveys, two cassettes from each lot of kits should be tested with a positive control, which can be obtained from WHO. **Do not** use kit lots that give a negative result when tested with the control.

iii. A cool box is not required for transporting QFAT for use in the field; however, care should be taken not to expose cassettes to extreme heat or direct sunlight for prolonged time.

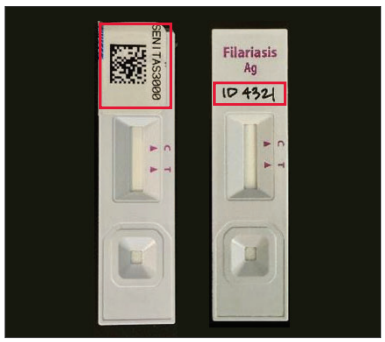
iv. QFAT must be read under bright unfiltered light. Faint lines can be difficult to see when lighting is not adequate. This is especially important when reading QFAT at night.

Test procedure

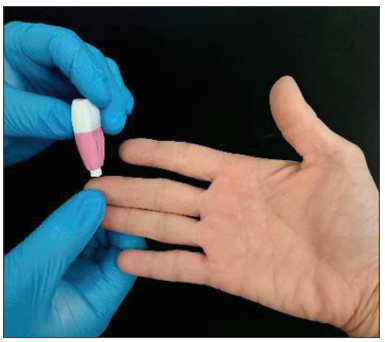
1

Allow all kit components to equilibrate to ambient temperature (15–40 °C) before testing. The materials provided include individually wrapped cassettes, buffer and fixed-volume (20 µL) sample collectors.
Remove the cassette from the foil pouch just before use.

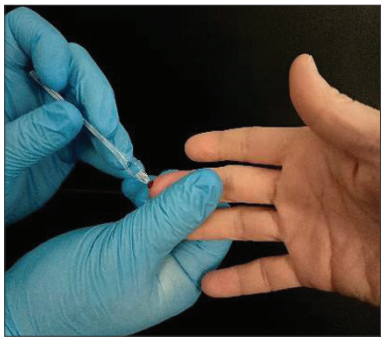
2



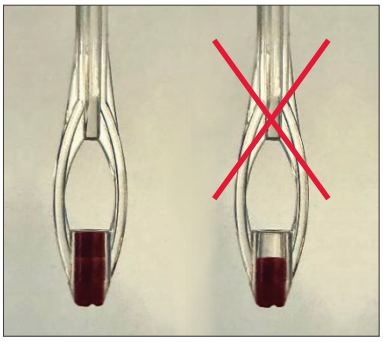
Cassettes should be labelled with appropriate unique identifiers before the sample is collected.
Perform a fingerstick to collect a blood sample for testing (refer to Annex 4).



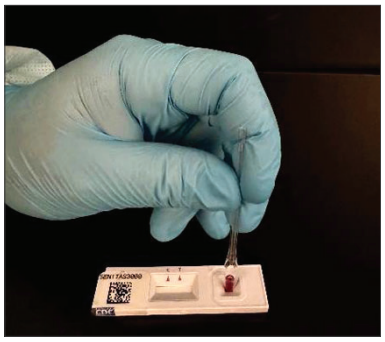
3



Gently touch the tip of the sample collector to the drop of blood, and allow capillary action to completely fill the tip. **Do not** press the tip directly to the finger, as this will disrupt the airflow necessary for capillary action. Sample collectors are calibrated to measure 20 µL of blood when completely filled. Ensure that the entire tip is full before proceeding. **Do not** add blood directly from the finger to the QFAT.



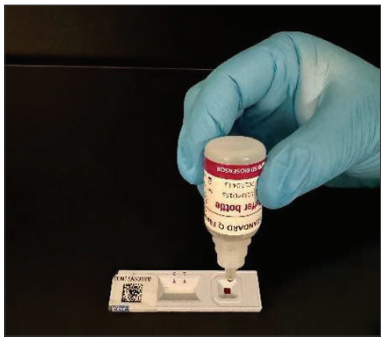
4



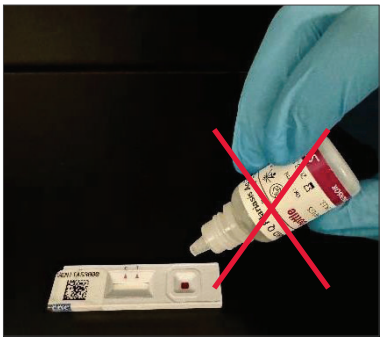
Gently touch the tip of the filled sample collector to the sample pad and allow all 20 µL of the blood to absorb into the pad. This process can take 3–5 seconds.

DO NOT tap vigorously or twist the sample collector to dispense the blood as this may damage the sample pad.

5



Immediately after the blood absorbs into the sample pad, hold the buffer bottle in a vertical position above the sample pad and gently squeeze to slowly add 2 drops of buffer. Ensure no air bubbles form when the bottle is squeezed.
DO NOT directly touch the tip of the buffer bottle to the sample pad.
DO NOT hold the buffer bottle at an angle as the volume of each drop of buffer will not be consistent.

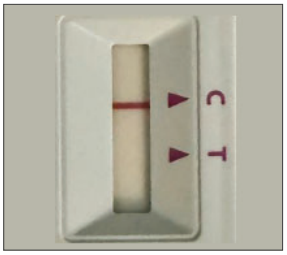


6

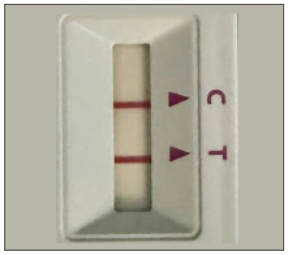
Test results should be read 10 minutes after adding the buffer. Note the time buffer was added on a clock and immediately record the reading time directly on the cassette.
Record the test result directly and clearly on the cassette.

