

**STRENGTHENING THE ASSESSMENT
OF LYMPHATIC FILARIASIS
TRANSMISSION AND DOCUMENTING
THE ACHIEVEMENT OF ELIMINATION**

MEETING OF THE NEGLECTED TROPICAL
DISEASES STRATEGIC AND TECHNICAL
ADVISORY GROUP'S MONITORING AND
EVALUATION SUBGROUP ON DISEASE-
SPECIFIC INDICATORS

LYMPHATIC FILARIASIS



GENEVA, SWITZERLAND, 27-29 AUGUST 2014



**World Health
Organization**

*Strengthening the assessment of
lymphatic filariasis transmission and
documenting the achievement of
elimination*

*Meeting of the Neglected Tropical Diseases Strategic and Technical Advisory
Group's Monitoring and Evaluation Subgroup on Disease-specific Indicators*

27–29 August 2014
World Health Organization, Geneva



WHO Library Cataloguing-in-Publication Data

Strengthening the assessment of lymphatic filariasis transmission and documenting the achievement of elimination: meeting of the Neglected Tropical Diseases Strategic and Technical Advisory Group's Monitoring and Evaluation Subgroup on Disease-specific Indicators.

1.Elephantiasis, Filarial – prevention and control. 2.Helminthiasis - transmission. 3.Soil – parasitology. 4.Neglected Diseases. 5.Program Evaluation. I.World Health Organization.

ISBN 978 92 4 150879 7

(NLM classification: WC 880)

© World Health Organization 2016

All rights reserved. Publications of the World Health Organization are available on the WHO website (www.who.int) or can be purchased from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel.: +41 22 791 3264; fax: +41 22 791 4857;

e-mail: bookorders@who.int).

Requests for permission to reproduce or translate WHO publications –whether for sale or for non-commercial distribution– should be addressed to WHO Press through the WHO website (www.who.int/about/licensing/copyright_form/en/index.html).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.

Printed in France

WHO/HTM/NTD/PCT/2016.09

Contents

Abbreviations.....	v
1. Opening session	1
2. Purpose and objectives.....	1
2.1 Declarations of interest.....	1
3. Background methods used to assess transmission of lymphatic filariasis: mapping, sentinel-site monitoring and the TAS	1
3.1 Discussion	2
4. Supplemental guidance for areas where the classification of endemicity is uncertain	2
4.1 United Republic of Tanzania.....	2
4.2 Indonesia	3
4.3 Bangladesh	3
4.4 Proposed supplemental method to classify endemicity	4
4.5 Issues in settings where loiasis is coendemic.....	5
4.6 Proposed algorithms for decision-making.....	6
5. Comparison of tests for lymphatic filariasis antigen	8
5.1 BinaxNOW Filariasis ICT and the Alere Filariasis Test Strip	8
5.2 Laboratory comparisons.....	9
5.3 Field comparison overview.....	9
5.4 Discussion: performance of the FTS and operational characteristics	13
6. Improving the efficiency of implementing and interpreting the TAS.....	15
6.1 TAS Eligibility and Reporting.....	15
6.2 Interpreting the results of a TAS	16
6.3 Comprehensive surveillance in Sri Lanka	18
7. Processes of validation, verification and certification of elimination.....	18
7.1 Background.....	18
7.2 Elimination criteria: morbidity	19
7.3 Elimination criteria: transmission.....	20
7.4 Developing a template for the dossier used to document elimination	22
8. Meeting conclusions and recommendations.....	24
8.1 Objective 1: strategies to delineate endemicity and determine when to initiate MDA	24
8.2 Objective 2: programmatic use of the new Alere Filariasis Test Strip	25
8.3 Objective 3: documenting targets for the achievement of elimination.....	25
8.4 General recommendations.....	25
9. Closure of the meeting.....	26
Annex 1. List of participants.....	27
Annex 2. Agenda	31

Annex 3. Comparison of survey methods recommended for use since the inception of the Global Programme to Eliminate Lymphatic Filariasis.....	34
Annex 4. Rationale and description of an example decision-making prevalence survey proposed for remapping the endemicity of lymphatic filariasis.....	39
Annex 5. Comparisons of the BinaxNOW Filariasis immunochromatographic test and the Alere Filariasis Test Strip.....	42

Abbreviations

ADL	adenolymphangitis
CDC	United States Centers for Disease Control and Prevention
DEC	diethylcarbamazine
DOLF	Death to Onchocerciasis and Lymphatic Filariasis
EDTA	ethylenediaminetetraacetic acid
ELISA	enzyme-linked immunosorbent assay
EU	evaluation unit
FTS	Filariasis Test Strip (Alere, Scarborough, ME, United States)
GAELF	Global Alliance to Eliminate Lymphatic Filariasis
GPELF	Global Programme to Eliminate Lymphatic Filariasis
ICT United	immunochromatographic test (BinaxNOW Filariasis ICT, Alere, Scarborough, ME, States)
IRS	indoor residual spraying
IU	implementation unit
LF	lymphatic filariasis
MDA	mass drug administration
MMDP	morbidity management and disability prevention
NTD	neglected tropical disease
PC	preventive chemotherapy
PCR	polymerase chain reaction
PPES	probability proportional to estimated size
RPRG	Regional Programme Review Group
SS	systematic sample
STAG	Strategic and Technical Advisory Group
STH	soil-transmitted helminthiases
TAS	transmission-assessment survey
WHO	World Health Organization

1. Opening session

Dr Dirk Engels opened the meeting by asking participants to examine the performance of the new diagnostic test for the *Wuchereria bancrofti* antigen (the Alere Filariasis Test Strip, manufactured by Alere, Scarborough, ME, United States).¹ He requested that the meeting decide whether guidance from the Global Programme to Eliminate Lymphatic Filariasis (GPELF) on mapping, monitoring and stopping mass drug administration (MDA) would need to change if the new test were implemented.

2. Purpose and objectives

The group selected Dr Patrick Lammie to chair the meeting. Dr Lammie noted that the meeting had three objectives:

1. to recommend new or modified strategies to supplement mapping and delineate the endemicity of lymphatic filariasis (LF);
2. to develop recommendations on the programmatic use of the new Alere Filariasis Test Strip (FTS) if necessary, as determined by the presentation and discussion of results of the comparative studies; and
3. to determine what information should be included in the template for a dossier to be used to document the achievement of elimination targets.

Participants were introduced (*Annex 1*) and the proposed agenda was approved (*Annex 2*).

2.1 Declarations of interest

All the invited experts completed a form of declaration of interests for WHO experts, which were submitted to and assessed by the WHO Secretariat prior to the meeting. WHO decided that all participants could contribute to the discussions of all technical sessions. The following was disclosed:

Dr. Eric Ottesen receives research support in the areas relevant to the topics discussed.

Dr Gary Weil is affiliated with an institution that holds the license to materials used in both the BinaxNOW Filariasis ICT and Alere Filariasis Test Strip. Dr. Weil does not receive any financial benefits or research support from royalties. All royalties go to a non-profit charity, The Foundation for Barnes Jewish Hospital.

3. Background methods used to assess transmission of lymphatic filariasis: mapping, sentinel-site monitoring and the TAS

Dr Jonathan King reviewed the 2012 global status of LF. In 2012, a total of 596 000 000 people were treated during MDA – that is, 43.2% of those who required treatment received it. Thirteen endemic countries had not started delivering MDA; 23 were implementing MDA; 22 had achieved 100% geographical coverage of MDA; and 15 were in the post-MDA surveillance stage. In 2012, approximately 50% of countries where LF was endemic needed intensive scale-up to meet the global elimination goal by 2020. In addition, 29 countries had reported some data on morbidity management and disability prevention (MMDP) during the previous 5 years.