***Note*: Multiple tests are often run in close succession in the field. Recording the reading time on the cassette is recommended to streamline workflow in field settings.**

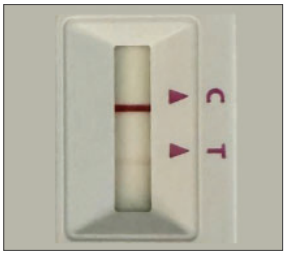
Test interpretation
(C = control T = test)



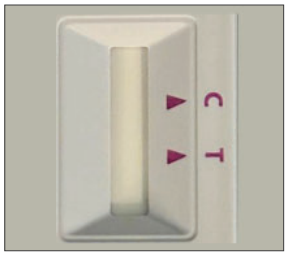
NEGATIVE
Control line only



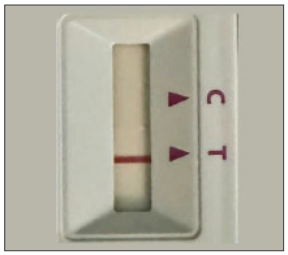
POSITIVE
Any visible pink line in the test area should be interpreted as a positive result



POSITIVE (weak)



INVALID
No lines appear



INVALID
Test line only

Annex 8. Checklist for preparation of an EMS

No.	Question	Answer	Recommended follow-up action
Programme monitoring			
Effective coverage			
1	Has at least 65% of the total population been reported to have ingested the medicines during the appropriate number of rounds of mass drug administration (MDA)?		If no, EMS should not be conducted. Further MDA rounds should be conducted until the appropriate number of effective rounds have been completed.
2	If monitoring and evaluation tools (supervisor's coverage tool, coverage evaluation surveys, microplanning) have been used, do the results support the conclusion that effective coverage has been achieved?		If not, consider conducting further MDA rounds to ensure that the appropriate number of effective rounds have been completed.
Never treatment			
3	Is there evidence of people who were never treated in any MDA round? ▪ In which population groups is the reported or surveyed coverage lowest? ▪ Is there any evidence of never treatment in these or other sub-groups of the population requiring MDA? ▪ Were strategies in place for inclusion of migrants in MDA?		If certain population groups are known or suspected to have low coverage, data collection in sentinel and spot-check sites should include these groups. Migrant communities could be selected as an additional spot-check site.
Formation of evaluation units (EUs)			
4	Is the total population of the EU < 500 000 people? With projected population growth, will it still be < 500 000 people by TAS3/IIS3?		If there are ≥ 500 000 people, re-form the EU to have < 500 000 people, e.g. include fewer implementation units (IU) or split IUs into more than one EU.
5	In an EU with more than one IU, are all the IUs comparable in terms of baseline prevalence, number of MDA rounds and coverage, or other factors that may affect transmission?		If not, re-form the EU to ensure that all the IUs are comparable.
Selection of appropriate site for an EMS			
6	Will at least one sentinel and one spot-check site be assessed per EU during EMS?		Ensure that at least two sites at highest risk of ongoing transmission are included in each EU.
7	Were spot-check sites chosen based on low MDA coverage and/or high baseline prevalence?		
8	In areas with heightened potential for ongoing risk of transmission, will extra spot-check sites be assessed?		

Sampling for EMS			
9	Are resources available to collect at least 300 samples from each sentinel or spot-check site, from people aged ≥ 20 years?		Ensure that enough days are scheduled to reach the sample size, especially when sampling only adults.
Testing for microfilaraemia (Mf)			
10	Will EMS be conducted at least 6 months after the last round of MDA in areas that received one- or two-drug LF regimens? Will EMS be conducted at least 9 months after the last round of MDA in areas that received ivermectin, DEC and albendazole (IDA)?		If not, plan to survey sentinel and spot-check sites at least 6 or 9 months after the last LF MDA.
11	Will blood slides for Mf be taken at peak circulation times according to known periodicity of the parasite?		If not, Mf prevalence will be underestimated.
12	During examination of blood slides for Mf, will 10% of negatives and all positives be re-read by experienced technicians for quality control?		If not, develop a plan to cross-check the slides.
Rapid diagnostic tests			
13	What is the expiry date of the diagnostic tests?		Ensure that the survey will be completed before the tests expire. If this is not possible, do not use the tests.
14	What lots are being used for the survey?		Ensure that a list of the lots used in each survey is kept at central level in case follow up is necessary.
15	Does the team have extra diagnostic tests in case retesting or oversampling is required?		Ensure that survey teams have at least 10% extra tests.
16	Are the diagnostic tests stored appropriately at customs and at sub-national level (if applicable)?		Ensure that the tests are stored according to the manufacturer's guidance. If storage conditions were compromised, test positive and negative controls before use in the field.
17	Have at least 5 tests from each lot been left at central level in case further testing is necessary?		If not, keep 5 tests from each test lot at central level.
18	Was at least 1 test from each lot tested with a positive control? If so, when?		One test from each lot should be tested with a positive control. Positive controls for antigen tests are available from WHO. Testing should be done within 6 weeks of usage.
19	Was at least 1 test from each lot tested with a negative control? If so, when?		One test from each lot should be tested with a negative control. Testing should be done within 6 weeks of usage.
Training			
20	Have all teams been trained in survey methods and use of diagnostic tests?		Training in Mf collection, staining and reading is especially important. Standardized materials are being developed.
Data quality, management and reporting			
21	Are there printed standard operating procedures (SOP) for data recording, management and reporting?		Data recording, management and reporting should be included in the survey protocol and distributed to survey teams at all levels.
22	Has a national focal point been designated to provide the survey results in the WHO EPIRF?		One person at the national level should be designated to communicate survey results to WHO through the EPIRF.

EMS, epidemiological monitoring survey; EPIRF, epidemiological data reporting form; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IIS, IDA impact survey; IU, implementation unit; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; SOP, standard operating procedure; TAS, transmission assessment survey; WHO, World Health Organization.