The steps recommended by the GPELF for interrupting transmission are for countries to: (i) map the endemicity of LF, (ii) deliver MDA for a minimum of 5 years, (iii) conduct a transmission-assessment survey (TAS), (iv) conduct post-MDA surveillance, (v) develop a dossier that documents the achievement of elimination targets, and (vi) for reviewers to validate the claim that elimination criteria have been achieved. Thus, the critical programmatic decisions include classifying the level of endemicity, determining when to stop

¹ Both the Alere Filariasis Test Strip (referred to throughout the text as the FTS) and the BinaxNOW Filariasis immunochromatographic test (referred to throughout the text as the ICT) are manufactured by Alere, Scarborough, ME, United States.

MDA (through monitoring and administering TASs), and demonstrating that the disease has been eliminated (that is, through surveillance and by passing the third TAS). Dr King reviewed how programmatic guidance for these stages had changed from 2000 to 2014 (*Annex 3*).

The method used to map LF was not designed to measure prevalence but rather has been biased towards scaling-up MDA, by assuming that the areas most at risk could be identified. Mapping has been implemented in a variety of ways among WHO's regions. Assessments of sentinel sites and spot-check sites were designed to monitor the impact of MDA over time, to provide a baseline in areas where endemicity has not been determined by collecting data about parasites or antigens, and to gauge the eligibility of implementation units (IUs) for the TAS. Surveys used to determine whether to stop MDA have been robust and epidemiologically rigorous, and have used large sample sizes to estimate prevalence in the targeted age group. The guidelines for the TAS have been standardized and are more practical than they were previously. The objective of post-MDA surveillance is to respond to any continuing transmission that has been identified to ensure that LF transmission has been interrupted. However, WHO has not provided specific protocols that address continuing nationwide surveillance or responding to positive cases found during surveillance.

3.1 Discussion

Many questions were raised about the requirements for post-MDA surveillance, such as whether a TAS is sufficient for proving that LF has been eliminated, and whether and how infection levels in vectors should be used for program monitoring and evaluation. Evidence from both epidemiological and entomological surveys is required to prove that onchocerciasis has been eliminated in the Region of the Americas. The group agreed that xenomonitoring might be important to allow the results of the TAS to be cross-validated. In addition, the question of how to find and how to follow up on hot spots, or areas of potential continuing transmission within an evaluation unit (EU), was discussed. The group agreed that a meeting focusing on post-MDA surveillance methods should be convened in 2015 in order to review operational research protocols and the results of studies, and to propose detailed options to be used by country programmes.

4. Supplemental guidance for areas where the classification of endemicity is uncertain

Presentations about the situation in three countries illustrated specific instances where the classification of endemicity was difficult. Proposed algorithms to aid in decision-making in uncertain areas then were presented and discussed.

4.1 United Republic of Tanzania

Dr Upendo Mwingira explained that from 1998 to 2004 LF had been mapped in the United Republic of Tanzania using the BinaxNOW Filariasis immunochromatographic test (ICT) (Alere, Scarborough, ME, United States) to sample 50–100 people aged older than 5 years in 1–2 villages in each district (approximate population in each district, 200 000). All districts with with an antigenaemia prevalence of at least 1% in at least 1 village had been classified as endemic. Some districts that had less than 1% antigenaemia prevalence but in which there were people with chronic cases of LF also were classified as endemic. MDA was started along the coast in 2000, and has been implemented in 101 of 160 districts. Most of the 56 districts where MDA has not been started had low baseline prevalence (1–8% antigenaemia) and few chronic cases.

The prevalence of antigenaemia has been found subsequently to have been significantly reduced in 16 districts that have not yet started MDA. These districts are in areas where *Anopheles* is present, and some have high burdens of malaria. Two districts surveyed sentinel sites for baseline data and found 0% antigenaemia. Three districts, where baseline mapping found antigenaemia rates of 9–15%, were resurveyed for LF using ICTs and antibodies as part of an indoor residual spraying (IRS) survey, and no evidence of infection was found. In eight districts, TASs were implemented and all districts passed – that is, no transmission was identified. In another three districts, where mapping originally identified up to 30% antigenaemia, the Death to Onchocerciasis and LF (DOLF) project reassessed endemicity by measuring the prevalence of LF antigens and microfilariae among

1000 people from the villages that had been originally mapped, and found 0% prevalence of antigenaemia and microfilaraemia.

Because the perception of the risk of LF is low, it has been difficult to get support from some districts and communities for treatment, so MDA has not been implemented in some areas. The country's programme would like to know whether districts should be remapped.

4.1.1 Discussion: United Republic of Tanzania

Some group members warned that using TASs in areas where MDA had not been implemented could be misleading because children might have lower infection rates and less exposure than the total population; therefore, it might be more useful to test adults.

4.2 Indonesia

Ms Molly Brady presented two questions that had been raised by the Indonesian LF programme.

1. Six districts (three with *W. bancrofti* and three with *Brugia spp.*) were mapped from 1993 to 2004 using blood films, and were classified as endemic, with a microfilaraemia prevalence ranging from 0% to 2.8%. The districts were remapped during 2012–2014 using blood films, and 0% microfilaraemia was found in all sites. Are the new data sufficient to reclassify the districts as non-endemic?
2. Five districts in *W. bancrofti* areas were mapped using ICTs and blood films. Although antigenaemia positivity was 1% or higher in at least 1 site in each district (and this ranged up to 18%), the prevalence of microfilaraemia was 0%. These districts were classified as non-endemic based on the microfilaraemia results, but the programme would like to confirm whether this was appropriate.

4.2.1 Discussion: Indonesia

Participants gave various examples from other settings in which blood films had not been subject to appropriate quality control, and agreed that decisions should not be made based on blood films in areas where there has not been extensive training and supervision of staff. However, the group agreed that the results of the ICTs should be used to determine endemicity in *W. bancrofti* areas, regardless of the results of the blood films.

4.3 Bangladesh

Dr Ramaiah Kapa reported on areas with low endemicity in Bangladesh. LF caused by *W. bancrofti* is endemic in Bangladesh, and is transmitted by *Culex* mosquitoes. Originally, 19 districts were classified as endemic based on the presence of clinical cases (that is, 100–10 000 clinical cases) and microfilaraemia rates ranging from 0.2% to 16%. Six to 12 rounds of MDA have been implemented in these districts. Fifteen districts had been classified as being low-endemic areas based on the presence of sporadic clinical cases and microfilaraemia rates of less than 0.6%. These districts, which are scattered throughout the country and border endemic areas, have not implemented MDA. Thirty districts have been classified as non-endemic. TASs were conducted in seven low-endemic districts, and all passed (three EUs had one positive case each); the other low-endemic districts are planning to implement TASs. The programme sought advice on whether the TAS method is appropriate for classifying low-endemic districts as non-endemic, and what type of surveillance or surveys should be done in non-endemic districts that border endemic districts.

4.3.1 Discussion: Bangladesh

The group was concerned about the implications of the mapping results, given the size of the IUs (more than 2 million people in some districts) and the use of the prevalence of microfilaraemia instead of antigenaemia. Further, it was noted that if global guidance recommended that a TAS should be implemented in every non-endemic district to confirm non-endemicity, this would be quite challenging from both the political and financial standpoints. Dr King assured the group that there is no recommendation for a TAS to be conducted in non-endemic areas, but if new clinical cases or new research shows that there is the possibility of transmission

in these areas, programmes should consult WHO to determine which type of survey or surveillance should be implemented to determine need for MDA.

4.4 Proposed supplemental method to classify endemicity

Dr Maria Rebollo presented a proposed method for reassessing the endemicity of LF, which will be piloted in Ethiopia. In 2013, the Ethiopian programme used ICTs to map endemicity, sampling 100 people aged 15 years or older in 2 communities in each district. The two communities were chosen because lymphoedema cases were present but there were no cases of onchocerciasis. Another common cause of lymphoedema in Ethiopia is podoconiosis which is not related to LF. Selecting sites based on lymphoedema only may not have led the teams to sites where LF was endemic. Of the 658 districts mapped, 45 districts found only 1 positive ICT result among the 200 people sampled – that is, 1 site with a 1% prevalence of antigenaemia.

A reassessment of LF has been proposed for these 45 districts and for 4 additional districts with antigenaemia prevalence greater than 1%. The programme debated whether to repeat the standard mapping protocol in these districts, but was concerned with the representativeness of this method, particularly when the choice of sites could be biased as a result of the presence of podoconiosis. The programme also considered conducting a TAS, but felt the cost was prohibitive.

The proposed method will use cluster sampling with the probability proportional to estimated size (PPES) to assess children aged 9–14 years in schools (*Annex 4*). A total sample of 480 children from 30 schools will be surveyed in each mapping unit to determine whether the prevalence of antigenaemia in the entire mapping unit (typically the district) is above or below 1% in this age group. The sample size assumes a design effect of 1.5 and is powered to allow no more than a 5% chance of being wrong when classifying a district as non-endemic if the district is truly endemic for LF. The concept, design and threshold are similar to those used in the TAS. The critical cut-off value is no more than three positive children. If three or fewer are antigen positive, programmes can be 95% confident that the prevalence of antigenaemia is below the threshold for LF transmission, and therefore no MDA is warranted. In settings where there are few schools (that is, fewer than 40) or where it is preferable to survey all schools in the mapping area, national programmes should conduct a systematic sample (SS) survey rather than a cluster survey. For an SS survey, 320 children are selected by sampling a fixed fraction of children from all schools in the mapping area. If an SS is used, the critical value should be no more than two positives. Children aged 9–14 years are the target population to be surveyed because this age group provide a more representative indicator of the prevalence in the total population than children aged 6–7 years, and they are likely to have the highest attendance in school. The method was developed for Ethiopia, so differing threshold levels for different vectors were not proposed.

The cost of this survey is estimated to be around US\$ 6000 per district, including the ICT and is much less costly than incorrectly classifying a district as endemic and implementing MDA for 5 rounds when it is unwarranted. For example, assuming 150 000 persons are treated in a district at US\$ 0.10 per person treated, the annual cost of MDA would be US\$ 15 000, which if implemented for 5 years would require US\$ 75 000. Using this robust survey could save programme resources.

4.4.1 Discussion: proposed supplemental method to classify endemicity

The group agreed that the proposed protocol would be advantageous when programmes could not predict areas of potential LF transmission. Indeed, the remapping protocol complements the original mapping (which was based on the programme's knowledge of high-risk areas), so that high-risk areas already should have been sampled. In addition, the methods are similar to that used for the TAS and are based on the average prevalence, thus giving a better estimate of the local epidemiology in a district. If by chance high-risk areas are not selected and the average prevalence in the survey is estimated to be below the 1% threshold, the assumption is that over time transmission will fall because these areas are surrounded by areas of lower prevalence. This is the same assumption made in the TAS. With both the TAS and this proposed remapping strategy, there is only a 5% chance of being wrong when a district is classified as non-endemic and therefore does not require MDA.

The group debated the number of clusters needed for the method, given that surveys to determine the district-level prevalence of trachoma and schistosomiasis use 18–20 clusters. The biostatisticians who developed the survey recommended 30 clusters because (i) with fewer clusters, more people are needed per cluster and this takes the survey further away from being a simple random sample, and (ii) with fewer clusters, the design effect increases and the sample size must be increased. Data from these surveys should be made available to statisticians so that the sampling strategy can be assessed and it can be determined whether the same conclusions can be drawn from fewer clusters.

It was recommended that future meetings on surveillance should include further discussion of how to recognize hot spots in mapping and monitoring, particularly in areas where *Culex* is the primary vector. Finally, it was suggested that a cost analysis should be done to look at the costs of improving methods (of mapping, the TAS and post-MDA surveillance) to reduce uncertainties compared with the costs of making the wrong decision (for example, by having to restart MDA or finding hot spots later).

4.5 Issues in settings where loiasis is coendemic

Dr Peter Fischer presented data from a study by Didier K Bakajika and others that originally aimed to assess the impact on LF of administering albendazole twice yearly.² Baseline data were collected in an area in the north-east of the Democratic Republic of the Congo where there are clinical cases of lymphoedema that are coendemic for multiple parasites; nighttime samples of capillary blood were taken from 2724 people in 30 villages for blood films and ICTs. Twenty-eight villages had a prevalence of antigenaemia of more than 1%. However, microscopy of blood films – both in the field and at Washington University (St Louis, MO, United States) – found *Mansonella perstans* and *Loa loa* parasites (average prevalence, 22%; range, 4–40%) but no *W. bancrofti* parasites. Several people had more than 20 000 *L. loa* microfilariae per millilitre. It was difficult to differentiate between *L. loa* and *W. bancrofti* parasites, particularly in slides with many microfilariae.

To follow up these results, the project extracted DNA from the blood films and ran polymerase chain reaction (PCR) on samples from 147 people with positive ICTs and 190 people with negative ICTs. Of these, 294 of the 337 tested positive for *L. loa*, and 1 sample (from a recent migrant to the area) tested positive for *W. bancrofti*. The researchers found that ICT positivity increased as the density of *L. loa* microfilariae increased – that is, in people with a density of more than 2000 *L. loa* microfilariae per millilitre, 59% of ICTs were positive. This association was statistically significant in multivariate analysis. No statistically significant association was found with counts of *M. perstans* microfilariae.

Finally, the project observed a varying periodicity of *L. loa* microfilariae among seven patients, and demonstrated that *L. loa* parasites could be present in nighttime blood samples. In conclusion, the study found that in Central Africa high densities of large, sheathed microfilariae in films made from nighttime blood samples do not necessarily indicate that *W. bancrofti* is present. Furthermore, ICTs are cross-reactive with *L. loa*, and this reactivity depends on the density of *L. loa* microfilariae. Therefore, positive ICT results in a loiasis-endemic area do not necessarily mean that the area is endemic for LF. Further research is necessary to confirm results from other geographical regions; to identify the cross-reactive antigen in *L. loa* serum samples; to determine how common coinfection with loiasis and LF is in individuals, villages and EUs; to determine whether the increased sensitivity of the new FTS leads to increased cross-reactivity in coendemic areas; and to evaluate alternative strategies for mapping LF, and monitoring and evaluating progress in loiasis-endemic areas.

4.5.1 Discussion: *Loa loa* issues

The group agreed on the importance of this issue: of the 12 countries in Africa that have not started MDA, 9 are countries where loiasis is coendemic with LF. The group agreed that an alternative diagnostic approach is needed to assess LF in areas where loiasis is coendemic. The ideas proposed were to use reference laboratories to perform PCR in areas that are highly endemic for loiasis or to assess antibodies – perhaps Wb123 to identify *W. bancrofti* infection – or both. The specificity of the Wb123 antibody is understood to be able to discriminate between infections with *W. bancrofti* and *L. loa*, but this should be confirmed by additional studies.

² Bakajika DK et al. Filarial antigenemia and *Loa loa* night blood microfilaremia in an area without bancroftian filariasis in the Democratic Republic of Congo. *American Journal of Tropical Medicine and Hygiene*. 2014, 91:1142–1148.