Annex 9. Checklist for supervision of an EMS

No.	Question	Answer	Recommended follow-up action
Responsibilities			
1	Have supervisory responsibilities been attributed to each team and/or sub-team?		If no, draft a short description and send to each team member.
Logistics and communication			
2	Does the supervisor have contact numbers for each team?		If no, generate a line-list of mobile telephone numbers for each team member and supervisor. WhatsApp groups are useful for reporting real-time results and solving problems.
3	Has an SOP been established for the team to communicate with the supervisor?		If no, draft a summary SOP and send to each team.
Sampling			
4	Are enough people being sampled in each site?		Supervisors should monitor this daily. If it appears that the sample size will not be achieved, supervisors should plan re-visits to households from which members were absent.
5	Is the correct age group (e.g. adults aged >20 years) being surveyed?		
6	Is the correct sampling procedure being followed? For EMS, random sampling by segmentation or systematic sampling of households is recommended.		If not, correct, and ensure the recommended sampling procedure is being followed.
Use of diagnostic tests			
7	Are technicians following recommended procedures for conducting the test, including quantity of blood, method of application to sample pad and universal safety precautions?		If not, teams should be re-trained immediately. See section 3 for more details.
8	Are the results being read at the recommended time?		
9	Are the times of reading and the results written on the test?		If not, trainers and supervisors should emphasize that the time of reading the test and the results should be written on the tests themselves.
10	Are people with invalid results tested again?		If not, supervisors should ensure that all teams retest people with invalid results, immediately.
11	Are positive results confirmed by more than one team member or supervisor?		Confirm positive results with another team member or supervisor within the appropriate timeframe.
12	Are photos being taken of positive results?		If possible, photos should be taken of positive results against a neutral background, in good light.

Data quality, management and reporting			
13	Are diagnostic test issues being documented by technicians and reported to WHO?		Programmes should use the WHO LF Diagnostic Test Feedback Form to report issues.
14	Are results linked accurately to the surveyed person and site?		Unique identifiers should be used to link diagnostic test results to the site and person.
15	Is a supervisor collecting and aggregating data from each team?		If not, identify a responsible person to do so, and communicate the SOP to all teams.

EMS, epidemiological monitoring survey; LF, lymphatic filariasis; SOP, standard operating procedure; WHO, World Health Organization.

Annex 10. Checklist for preparation of a TAS or an IIS

No.	Question	Answer	Recommended follow-up action
Programme monitoring			
Effective coverage			
1	Has at least 65% of the total population been reported to have ingested the medicines for the appropriate number of effective rounds of MDA?		If no, TAS or IIS should not be conducted. Further MDA rounds should be conducted the appropriate number of effective rounds have been completed.
2	If monitoring and evaluation tools (supervisor's coverage tool, coverage evaluation surveys, microplanning) have been used, do the results support the conclusion that effective coverage has been achieved?		If results do not support effective coverage was achieved, consider conducting further MDA rounds to ensure that the appropriate number of effective rounds are completed.
Never treatment			
3	Is there evidence of people who were never treated in any MDA rounds? ▪ In which population groups is the reported or surveyed coverage lowest? ▪ Is there any evidence of never treatment in these or other sub-groups of the population requiring MDA? ▪ Were there strategies in place for inclusion of migrants in MDA?		If certain population groups are known or suspected to have low coverage, data collection in sentinel and spot-check sites should include these groups. Migrant communities could be selected as an additional spot-check site.
Formation of an EU			
4	Is the total population of the EU < 500 000 people? With projected population growth, will it still be < 500 000 people by the time of the TAS3/IIS3?		If there are ≥ 500 000 people, re-form the EU to have < 500 000 people, e.g. include fewer IUs, or split IUs into more than one EU. TAS/IIS results from smaller EUs will better reflect the true mean incident of infection.
5	In an EU with more than one IU, are all the IUs comparable in terms of baseline prevalence, number of MDA rounds and coverage, or other factors that may affect transmission risk?		If not, re-form the EU to ensure all the IUs are comparable.
Selection of an appropriate sites for an EMS			
6	Were at least one sentinel and one spot-check site per EU assessed during EMS?		Ensure that at least two sites at highest risk of ongoing transmission are included in each EU.
7	Were spot-check sites chosen based on low MDA coverage and/or high baseline prevalence?		
8	In areas with heightened potential for ongoing risk of transmission, were extra spot-check sites assessed?		

Sampling for EMS			
9	Were at least 300 samples taken from people aged ≥ 20 years at each sentinel or spot-check site?		If the sample size was not achieved, further samples should be taken to achieve the minimum sample to confirm eligibility for TAS1 or IIS1.
Diagnostic tests for EMS (see also questions 15–21 if rapid diagnostics were used)			
10	Was EMS conducted at least 6 months after the last round of MDA in in areas that received one- or two-drug LF regimens? Was EMS conducted at least 9 months after the last round of MDA in areas receiving IDA?		If not, then sentinel and spot-check sites should be re-surveyed at least 6 or 9 months after the last MDA.
11	Were blood slides for Mf taken at peak circulation times according to the known periodicity of the parasite?		If not, Mf prevalence will be underestimated.
12	During examination of blood slides for Mf, were 10% of negatives and all positives re-read by experienced technicians for quality control?		If not, cross-check the slides.
Infection thresholds for EMS			
13	Was Mf <1% in each sentinel and spot-check site? Or < 2% antigen in *W. bancrofti* areas if Mf testing could not be done?		If not, the EU is not eligible for TAS1 or IIS1. Two additional rounds of enhanced MDA should be conducted before conducting EMS.
Preparation of TAS or IIS			
14	Has the TAS Eligibility and Planning Form been submitted and reviewed by WHO?		The TAS Eligibility and Planning Form should be submitted to WHO for review at least 6 months before the survey if diagnostic tests are being requested.
Rapid diagnostic tests			
15	What is the expiry date of the diagnostic tests?		Ensure that the survey will be completed before the tests expire. If this is not possible, do not use the tests.
16	What lots are being used in the survey?		Ensure that a list of the lots used in each survey is kept at central level in case follow-up is necessary.
17	Does the team have extra diagnostic tests in case retesting or oversampling is necessary?		Ensure that survey teams have at least 10% extra tests.
18	Are the diagnostic tests stored appropriately at customs and sub-national level (if applicable)?		Ensure that the tests are stored according to the manufacturer's guidance. If storage conditions were compromised, test with positive and negative controls before use in the field.
19	Have at least 5 tests from each lot been left at central level in case further testing is necessary?		If not, keep 5 tests from each test lot at central level.
20	Was at least one test from each lot tested with a positive control? If so, when?		One test from each lot should be tested with a positive control. Positive control for antigen tests is available from WHO. Testing should be done within 6 weeks of usage.
21	Was at least one test from each lot tested with a negative control? If so, when?		One test from each lot should be tested with a negative control within 6 weeks of usage.