4.6 Proposed algorithms for decision-making

Dr Eric Ottesen presented a series of algorithms that can be used to generalize discussions of specific situations and provide generic guidance to national programmes. The aim was to decide what evidence is needed to delineate LF endemicity. After much discussion, the following final algorithms were agreed upon by the group. *Figure 1* provides the single summary algorithm that addresses what to do in each scenario discussed.

- In the first scenario (exemplified by the report from the United Republic of Tanzania), the original mapping surveys found a prevalence of antigenaemia or microfilaraemia of 1% or higher, but subsequent assessments or data collected at sentinel sites found antigenaemia or microfilaraemia of less than 1%. The group agreed that if results were negative then additional data from sentinel sites or spot-check sites, or remapping using the same protocol as had been used earlier, would not be sufficient to reclassify the IU as non-endemic. Instead, the IU should either start MDA based on the original mapping results or use a more statistically robust protocol (for example, the new protocol proposed for Ethiopia) to determine endemicity. For the remapping protocol, MDA is recommended when more than the critical number of positive cases has been identified. A result that is less than or equal to the critical number of positive cases would be sufficient to reclassify the IU as non-endemic. As with the original mapping results, the protocol and results of the reassessment should be reviewed by the Regional Programme Review Group (RPRG).
- The second scenario includes IUs with low endemicity that have not planned MDA or collected baseline information from a sentinel site. The group agreed that in IUs where MDA had not been started due to low endemicity (1–2%), the IUs should either start MDA according to WHO's guidelines or use a more statistically rigorous protocol (as mentioned in the first scenario). If after implementing a more rigorous survey the results are below the threshold, the IU could then be reclassified as non-endemic.
- The third scenario includes areas that need to be mapped but where there might be a significant time lag between mapping and collecting baseline data from a sentinel site. The group agreed that when countries desire to speed up their programme, the baseline collection of data from a sentinel site should not be required. Since data from sentinel sites collected by the GPELF have clearly indicated that MDA is effective where coverage targets are achieved, baseline sentinel-site information is less important in areas where community data are available from mapping; in this case, the mapping site with the highest prevalence of antigenaemia or microfilaraemia can be considered as the baseline sentinel site. Using such a shortcut will allow the programmatic priority to be placed on scaling-up MDA and ensuring that coverage reaches more than 65%. The group agreed that in unmapped areas national programmes should follow WHO's current standard mapping protocol – for example, the guidance for the African Region or the 2011 TAS manual.^{3,4}
- The fourth scenario includes loiasis-endemic areas that have been determined to be endemic for LF based on mapping using ICTs or the prevalence of microfilaraemia but that might have been misclassified due to potential cross-reactivity identified by ICTs or because of the difficulty of differentiating *W. bancrofti* from *L. loa* microfilariae in blood slides. Concerns were raised that overtreatment may occur in loiasis-endemic areas if MDA for LF is implemented based on ICT results, and this might not be acceptable to ministries of health, despite the benefits of also controlling soil-transmitted helminthiasis (STH) when MDA is administered for LF. However, the group concluded that the new strategy of delivering albendazole monotherapy twice a year together with vector-control efforts should be implemented in coendemic areas based on results obtained using ICTs. At the same time, it is critical that operational research is conducted to develop new tools to monitor the impact of MDA on the prevalence of LF in loiasis-endemic areas.

³ *Operational guidelines for rapid mapping of bancroftian filariasis in Africa*. Geneva, World Health Organization, 2000 (WHO/CDS/CPE/CEE2000.9) (also available at http://whqlibdoc.who.int/hq/2000/WHO_CDS_CPE_CEE_2000.9.pdf).

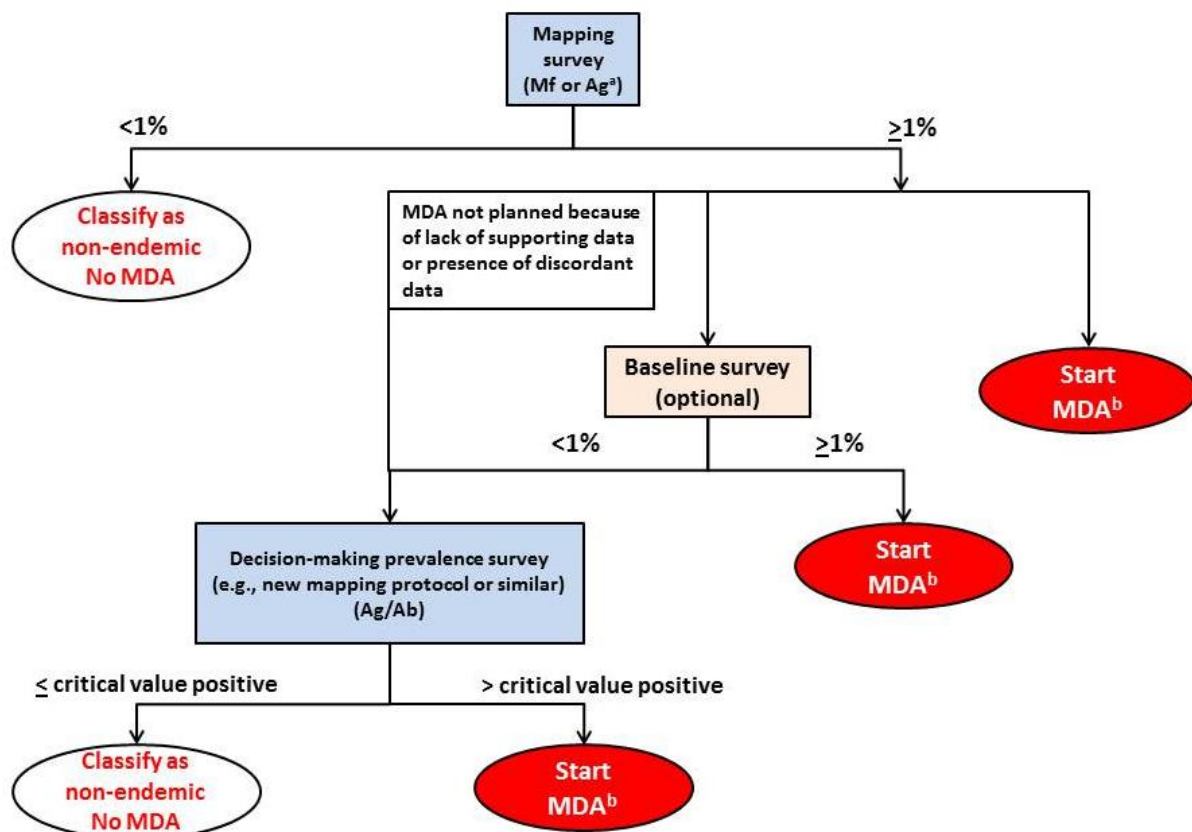
⁴ *Training in monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis*. Geneva, World Health Organization, 2011 (also available at http://www.who.int/lymphatic_filariasis/resources/TAS_training_materials/en/).

4.6.1 Discussion: proposed algorithms

The group recommended that in districts in loiasis-endemic areas that have yet to be mapped, ICTs should continue to be used but supplemental blood specimens need to be collected. If positive results are found with ICTs using nighttime blood samples, then positive samples could be pooled for PCR testing. Blood spots for antibody testing could also be collected. If evidence of *W. bancrofti* infection is found, then MDA should be planned. If supplemental assays do not confirm *W. bancrofti*, then MDA is not required. PCR testing of night-blood spots could be done by any of a number of reference laboratories (for example, at Washington University, the Kenya Medical Research Institute or Noguchi Memorial Institute for Medical Research in Legon, Ghana). The group recommended that a list should be made of all IUs in areas where LF and loiasis are potentially coendemic to determine whether the resources exist to implement additional diagnostic assays in all areas.