Sampling			
22	For TAS, is the net primary school enrolment rate < 75%?		If yes, a school-based survey should not be done. Instead, a community-based survey should be done, with enumeration units as clusters.
23	Were schools or enumeration areas listed in geographical order before sampling with the TAS or IIS SSB?		If no, list them in geographical order, and rerun the SSB.
24	In school-based surveys, has attendance and/or a requirement for written permission been considered in the "non-response" rate? In community-based surveys, has information about previous non-response rates been used in the SSB calculations?		Past survey non-response rates and information about whether written permission is necessary should be considered before running the SSB.
25	In school-based surveys, has the list of schools and the number of students in levels 1 and 2 been confirmed?		If no, confirm the number of schools and students, and revise SSB in the field if necessary. Ensure that extra schools have been placed on "stand by". More than 5 extra schools might be required.
Training			
26	Have all teams been trained in the survey method and use of diagnostic tests?		Standardized LF survey training modules are available from WHO.
Data quality, management and reporting			
27	Is there a printed SOP for data recording, management and reporting?		Instructions for data recording, management and reporting should be included in the survey protocol and distributed to survey teams at all levels.
28	Has a national focal point been designated to enter survey results into the WHO EPIRF?		One person at the national level should be designated to communicate survey results to WHO through the EPIRF.

EMS, epidemiological monitoring survey; EPIRF, epidemiological data reporting form; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IIS, IDA impact survey; IU, implementation unit; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; SOP, standard operating procedure; SSB, Survey Sample Builder; TAS, transmission assessment survey; WHO, World Health Organization.

Annex 11. Checklist for supervision of a TAS/IIS

No.	Question	Answer	Recommended follow-up action
Responsibilities			
1	Have supervisory responsibilities been attributed to each team and/or sub-team?		If no, draft a short description and send to each team member.
Logistics and communication			
2	Does the supervisor have contact numbers for each team?		If no, generate a list of mobile telephone numbers for each team member and supervisor. WhatsApp groups are useful for reporting real-time results and solving problems.
3	Has an SOP been established for team communication with the supervisor?		If no, draft a summary SOP and send to each team.
Sampling			
4	Are enough people being sampled in each site or cluster?		Supervisors should monitor this daily. If it appears that the sample size will not be achieved – for example, due to a higher-than-expected number of absentees from school for TAS – supervisors should plan to re-visit the schools or communities. They should contact visit schools or community clusters on the "stand-by" list and survey them as soon as possible.
5	Are the correct age groups being surveyed?		In EMS and IIS, are adults aged ≥ 20 years being surveyed? In TAS of community and school-based surveys, if a few outliers (aged ≥ 10 years) are found, they should be included in the sample. If many are found on the first day or two, TAS teams should consider only 6- and-7-year-olds as eligible for sampling (as opposed to grade 1 and 2 students).
6	Ils the correct sampling procedure being followed? For EMS, random sampling by segmentation or systematic sampling of households is recommended. For TAS, systematic or random sampling according to SSB results is recommended. For IIS, random sampling by segmentation is recommended.		If not, correct, and ensure that the recommended sampling procedure is being followed.

Diagnostic test use			
7	Are technicians following recommended procedures for conducting the test, including quantity of blood, method of application to sample pad and universal safety precautions?		If not, teams should be immediately retrained. See section 3 for more details.
8	Are the results being read at the recommended time?		
9	Are the time of reading and the results being written on the test?		If not, trainers and supervisors should emphasize that the time of reading the test and the results should be written on the tests themselves.
10	Are people with invalid results tested again?		If not, supervisors should ensure that all teams retest people with invalid results, immediately.
11	Are positive results confirmed by more than one team member or supervisor?		Confirm positive results with another team member or supervisor within the appropriate timeframe.
12	Are photos being taken of positive results?		If possible, photos should be taken of positive results against a neutral background, in good light.
Data quality, management and reporting			
13	Are diagnostic test issues documented by technicians and reported to WHO?		Programmes should use the WHO LF Diagnostic Test Feedback Form to report issues.
14	Are results linked accurately to the surveyed person and site?		Unique identifiers should be used to link diagnostic test results to the site and person.
15	Is a supervisor collecting and aggregating data from each team?		If not, identify a responsible person to do so, and communicate the SOP to all teams.

EMS, epidemiological monitoring survey; IIS, IDA impact survey; LF, lymphatic filariasis; SOP, standard operating procedure; SSB, Survey Sample Builder; TAS, transmission assessment survey; WHO, World Health Organization.

Annex 12. Checklist for investigation of EMS results above threshold

No.	Question	Answer	Assessment	Recommended follow-up action
Population selected				
1	Was the sample size lower than the target?			Return to site to ensure that there are ≥ 300 samples in each site.
Distribution of results				
2	How were positive results distributed by team?		Analyse the data by team to determine whether positive results were clustered in certain teams	If only certain field teams found positive results, this might indicate that tests were read or used incorrectly. Discuss with the teams and reassess their capacity to apply and read the test. Re-test positive people originally tested by teams found to have low capacity. Re-train these teams before future surveys.
Diagnostic test quality				
3	Were tests used before their expiration date?			If no, the survey should be repeated.
4	Was the lot used in a failed EU also used in EUs that passed the surveys?		If one lot was used only in EUs that failed the survey (and not in those that passed) and tests remain from that lot, test with positive and negative controls.	If there is evidence that the diagnostics were faulty, the survey should be repeated.
5	Were positive and negative controls conducted on all lots within 6 weeks of the survey?		If controls were not conducted on all lots, test any leftover tests from that lot with positive and negative controls.	If there is evidence that the tests were faulty, the survey should be repeated.

6	Did team members participate in LF survey training and demonstrate capacity to use the test and interpret results?			If no, ensure that all participants in future training pass the post-test and demonstrate ability to use and interpret RDTs appropriately.
7	Were teams evaluated frequently by the supervisor in the field?			If no, improve the quality of supervision before the next survey.
8	Is the area co-endemic for *Loa loa*?			If yes, confirmatory testing should be done on all positives by dried-blood spot specimens for serology or PCR and night blood films.
9	Was EMS conducted at the appropriate timing after the last round of MDA?			
10	Were blood slides for Mf taken at peak circulation times according to the known periodicity of the parasite?		If not, Mf prevalence will be underestimated.	Ensure appropriate blood collection times during the next EMS.
11	During examination of blood slides for Mf, were 10% of negatives and all positives re-read by experienced technicians for quality control?		If not, cross-check the slides.	
EU setting				
12	Was the baseline infection prevalence in areas in the EU considered to be high?		If the prevalence of antigen was high (> 10%), > 5 MDA rounds were probably necessary according to epidemiology alone.	Implement 2 more rounds of MDA, ensuring high treatment coverage, and add vector control (if feasible).
13	Are contiguous areas endemic (including cross-border areas), and are they implementing MDA?		If contiguous areas are endemic and have a high baseline prevalence, there is a risk of resurgence due to movement of people or vectors.	
14	Are other health programmes in the EU finding it difficult to achieve good coverage or decrease the disease burden?		Collect data from other health programmes to determine whether they have similarly low coverage or persistent prevalence. Consider interviews with staff of other programmes and district staff in EUs to identify challenges and suggest improvements.	Consider lessons learnt by other health programmes and how they might be used to improve next 2 MDA rounds.

15	Are there mobile populations in the EU, such as nomadic pastoralists or economic migrants?		Mobile populations might be at greater risk of infection with LF because of exposure to vectors and/or more likely to be missed by MDA. Investigate how best to reach mobile populations in MDA. Consider testing them for LF infection, as they might have been missed in previous surveys.	Use results to ensure that MDA reaches mobile populations, e.g. is conducted at an appropriate time with appropriate outreach. In repeated EMS, consider adding a spot-check site focused on this population.
16	Is the EU in an insecure or conflict-affected area?		Collect information from various sources and other health programmes about the area and what can be achieved.	Contact other stakeholders (WHO, UNHCR, MSF, implementing partners, military) about the situation and what can be implemented If safe and feasible, adapt activities to the situation; e.g. use only local supervisors, be prepared to implement activities quickly when conditions allow.
MDA coverage				
17	Was coverage calculated and reported correctly?		Analyse the source of the total population requiring MDA that is used, as it could affect the accuracy of reported coverage. Review the calculations used to determine coverage. Determine whether drug registers were updated before each MDA, if applicable.	Determine whether other data should be used as the total population figure. Ensure that coverage is being defined and reported as proportion treated out of the total population during next 2 MDA rounds (see section 5). Consider updating registers or conducting a pre-MDA census before the repeated MDA round.
18	Are there sub-district areas with low coverage?		Analyse data by sub-district. Determine whether low-coverage areas are matched with clusters with positive results during the survey.	Consider microplanning, and an additional focus on training and supervision in areas with previous low coverage. Consider use of the supervisor's coverage tool or coverage evaluation surveys in these areas. Ensure that a spot-check site in those areas is included in the repeated EMS.

19	Are there any specific population groups (e.g. by age, sex, ethnic group, occupation) with low coverage?		Analyse MDA coverage data by population group. If certain groups have low coverage, collect further data on MDA coverage to determine the reason, e.g. whether they were never treated.	During the next 2 MDA rounds, modify distribution strategies to ensure that all population groups are covered.
20	Is there evidence that certain people consistently refuse to take medicines?		Analyse never treatment and other data from EMS, the supervisor's coverage tool and coverage evaluation surveys to determine who is refusing treatment. Potentially interview key informant, focus group discussions or other qualitative research to determine the reasons for refusal and how they could be overcome.	If there is evidence, before the next 2 MDA rounds, conduct e.g. microplanning, targeted social mobilization, meeting with leaders of groups who refuse.
21	Is there evidence that certain people are consistently not offered medicines?		Analyse never treatment and other data from EMS, the supervisor's coverage tool and coverage evaluation surveys to determine who is not being reached. Potentially conduct key informant interviews, focus group discussions or other qualitative research to determine the reasons for not being reached and how to overcome them.	If evidence exists, before the next 2 MDA rounds, conduct strategies to address (e.g. microplanning, changing timing or hours of MDA distribution, changing distribution platforms).
Quality of MDA				
Timing, compliance and platforms				
22	Was directly observed treatment (DOT) used?		Analyse supervisor reports, post-MDA review meeting reports, coverage evaluation survey reports to determine the frequency of DOT.	If not, before the next 2 MDA rounds, retrain EU staff and drug distributors in the importance of DOT. Increase supervision during the next 2 MDA rounds.
23	Was MDA conducted at a time of year when most people are available? E.g. was MDA conducted during the rainy season or farming period? What is the most appropriate month for treatment?		Conduct participatory methods qualitative research, including preparing seasonal calendars.	If groups were missed because of the timing of MDA, revise it for the next 2 rounds. If all population groups (including migrants and seasonal workers) cannot be reached in a single annual distribution, consider an additional targeted MDA during the year to cover these groups.

24	What drug distribution platforms were used? Did the drug distribution platforms ensure delivery of medicines to all communities and groups?		Review information on local drug distribution platforms. Determine whether buffer stocks of medicines and supplies were available during MDA at all levels.	If coverage was not reached, consider changing drug distribution platforms, e.g. adding house-to-house mop-up, including factories, mines and refugee camps as fixed posts. Consider using the supervisor's coverage tool after the first repeated MDA round to determine whether coverage was met, and conduct mop-up campaigns if necessary.
25	Was the dosage of medicines appropriate for all communities and groups?		Check calibration of dose poles or dosing schedules used by drug distributors. Ensure calibrations for dosage fit the demographic profile of the targeted population to achieve an appropriate mg/weight ratio.	Consider checking a sample of dose poles from communities before next round of MDA to determine whether they should be changed to ensure accuracy. Review data on distribution of height and weight of the population to ensure appropriate dosing.
26	If drugs are locally procured, have they been controlled for quality?		Assess the sources of medicine used in MDA. Have the sources undergone any panel review or pre-qualification?Are there data to verify the active ingredient, absorption and stabilization?	If drugs were not quality controlled according to WHO standards, leftover drugs can be assessed. Consult WHO for the recommended protocol.
27	What is the ratio of the number of people targeted to the drug distributor?		Less than 250:1 is usually appropriate but might have to be modified for remote areas.	Determine whether more drug distributors are required for certain areas when planning the next 2 MDA rounds. Use of the WHO microplanning manual can be useful.
28	Was there provision for mop up after MDA in communities in which targets were not met? Was mop-up completed?		Determine whether mop-up was conducted in areas with low coverage and, if not, why not.	Ensure adequate supplies for mop-up and regular monitoring and communication to teams that should conduct mop-up.
29	Did the MDA take > 2 months to implement?		Review information on length of MDA.	Complete each of the next 2 MDA rounds within 2 months.