The group also discussed mosquito vector-control interventions that have been recommended to accompany the use of twice-annual albendazole for MDA in loiasis-endemic areas. LF programmes do not have targets for vector-control interventions (or funding for these interventions), but have the responsibility to encourage the use of vector control in LF-endemic areas. LF programmes should be responsible for coordinating with malaria prevention programmes to help guide the integrated vector management strategy, to ensure that the interventions cover LF-endemic areas, and to collect secondary data to use for LF reporting (for example, about bednet use, the number of nets per sleeping space, and coverage of IRS). LF activities are useful to malaria programmes because they provide a platform for resupplying nets, implementing social mobilization, and integrating MDA and surveys of bednet coverage.

Figure 1. Algorithm for determining the endemicity of lymphatic filariasis (LF) and the need for mass drug administration (MDA)



5. Comparison of tests for lymphatic filariasis antigen

5.1 BinaxNOW Filariasis ICT and the Alere Filariasis Test Strip

Ms Kimberly Won summarized the differences between the BinaxNOW Filariasis ICT and the Alere FTS (both manufactured by Alere, Scarborough, ME, United States). In areas where *W. bancrofti* is present, the ICT is the only test recommended currently for use in TAS, and significant programmatic decisions are made based on the results.⁵ However, there are challenges to using ICTs including their limited shelf-life (3 months); the requirement for cold storage until time of use; the need to read results at 10 minutes (which limits options for having a supervisory team conduct quality control); its relatively high cost (range, US\$ 3.00–10.00); and difficulties with procurement. Because hands-on training in administering the TAS is necessary even for experienced teams, an entire theoretical and practical module on diagnostics is included as part of WHO's training on the TAS. An ICT bench aid is available as part of the TAS training materials and on the web site of the Neglected Tropical Diseases (NTDs) Support Center.⁶

The Bill & Melinda Gates Foundation funded the manufacturer to reformat the ICT to address issues of cold storage, cost and shelf-life. The manufacturer then developed the FTS, which is a lateral flow test like the ICT (Table 1). The FTS is interpreted similarly to the ICT, and includes a control line to ensure that the test is working properly; also, the presence or absence of a test line is used to determine positivity. A bench aid has also been developed for the FTS. The United States Centers for Disease Control and Prevention (CDC) noted some issues that may affect the use of the FTS: (i) training is required to collect the correct quantity of blood using the new plastic, calibrated micropipette; (ii) each test strip must be secured to the provided plastic tray with a barcode label or tape so that the strips do not fly away or are not mislabelled; (iii) there is no easy way to mark each person's unique identification code, the time the sample was collected or the result directly on the test strip; and (iv) it might be necessary to use only heparin tubes (not tubes containing ethylenediaminetetraacetic acid, or EDTA) to collect plasma.

Table 1. Comparison of the BinaxNOW Filariasis immunochromatographic test (ICT) with the Alere Filariasis Test Strip (FTS)^a

	ICT	FTS
Sample volume required	100 µl	75 µl
Sample type	Whole blood, plasma or serum	Whole blood, plasma, ^b or serum
Time to result	10 minutes	10 minutes
Shelf-life ^{c,d}	9–12 months at 2–8 °C 3 months at >8 °C	16–24 months at 2–37 °C
Cost per test	About US\$ 3.00	< US\$ 1.50

^a Both tests are manufactured by Alere, Scarborough, ME, United States.

^b Only heparin collection tubes can be used to collect plasma not EDTA tubes.

^c The BinaxNOW Filariasis ICT can be kept in cold storage for 9–12 months; in ambient temperatures (once deployed for use in surveys), the tests are functional for up to 3 months.

^d The Alere FTS does not need cold storage; tests have been reported to be functional at ambient temperatures for 16–24 months.

⁵ *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>, accessed 28 August 2014).

⁶ *Immunochromatographic card test (ICT) bench aid*. Decatur, GA, Neglected Tropical Diseases Support Center (<http://www.ntdsupport.org/resources/immunochromatographic-card-test-ict-bench-aid>, accessed 28 August 2014).

5.1.1 Discussion: the ICT and the FTS

A process was proposed in which WHO would serve as a focal point of reference for the FTS manufacturer for forecasting needs and ordering tests. A consortium of sponsoring agencies has indicated interest in financing the purchase of these tests for national programmes to enable them to implement the TAS. Countries would fill out WHO's TAS Eligibility and Planning Form to determine whether it is appropriate to implement the survey.⁷ It has been proposed that a new section on this form would allow countries to request subsidized diagnostic tests. The subsidy from the sponsoring agencies would include delivery to national medical stores, and WHO would be used as the consignee for customs clearance. The process for making available controls for local quality testing of the received tests has not been decided.

5.2 Laboratory comparisons

5.2.1 Washington University, United States

Dr Gary Weil presented the results of laboratory comparisons of the two tests. Both tests use labelled polyclonal antibody for detection, and monoclonal antibody for trapping antigen on a nitrocellulose membrane. Antigen levels depend on the numbers of adult worms, and both the prevalence and level of antigen decline following MDA.

Both Washington University and the CDC tested samples from specimen banks using the FTS and the ICT. The tests were performed and read blind by separate technicians. There was 99% agreement between the FTS and the ICT. No positives were found in samples from non-endemic countries (Argentina, Haiti or the United States). The FTS was able to detect significantly lower levels of antigen than the ICT in serial dilutions. In terms of stability, it was more common for tests to turn positive later when whole blood was tested. In general, the FTS had 100% sensitivity and 98% specificity for the samples tested. These data have been published in *American Journal of Tropical Medicine and Hygiene*.⁸

5.2.2 Vector Control Research Centre, India

Dr K Krishnamoorthy updated the group on the progress of laboratory testing in India. The team in India received the ICT and the FTS in July 2014, so testing was scheduled to start in late September. The plan was to test the following samples: 50 samples known to be negative by enzyme-linked immunosorbent assay (ELISA) using Og4C3; 50 known positives using TG3 detected by Og4C3; 50 known positives using TG4 and detected by Og4C3; 10 samples from dogs that were positive for *Dirofilaria immitis*; 10 samples from animals with *Brugia* infections; and 10 samples from non-endemic areas. Dr Krishnamoorthy also noted that the strips were difficult to handle unless they were fixed to something.

5.2.3 Discussion: laboratory comparisons

Group members suggested that since the *Dirofilaria* samples would test positive, the Indian team could instead test more samples from non-endemic areas.

5.3 Field comparison overview

Results of using the FTS in programmatic settings were presented and discussed. The field comparisons were not part of a multicentre trial, but rather the findings from continuing, recommended monitoring and evaluation activities regularly conducted by national programmes. The sampling methods and the populations surveyed varied according to the type of monitoring or evaluation activity, but followed standardized WHO guidelines where applicable, for example, in terms of mapping, sentinel-site evaluation and TAS. In each site, at minimum, whole blood was collected from consenting survey participants and tested with both the ICT and the FTS. In some sites, night blood films were collected from persons testing positive for circulating filarial antigen by either test.

⁷ TAS eligibility and planning form. Geneva, World Health Organization, 2015 (http://www.who.int/entity/lymphatic_filariasis/resources/WHO_TAS_EPF.XLSM, accessed 2 March 2015).

⁸ Weil GJ et al. Laboratory and field evaluation of a new rapid test for detecting *Wuchereria bancrofti* antigen in human blood. *American Journal of Tropical Medicine and Hygiene*, 2013, 89:11–15.