Training				
30	Were drug distributors trained? Did training aides or manuals provide appropriate information? Were drug distributors given adequate information to respond to common questions from the community?		Review information from training, such as supervision forms, trip reports. If necessary, collect new qualitative information on what motivates drug distributors and how they are being trained.	Update training aides or manual. Re-train drug distributors before the next 2 2 MDA rounds.
31	Were drug distributors selected because they were well known and respected by the community?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new qualitative information to better understand selection and role of drug distributors.	Before the next MDA, update process for selecting drug distributors.
32	Were the roles and responsibilities of drug distributors written and distributed?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new qualitative information from NTD programme staff at all levels, health facility workers and drug distributors to better understand the selection and role of drug distributors.	Develop or update roles and responsibilities of drug distributors. Distribute them in appropriate languages for appropriate literacy levels during MDA re-training.
33	Was information on responding to real or perceived side-effects included in training?		Review training materials to determine whether responding to side-effects was included.	Update training materials to include information on responding to real or perceived side-effects. See WHO MDA safety manual for examples.
34	Were standard post-tests used to test the ability of drug distributors after training?		Review training and supervision reports to determine whether post-tests were applied.	Update training agenda to ensure that post-tests are conducted. Develop or update post-tests, and determine how to collect such information systematically at all levels of training.
Social mobilization				
35	Were community leaders involved in planning the MDA?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new qualitative information to better understand how social mobilization was conducted.	Involve community leaders and other local influencers in social mobilization before a the next 2 MDA rounds.

36	Were individuals with clinical manifestations of LF involved in the campaign, if willing?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new qualitative information to better understand how social mobilization was conducted.	Issue inclusive, appropriate social mobilization messages that include the perspectives of people with clinical manifestations of LF.
37	Were one-page job aids with photos of people with LF used as visual aids in discussions with communities?		Review information, education and communication (IEC) materials.	Create visual aids to help community members understand the impact of LF and the importance of participating in LF MDA.
38	Did social mobilization strategies and IEC materials contain appropriate messages and were they disseminated by community preferred means?		Review IEC materials.	Use knowledge, attitudes and practice and/or other qualitative information on effectiveness of IEC materials, change IEC strategy as necessary to improve knowledge and compliance before the next 2 2 MDA rounds.
39	Were side-effects addressed in communications?		Review IEC materials.	Add information about side-effects. Pilot-test IEC materials with various groups to ensure understanding and appropriateness.
40	Was information about how and where to receive treatment for side-effects provided?		Review IEC materials.	Add information to IEC materials about how and where to receive treatment for side-effects. Pilot-test with various groups to ensure understanding and appropriateness. Consider issuing a one-page communication for drug distributors to have as a reference.
Supervision				
41	Was there a system for addressing reports of side-effects or adverse events?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	If the system was inadequate, consider revising safety protocols and training. See the WHO MDA safety manual, for examples.
42	Did side-effects or adverse events occur in the community after MDA? If so, how were they responded to?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	If the response was inadequate, consider revising safety protocols and training. See the WHO MDA safety manual for examples.
43	Were roles and responsibilities for supervisors at each level written and distributed?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	Create or update written roles and responsibilities for supervisors at each level, and include their discussion in training before MDA.

44	Did supervisors use standard supervision monitoring forms?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	Use an MDA supervision checklist. See WHO microplanning manual Annex 9 for an example. Ensure that supervisors are trained in use of forms before MDA. Consider electronic collection of supervision data.
45	What is the ratio of drug distributors to supervisor?		No more than 10:1 is usually appropriate but might have to be modified for remote areas.	Determine whether certain areas require more supervisors during planning for the next MDA, e.g. in the WHO microplanning manual.
46	Were meetings held with communities during and/or after MDA to solve problems?			Hold daily data monitoring sessions with MDA teams during MDA to solve problems and make adjustments in the next 2 MDA rounds. Hold post-MDA review meetings after MDA, inviting community members to take part.

DOT, directly observed treatment; EMS, epidemiological monitoring survey; EU, evaluation unit; IEC, information, education, and communication; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; MSF, Médecins Sans Frontières; NTD, neglected tropical disease; PCR, polymerase chain reaction; RDT, rapid diagnostic test; UNHCR, United Nations High Commissioner for Refugees; WHO, World Health Organization.

Annex 13. Checklist for investigation of TAS/IIS results above threshold

No.	Question	Answer	Assessment	Recommended follow-up action
Distribution of results				
1	How were positive results distributed by cluster?		Analyse the data spatially to determine whether positive results were geographically clustered (e.g. more positives in a few isolated clusters) or not (few positives were found in many clusters throughout the EU).	Additional information should be collected to assess the reasons for clustering. If the EU is found to be heterogeneous in terms of risk, split the EU into several EUs and conduct another survey or an MDA. Use the information to enhance coverage in the next 2 MDA rounds. Consult WHO for assistance.
2	How were positive results distributed by team?		Analyse the data by team to determine whether positive results were clustered in certain teams.	If only certain teams found positive results, this might indicate that tests were read or used incorrectly. Discuss with the teams and reassess their capacity to apply and read the test. Re-test positive children originally tested by teams found to have low capacity. Retrain the teams before future surveys.
Quality of diagnostic tests				
3	Were the tests used before their expiration date?			If not, the survey should be repeated.
4	Was the lot used in the failed EU also used in EUs that passed the surveys?		If one lot was used in all EUs that failed the survey (and not in areas that passed) and there are leftover tests from that lot, test with positive and negative controls.	If there is evidence that the diagnostic tests were faulty, the survey should be repeated.
5	Were positive and negative controls conducted on all lots within 6 weeks of survey?		If controls were not conducted on all lots, if there are leftover tests from that lot, test with positive and negative controls.	If there is evidence that the diagnostic tests were faulty, the survey should be repeated.

6	Did team members participate in LF survey training and demonstrate capacity to use the test and interpret the results?			If not, ensure that all participants in future training pass the post-test and can demonstrate ability to use and interpret RDTs appropriately.
7	Were teams evaluated frequently by the supervisor in the field?			If no, improve the quality of supervision before the next survey.
8	Is the area co-endemic for *Loa loa*?			If yes, confirmatory testing should be done on all positives by dried blood spot specimens for serology and/or night blood films.
9	Was EMS conducted at least 6 months after the last round of MDA in areas that received one- or two-drug LF regimens? Was EMS conducted at least 9 months after the last round of MDA in areas that received IDA?			If not, then survey sites at least 6 or 9 months after the last MDA in the next EMS.
10	Were blood slides for Mf taken at peak circulation times according to the known periodicity of the parasite?		If not, Mf prevalence will be underestimated.	Ensure appropriate blood collection times during the next EMS.
11	During examination of blood slides for Mf, were 10% of negatives and all positives re-read by experienced technicians for quality control?		If not, cross-check the slides.	
EU setting				
12	Was the baseline prevalence of infection considered to be high in areas in the EU?		If the prevalence was high (> 10% antigen), more than five MDA rounds was probably required according to epidemiology alone.	Implement 2 more rounds of MDA with an emphasis on ensuring high treatment coverage and add vector control (if feasible).
13	Are contiguous areas endemic (including cross-border areas), and are they implementing MDA?		If contiguous areas are endemic and have a high baseline prevalence, there is a risk of resurgence due to movement of people or vectors.	

14	Do other health programmes in the EU find it difficult to achieve good coverage or to lower the disease burden?		Consult data from other health programmes to determine whether they have had similarly low coverage or persistent prevalence. Consider interviews with informants in other health programmes and district staff to identify challenges and possible solutions.	Consider lessons learnt by other health programmes and how they might be used to improve the next 2 MDA rounds.
15	Are there mobile populations in the EU, e.g. nomadic pastoralists or economic migrants?		Mobile populations might be at greater risk of LF due to exposure to vectors and/or the likelihood of being missed for MDA. Investigate how best to reach mobile populations in the next MDA. Consider testing them for LF infection, as they might have been missed in previous surveys.	Use results of investigation to ensure MDA reaches mobile populations, e.g. is conducted at the appropriate time with appropriate outreach. In repeated EMS, consider adding a spot-check site for this population.
16	Is the EU in an insecure or conflict-affected area?		Collect information from various sources and other health programmes about the area and what can be implemented.	Consult other stakeholders (WHO, UNHCR, MSF, implementing partners, military) about the situation and what can be implemented. If safe and feasible, adapt activities to the situation, e.g. use only local supervisors, be prepared to implement activities quickly when conditions allow.
MDA coverage				
17	Was coverage calculated and reported correctly?		Analyse the source of the total population requiring MDA that is used, as it could affect the accuracy of reported coverage. Review the calculations used for determining coverage. Determine whether drug registers were updated before each MDA, if applicable.	Determine whether other data sources should be used as the total population figure Ensure that coverage is defined and reported as the number treated over the total population in next 2 MDA rounds (see section 5). Consider updating registers or conducting a pre-MDA census before a repeated MDA round.

18	Are there sub-district areas with low coverage?		Analyse data by sub-district. Determine whether low-coverage areas are matched with clusters with positive results during the survey.	Consider microplanning and an additional focus on training and supervision in areas with previous low coverage. Consider use of the supervisor's coverage tool or coverage evaluation surveys in these areas. Ensure that a spot-check site in those areas is included in the repeated EMS.
19	Do any special population groups (e.g. by age, sex, ethnic group or occupation) have low coverage?		Analyse MDA coverage data by population group. If certain groups have low coverage, collect further data on MDA coverage to determine the reason, e.g. whether the groups were never treated.	During the next 2 MDA rounds, modify distribution strategies to ensure that all population groups are covered.
20	Do certain people consistently refuse to take medicines?		Analyse never treatment and other data from EMS, the supervisor's coverage tool and coverage evaluation surveys to determine who is refusing treatment.Potentially conduct interviews with key informants, hold focus group discussions or implement other qualitative research to determine the reasons for refusal and how to overcome them.	If evidence exists, before the next 2 MDA rounds, implement strategies to address (e.g. microplanning, targeted social mobilization activities, and meetings with leaders of groups who refuse).
21	Is there evidence that certain people consistently do not receive or are offered medicines?		Analyse never treatment and other data from EMS, the supervisor's coverage tool and coverage evaluation surveys to determine who is not being reached. Potentially conduct key informant interviews, focus group discussions, or other qualitative research to determine reasons for not being reached and how to overcome.	If evidence exists, before the next 2 MDA rounds, implement strategies to address (e.g. microplanning, changing the timing or hours of MDA distribution and changing distribution platforms).
Quality of MDA				
Timing, compliance and platforms				
22	Was DOT used?		Analyse supervisor reports, post-MDA review meeting reports and coverage evaluation survey reports to determine the frequency of DOT.	If not, before the next MDA round, re-train EU staff and drug distributors, including on the importance of DOT. Increase supervision during next 2 MDA rounds.