The following minimum information from each site was presented:

- the programmatic context in which the FTS was applied;
- the protocol followed;
- the description of the sample population surveyed;
- quantitative results –
 - including the percentage of agreement between the FTS and the ICT
 - the prevalence estimate or point estimate of antigenaemia as determined by each test;
- qualitative results –
 - the programme decision indicated by each test
 - operational observations
 - Feedback from technicians;
- Conclusions of and recommendations made by those implementing the activities.

The results from 14 field studies were summarized (*Table 2*). For the five sites using the tests for mapping, all five came to the same conclusion about endemicity. Different conclusions about eligibility for a TAS were reached depending on which test was used for the one pre-TAS evaluation. All four sites that used the tests to decide whether to stop MDA came to the same conclusion with both tests. In the context of post-MDA surveillance, although more FTS tests were positive than ICTs, in three of the four sites the same interpretation was made. The site-specific results are presented in *Annex 5, Table A5.1*.

Summary results were presented from studies done by DOLF in coordination with national LF programmes in Côte d'Ivoire, the Democratic Republic of the Congo, Liberia and Sri Lanka. All countries within the DOLF project used the same operational protocol and training methods. The results from studies done by national programmes in Niger and Uganda were also presented by Dr Weil.

5.3.1 Liberia: mapping

The study in Liberia was conducted in the Foya district in north-eastern Liberia, an area of rural villages that has a moderately high prevalence of LF and is coendemic for onchocerciasis, schistosomiasis and STH. Data were collected in 2012 and 2014. In 2012, no MDA had occurred. In 2014, MDA for LF had not yet occurred in this area, but MDA for onchocerciasis using ivermectin had occurred 5 months prior to the study. The FTSs were read at 10 minutes, 30 minutes, and 24 hours.

Table 2. Summary of programmatic outcomes in field studies comparing the results of the BinaxNOW Filariasis immunochromatographic test (ICT) with the Alere Filariasis Test Strip (FTS)^a

Use for test	Total no. of sites	No. of sites with same conclusion from both tests	No. of sites with more positive tests identified by the FTS	No. of sites with more positive tests identified by the ICT	No. of persons tested	No. of discordant tests
Mapping	5	5	3	0	2381	56
Survey to determine eligibility for TAS	1	0	1	0	505	13
Survey to determine whether to stop MDA	4	4	1	3	7073	33
Surveillance	4	3	3	1	8292	91

TAS, transmission-assessment survey; MDA, mass drug administration.

^a Both tests are manufactured by Alere, Scarborough, ME, United States.

In 2012, blood was collected from 519 people who were older than 5 years in 5 villages; in 2014, blood was collected from 818 people. In 2012, the prevalence of antigenaemia was 19.5% by ICT; it was 9.9% in 2014. In 2012, the prevalence of antigenaemia was 24.6% by FTS; it was 10.3% in 2014. In 2012, 26% more positive cases were identified using the FTS; this dropped to 4% more positive cases in 2014.

In 2014, the agreement between the two tests was 94.4%. At 30 minutes, 0.7% of ICTs and 1.1% of FTSs had turned positive; at 24 hours, 63.3% of ICTs and 9.5% of FTSs had turned positive.

Data were also presented from the Harper district, another site coendemic for onchocerciasis. After one or two rounds of MDA, blood was collected from 1148 people who were older than 5 years. Of these, 207 (18%) were found to be positive by ICT and 230 (20%) by FTS. All areas tested using either ICTs or FTSs were found to be endemic for LF.

5.3.2 Côte d'Ivoire: mapping

In Côte d'Ivoire, a study was conducted at a site where onchocerciasis and STH were coendemic. Of 837 people tested who were older than 5 years, a total of 227 (27%) people were positive by ICT, and 244 (29%) were positive by FTS, thus the FTS identified 7.5% more positives. Both tests identified the area as endemic for LF.

5.3.3 Democratic Republic of the Congo: mapping

In the Democratic Republic of the Congo, the FTS identified 13 (45%) more positive cases among 187 people aged 5 years and older. A total of 29 (15.5%) were positive by ICT and 42 (22.5%) by FTS. Both tests found the area to be endemic for LF.

5.3.4 Niger: survey to determine whether to stop MDA

The study in Niger was completed in two EUs that had implemented a community-based TAS in children aged 6–7 years. Forty-one (1.9%) samples were positive by ICT and 25 (1.2%) by FTS. Sixteen of the ICT-positive samples were negative by FTS; none of the FTS-positive samples was negative by ICT. Given that this result is different from most others (that is, the ICT was more sensitive than the FTS), the result was double-checked with the team and they confirmed that it was correct. Results were not presented by EU; therefore, programmatic outcomes could not be compared by results from the ICT and the FTS.

5.3.5 Uganda: survey to determine whether to stop MDA

The study in Uganda was completed in an EU that had implemented a school-based TAS in children aged 6–9 years. Three (0.12%) children were positive by ICT and four (0.25%) by FTS. Two children had positive results on both tests; two were positive by FTS but negative by ICT; and one was positive by ICT but negative by FTS. Using either the results from the ICT or the FTS, the EU passed the TAS, indicating that MDA could be stopped. The researchers also noted that tap water (alone or used to dilute blood) caused the FTS (but not the ICT) to turn positive.

5.3.6 Sri Lanka: post-MDA surveillance

The study in Sri Lanka was implemented in two villages under post-MDA surveillance in an area with *W. bancrofti* transmitted by *Culex* mosquitoes (as well as some *B. malayi* infections in dogs and occasional infections in people). All households in each village were visited, and samples were taken from up to four people who were older than 8 years in each household. Initially, blood was collected using EDTA tubes and tests were performed in a central laboratory, but the team became concerned about the frequent number of positive cases identified by the FTS. When the same people were retested in the field using samples of whole blood, they were found to be negative by FTS. Therefore, the research team recommended that programmes do not use EDTA tubes to collect blood for the FTS because something in the tubes promotes binding of the antibody or gold conjugate to the test line in the FTS, leading to a false-positive result. In the Galle district, 9 (2.3%) samples were positive by ICT and 18 (4.6%) by FTS. In the Matara district, 9 (1.9%) samples were positive by ICT and 25 (5.4%) by FTS. There were no samples that were positive by ICT and negative by FTS.

5.3.7 Malawi: survey to determine whether to stop MDA

Professor Moses Bockarie presented results from a field study in Malawi where ICTs and FTSs were compared in two EUs implementing a school-based TAS. In the first EU, 10 people (0.6%) were positive by ICT and 3 (0.18%) by FTS. Of these, 3 people were positive by FTS but negative by ICT; and 10 people were positive by ICT but negative by FTS. There were also 162 people with invalid results by FTS. In the second EU, 1 person (0.06%) was positive by ICT; 0 were positive by FTS; and 163 people had invalid results by FTS. Most invalid tests occurred in samples from the first schools visited, and increasing the volume of blood collected from 75 µl to 100 µl decreased the number of invalid tests. Both EUs passed the TAS regardless of which diagnostic test results were used. If invalid results were not included in the analysis, the agreement between the two tests would be 99%. It was hypothesized that the whole blood was drying on the application pad before all the blood could be deposited. The Malawi team recommended providing a chase buffer with the test, attaching the test strip to the plastic tray during manufacturing to improve handling, or redesigning the tests to have a similar appearance to the ICT.

5.3.8 Nigeria: post-MDA surveillance

Dr Gregory Noland presented results from the field study in Nigeria, which was done in connection with a study comparing the results of a TAS and a 20-cluster all-ages household survey. Both tests were performed on 5900 people aged 3 years to 95 years. Eleven (0.19%) people were positive by ICT and 10 (0.17%) by FTS. Four people were positive by ICT but negative by FTS; and three people were positive by FTS and negative by ICT. Microfilaraemia was not found in any of the 14 people who were positive by either test. All five EUs passed the post-MDA surveillance survey using results from either test (ICT, 0–0.66%; FTS, 0–0.52%). There were no differences in the conclusions drawn from either the school-based survey or the population-based survey.

In terms of operational issues, the team did not have problems with the micropipettes. However, adding blood too quickly to the FTS inhibited the lateral flow, so blood needed to be added drop by drop. Using barcode labels to attach the strips to the plastic tray helped reduce the risk of losing the FTS.

5.3.9 Haiti: survey to determine eligibility for a TAS

Dr Lammie presented results from the study in Haiti, conducted as part of pre-TAS assessments of sentinel sites and spot-check sites in the Nippes département, an area with a low prevalence as determined by ICT. Blood was collected from 505 people older than 2 years. Of these, 1 (0.2%) was positive by ICT and 14 (2.77%) by FTS. Thirteen people were positive by FTS but negative by ICT. The FTS result would indicate that the programme should continue MDA, since it is above the antigenaemia cut-off for being eligible for a TAS. However, all antigen-positive results were negative for microfilariae, so the programme has not decided what to do.

The Haiti team appreciated not having to use cold storage for the FTS and appreciated the increased sensitivity of the test. However, they expressed concern about the difficulties in labelling the tests and the lack of a place to write the time and results.

5.3.10 United Republic of Tanzania: mapping and post-MDA surveillance

Dr Mwingira presented results from studies done in the Rorya and Bukombe districts, where mapping in 2004 found antigenaemia rates of 13.5% and 14.7%, respectively. No MDA has taken place, but the malaria programme has distributed bednets and scaled-up IRS in these areas. Blood was collected from 402 people in 1 village in the Rorya district and 436 people in 1 village in the Bukombe district; testing was done onsite. In the Rorya district, 38 people (9.5%) were positive by ICT and FTS (100% agreement); in the Bukombe district no positive cases were found by either test (100% agreement).

A field study was also done in coordination with a TAS for post-MDA surveillance in the Tandahimba district. In 2002, this district had a 6.8% baseline prevalence of microfilaraemia; in 2009, it passed a community-based TAS using ICTs (0.6% positive), and in 2011 it passed another TAS using ICTs (0.56% positive). In 2014, 300 µl of blood per person was collected in EDTA tubes in the community, but testing (by ICT, FTS and filter-paper blood spots) was done at the district's central laboratory. Of the 1629 samples, 4 (0.2%) were positive by ICT and 62 (3.8%) by FTS. Thus, if the FTS were used to make a programmatic decision, the EU would have failed the TAS.

The programme reported that there were challenges in collecting enough blood using a finger-prick, as well as logistical issues with the light weight of the tests and the lack of space on the test strip to record timing and results. The team recommended that the manufacturer should improve the weight, format and housing of the test. They also recommended that a training guide should be developed and information added to the 2011 TAS manual⁹ about how to interpret results, especially if differences occur when using the ICT and the FTS.

5.3.11 India: survey to determine whether to stop MDA

Dr Krishnamoorthy presented information on the methods that will be used for field studies in India, which were scheduled to take place by the end of October 2014. The ICT and the FTS will be compared in one district that is eligible for a TAS and that has had eight rounds of MDA. Samples will be collected from schools selected using Survey Sample Builder (NTD Support Center, Task Force for Global Health, Decatur, GA, United States). For comparison, a survey will also be conducted in a district that is not eligible for a TAS, but that has completed 7 rounds of MDA and found an antigenaemia prevalence of 9–20% in children aged 2–4 years.

5.3.12 Discussion: survey results

For the post-MDA surveillance comparison in the United Republic of Tanzania, it was noted that, given the experiences in Sri Lanka, the results might have been skewed by the use of EDTA tubes, which could have increased the number of false positives identified by the FTS.

The group discussed methods that may make it easier to collect blood samples in countries that have yet to use the FTS. The importance of having well-trained technicians collect the blood samples and using good lancets was emphasized. The group recommended that a short training video about using the FTS should be made available to researchers and country programmes. Group members also noted that malaria programmes often have good checklists for supervising or observing people implementing rapid diagnostic tests, and these could be adapted for training materials for the FTS.¹⁰

5.4 Discussion: performance of the FTS and operational characteristics

Dr King summarized the overall diagnostic characteristics shown in *Table 3*. The detailed results from each comparison study in 15 field sites are presented in *Annex 5, Table A5.1*.

Equivalent diagnostic characteristics were found in the controlled settings of the laboratory studies, but during serial dilutions the FTS detected 2 to 4 times lower levels of antigen than ICT.¹¹ In programmatic settings there were more FTS-positive cases than ICT-positive cases in 10 of the 15 separate surveys, which is consistent with the increased sensitivity of the FTS found in the laboratory investigation. For studies done before MDA, the ratio of FTS-positive cases to ICT-positive cases was 1.14. For studies done after MDA – that is, in areas before a TAS, in those conducted as part of a TAS, or for post-MDA surveillance – the ratio was 1.25.

Overall there was nearly perfect agreement on negative cases, indicating no loss in diagnostic capabilities compared to the ICT. There was variable agreement on positive cases, particularly in settings of very low endemicity – that is, those with a less than 2% prevalence of antigenaemia. In post-MDA settings, when using the ICT as the gold standard, the FTS had 72.2% sensitivity and 47.2% agreement on positive cases. These measures are limited because the recorded ICT result is assumed correct and by the few positive cases observed. As mentioned, there were still more persons FTS-positive (158/14,797) than ICT-positive (126/14,797) in these post-MDA settings. Yet in three of the 10 post-MDA sites, more ICT-positive than FTS positive results was observed. Of the discordant results from persons ICT positive but FTS negative almost half

⁹ *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>, accessed 28 August 2014).

¹⁰ Supervisory checklist for performing malaria RDTs. In: *Malaria rapid diagnostic tests: an implementation guide*. Geneva, Foundation for Innovative New Diagnostics (FIND), 2013:67–77 (also available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/243817/malaria_rdt_implementation_guide2013.pdf).

¹¹ Weil GJ et al. Laboratory and field evaluation of a new rapid test for detecting *Wuchereria bancrofti* antigen in human blood. *American Journal of Tropical Medicine and Hygiene*, 2013, 89:11–15.

(16/35) were reported from a single survey site. In another of these three sites it was noted that many FTSs had invalid results in the first clusters surveyed. However, this did not carry over to other clusters, perhaps indicating that there had been an improvement in learning how to operate the FTS. Feedback from the researchers indicated that such operational difficulties could be attributed to the design of the test strip.

Finally, Dr King reiterated that WHO needed the group to decide (i) whether to recommend the FTS for programmatic use, (ii) including the FTS in WHO's internal procurement catalogue of approved devices, and (iii) how to respond to the observed higher sensitivity of the FTS, remembering that if the aim is to interrupt transmission, then a more sensitive test that could detect continuing transmission would be conceptually more valuable but operationally more challenging.

Table 3. Measure of the diagnostic accuracy of the Alere Filariasis Test Strip (FTS), assuming the BinaxNOW Filariasis immunochromatographic test (ICT) as the gold standard^a

Measure of diagnostic accuracy	Overall estimate ^{b, c}	Pre-MDA settings ^b	Post-MDA settings ^{b, d}
Sensitivity	93.1 (90.9–95.2)	99.7 (99.2–100)	72.2 (64.4–80.0)
Specificity	99.3 (99.2–99.5)	97.2 (96.5–98.0)	99.5 (99.4–99.7)
Agreement between the FTS and ICT	99.1	97.6	99.3
Agreement on positive cases	76.9	87.5	47.2
Agreement on negative cases	99.1	97.2	99.3
Ratio FTS positive / ICT positive	1.14 (592:519)	1.14 (448/394)	1.25 (158/126)

MDA, mass drug administration.