23	Was MDA conducted at a time of year when most people are available? E.g. was MDA conducted during the rainy season or farming period? What is the most appropriate month for treatment?		Conduct participatory methods qualitative research, including preparing seasonal calendars.	If groups were missed because of the timing of MDA, revise the timing of MDA in the next 2 MDA rounds. If all population groups (migrants, seasonal workers) cannot be reached in a single annual distribution, consider an additional targeted MDA during the year to cover these groups.
24	What drug distribution platforms were used? Did the drug distribution platforms ensure delivery of medicines to all communities and groups?		Review information on local drug distribution platforms. Determine whether buffer stocks of medicines and supplies were available at all levels during MDA.	If coverage was not achieved, consider changing the drug distribution platform, e.g. adding house-to-house mop-up, including factories, mines and refugee camps as fixed posts. Consider using the supervisor's coverage tool after the first repeated MDA round to determine whether coverage was achieved, and conduct mop-up if necessary.
25	Was the dosage of medicines appropriate for all communities and groups?		Check calibration of dose poles or dosing schedules used by drug distributors. Ensure calibrations for dosage fit the demographic profile of the targeted population to achieve an appropriate mg/weight ratio.	Consider checking a sample of dose poles in communities before the next round of MDA to determine whether changes should be made to ensure their accuracy. Review data on the distribution of height and weight of the population to ensure appropriate dosing.
26	If drugs are locally procured, were they controlled for quality?		Assess the sources of the medicines used in MDA. Have they been reviewed or pre-qualified? Are there data to verify the active ingredient, absorption and stabilization?	If their quality was not controlled according to WHO standards, leftover drugs can be assessed. Consult WHO for the recommended protocol.
27	What is the ratio of the number of people targeted to drug distributors?		Less than < 250:1 is usually appropriate but might have to be modified for remote areas.	Determine whether certain areas should have more drug distributors during planning the next MDA rounds. The WHO microplanning manual may be useful.

28	Was there provision for mop-up after MDA in communities in which targets were not met? Was mop-up completed?		Check whether mop-up was implemented in areas with low coverage and, if not, why not.	Ensure that adequate supplies are available for mop-up and data are monitored and communicated regularly to mop-up teams.
29	Did the MDA take longer than 2 months to implement?		Review information on length of MDA.	Complete each of the next MDA rounds within 2 months.
Training				
30	Were drug distributors trained? Did training aides and manuals provide appropriate information? Were drug distributors given adequate information to respond to common questions from the community?		Review information from training, such as supervision forms and trip reports. If necessary, collect new, qualitative information on the motivation of drug distributors and how they are trained.	Update training aides and manuals. Re-train drug distributors before the next 2 MDA rounds.
31	Were drug distributors selected because they were well known and respected in the community?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new, qualitative information on the selection and role of drug distributors.	Before the next MDA, update the process for selecting drug distributors.
32	Were the roles and responsibilities of drug distributors written and distributed?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new, qualitative information from programme staff at all levels, health facility workers and drug distributors to better understand the selection and role of drug distributors.	Develop or update the roles and responsibilities of drug distributors. Distribute them in appropriate languages and at appropriate literacy levels during re-training in MDA.
33	Was information on responding to real or perceived side-effects included in training?		Review training materials to establish whether responding to side-effects was included.	Update training materials to include information on responding to real or perceived side-effects. See the WHO MDA safety manual for examples.
34	Were standard post-tests used to test the ability of drug distributors at the end of training?		Review training and supervision reports to determine whether post-tests were used.	Update training agenda to ensure that post-tests are conducted. Develop or update post-tests, and determine how to collect the information systematically at all levels of training.

Social mobilization				
35	Were community leaders involved in planning the MDA?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new, qualitative information to better understand how social mobilization was conducted.	Involve community leaders and other local influencers in social mobilization before a the next two MDA rounds.
36	Were individuals with clinical manifestations of LF involved in the campaign, if they were willing?		Review supervision reports, post-MDA review meeting reports and other data sources. If necessary, collect new, qualitative information to better understand how social mobilization was conducted.	Prepare inclusive, appropriate social mobilization messages that include the perspectives of persons with clinical manifestations of LF.
37	Were one-page job aids with photos of people with LF as visual aids used in discussions with communities?		Review IEC materials.	Create visual aids to help community members understand the impact of LF and the importance of participating in LF MDA.
38	Did social mobilization strategies and IEC materials contain appropriate messages, and were they disseminated through the preferred means of communities?		Review IEC materials.	Use knowledge, attitudes and perceptions and/or other qualitative information on the effectiveness of IEC to change the IEC strategy as necessary to improve knowledge and compliance before the next 2 MDA rounds.
39	Were side-effects addressed in communication messages?		Review IEC materials.	Add information about side-effects to IEC materials. Pilot-test with various groups to ensure understanding and appropriateness.
40	Was information about how and where to receive treatment for side-effects provided?		Review IEC materials.	Add information to IEC materials about how and where to receive treatment for side-effects. Pilot-test in various groups to ensure understanding and appropriateness. Consider preparing a 1-page reference for drug distributors.
Supervision				
41	Was there a system for addressing reports of side-effects or adverse events?		Review how reports of side-effects were addressed in trip reports, supervision reports and reports of post-MDA review meetings.	If the system was inadequate, consider revising the safety protocols and training. See the WHO MDA safety manual for examples.

42	Did side-effects or adverse events occur after treatment in the community? If so, what was the response?		Review how reports of side-effects were addressed in trip reports, supervision reports and reports of post-MDA review meetings.	If the response was inadequate, consider revising the safety protocols and training. See the WHO MDA safety manual for examples.
43	Were the roles and responsibilities of supervisors at each level written and distributed?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	Prepare or update written roles and responsibilities for supervisors at each level, and include their discussion in training before MDA.
44	Did supervisors use standard supervision monitoring forms?		Review how reports of side-effects were addressed in trip reports, supervision reports and post-MDA review meeting reports.	Use an MDA supervision checklist. See WHO Microplanning manual Annex 9 for an example. Ensure that supervisors are well trained in use of forms before MDA. Consider collecting electronic data on supervision.
45	What is the ratio of drug distributors to supervisors?		No more than 10:1 is considered appropriate but may have to be modified for remote areas.	Determine whether certain areas should have more supervisors in planning the next MDA. Use of the WHO Microplanning manual can be useful.
46	Were meetings held with communities during and/or after MDA review meetings to solve problems?			Hold daily data monitoring sessions with MDA teams during MDA to solve problems and make adjustments for MDA. Hold post-MDA review meetings after the next two MDA rounds, and invite community members to take part.

DOT, directly observed treatment; EMS, epidemiological monitoring survey; EU, evaluation unit; IDA, ivermectin + diethylcarbamazine + albendazole; IEC, information, education, and communication; IIS, IDA impact survey; LF, lymphatic filariasis; MDA, mass drug administration; Mf, microfilariae; MSF, Médecins Sans Frontières; RDT, rapid diagnostic test; TAS, transmission assessment survey; UNHCR, United Nations High Commissioner for Refugees; WHO, World Health Organization.

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