^a Both tests are manufactured by Alere, Scarborough, ME, United States.

^b Values are % (95% confidence interval) unless otherwise noted.

^c These estimates exclude data from the Tandahimba district, United Republic of Tanzania where samples were collected in EDTA (ethylenediaminetetraacetic acid) tubes

^d The information on post-MDA settings include data from Indonesia collected after the second round of MDA that were not presented in the meeting but are reported in *Annex 5*.

5.4.1 The FTS: conclusions and recommendations

The group agreed that they were satisfied that the FTS was as good as the ICT in terms of diagnostic characteristics. The group noted that the FTS has a longer shelf -life, better temperature stability and costs less, according to the manufacturer. The group agreed that any increased sensitivity of the FTS above that of the ICT is acceptable to the GPELF, and guidance on implementing a TAS and critical cut-off numbers would not be changed. It was also noted that, just as with the ICT, using the FTS in pre-TAS sentinel sites and spot-check sites (where adults are evaluated) might cause confusion because of the persistence of antigenaemia in adults, which would not necessarily represent an increased risk of transmission. Nighttime blood samples for microfilariae could be taken from all positive cases during pre-TAS assessments of sentinel sites and spot-check sites.

However, the group expressed concern about whether the FTS could be used easily in the field in its current form based on the inconsistency of results in areas where training was not supervised and on concerns expressed about the operation of the test by technicians collecting samples. All presenters noted the challenges of learning to collect blood with the plastic tubes and the proper technique for applying the blood to the sample pad. It was felt that the challenges of blood collection and application could be overcome with enhanced training in appropriate techniques that had been identified through these first field experiences. The critical challenges of using the test in the field were the “flight-risk” of the strip being blown away given its

current light weight, and the inability of labelling the FTS with a unique identifier. To overcome these operational challenges, it was recommended that WHO should ask the manufacturer to make simple improvements in the housing and format of the FTS that would not increase the size of the test packets or the cost. These improvements should be made before the test moves into production in consultation with people who have field-tested the FTS. The recommendations for the housing and format of the test were simply to enclose the test strip within a protective plastic cassette to add more weight, to devise a means of protecting the deposited blood, and to provide a large enough surface for labelling.

The group agreed that it would be beneficial to implement a transition period lasting at least until the end of 2015 to allow for the continued use of the ICT during the adoption of the FTS. This would provide time for the manufacturer to improve the design of the FTS, and allow training materials to be prepared and training to be conducted (perhaps in concert with regional TAS training sessions), and for a centralized process for procurement to be established.

In the meantime, country programmes could use either test. However, it was recommended that where possible programmes should use the FTS when conducting a TAS to decide whether to stop MDA so that the series of TAS surveys that define the surveillance strategy would be done using the same diagnostic tool. Additionally, there might be some instances in which an EU using the ICT passes the TAS used to decide whether to stop MDA or for post-MDA surveillance, but then fails the next TAS when the FTS is used. In these cases, programmes should follow the guidance in WHO's 2011 TAS manual and ask the RPRG for advice.¹²

Distributing the information to country programmes is the critical next step, and this should be done at meetings of programme managers, RPRGs, the Global Alliance to Eliminate Lymphatic Filariasis (GAELF), and through WHO's regional offices.

6. Improving the efficiency of implementing and interpreting the TAS

6.1 TAS Eligibility and Reporting

Dr Aya Yajima presented information on the forms currently used to assess TAS eligibility and the proposed new eligibility and reporting forms, as well as information on the processes involved in submitting and reviewing the forms. The previous TAS Eligibility and Reporting Form was used for only one EU at a time.¹³ Countries download the form as an Excel file and complete the tabs asking for information about eligibility and survey design with information about the progress of MDA and the results of surveys of sentinel or spot-check sites in the IUs included in a given EU; the form is then submitted to the RPRG, which decides whether to endorse eligibility. After the TAS has been completed, national programmes complete the form's results tab with information about the results of the TAS; the completed form is then submitted to the RPRG for endorsement. There has been inconsistent uptake in the use of this recommended process by countries, and it is not being used in all regions.

WHO also has a Preventive Chemotherapy (PC) Epidemiological Data Reporting Form and this should be submitted as part of the Joint Application Package for drug donations, which includes the Joint Request for Selected PC Medicines, the Joint Reporting Form, the Annual Work Plan and the PC Epidemiological Data Reporting Form.¹⁴ The original PC Epidemiological Data Reporting Form asks for information about the results of mapping and surveys at sentinel or spot-check sites, or both, and about morbidity, but not about TAS results.

¹² *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>, accessed 28 August 2014).

¹³ *TAS eligibility and reporting form*. Geneva, World Health Organization, 2013 (http://www.who.int/lymphatic_filariasis/resources/WHO_TAS_Eligibility_and_Reporting_Form.xlsx, accessed 09 January 2014).

¹⁴ All of the forms for the Joint Application Package can be found at http://www.who.int/neglected_diseases/preventive_chemotherapy/reporting/en/.

The previous TAS form was difficult to review if many EUs are planning to implement a TAS since multiple files were needed. The proposed new form includes information about all EUs in a country; these would be listed by geographical proximity. Each EU would provide information on its population and MDA coverage, results from testing at the sentinel site, and the design of the TAS. This information would be automatically summarized on an overview tab that reviewers could easily consult. The proposed form uses the same format as the data summary templates for the LF dossier, and once the form is finalized it would be useful to add it to the list of standard reports automatically generated by the integrated NTD database¹⁵. It has also been proposed that the TAS results should be added to the epidemiological data form so that WHO can accurately re-estimate the population requiring MDA and can determine whether IUs that have stopped MDA are truly no longer at risk or have just discontinued MDA.

The new review process proposes that national programmes be asked to submit their TAS eligibility form after the fifth round of MDA and as soon as sentinel-site and spot-check surveys have been completed (that is, preferably 4–5 months before the TAS may be implemented). The eligibility form would then be virtually reviewed by RPRGs or a global LF group, and feedback would be given to national programmes within 1 month. The TAS results would be included as part of the Joint Application Package, that is submitted annually by 15 August to WHO's headquarters. Results will be shared with a global LF group and WHO's Regional Offices so that RPRGs can also review them.

6.1.1 Discussion: TAS form

Representatives from some country programmes expressed the opinion that TAS Eligibility and Reporting Forms were unnecessary and that only results from the TAS should be reported, especially if endorsement by the RPRG would take several months. However, the group agreed that, particularly when diagnostic tests are donated, an independent review is necessary before the donated tests are distributed to countries. The group noted that if diagnostics are to be donated for post-MDA surveillance, the same mechanism of submitting requests or projections of need should also be applied. The group agreed that knowledge of TAS criteria and the context in a country were the most important characteristics for independent reviewers, as well as the ability to quickly review and send recommendations to countries.

6.2 Interpreting the results of a TAS

Dr Michael Deming presented a variety of scenarios to illustrate how to accurately interpret the results of a TAS. The question and answer format of the scenarios is summarized below.

- Question: Can the TAS be used to calculate the prevalence of antigenaemia or antibody positivity?
 - Answer: Yes it can because the TAS uses an equal probability sample of children aged 6–7 years or in first and second grades. The calculation is the number of positive children divided by the total number of children sampled. Confidence limits could be calculated around the point prevalence, but software would be needed to do this correctly.
- Question: The TAS identified more positive cases than the critical cut-off value. But the calculation of the prevalence of antigenaemia in the TAS was 1.3% (22/1692), which is less than 2%, so why did we fail?
 - Answer: The target probably was met, but there were too many positive children to be 95% certain that it had been met; therefore, the TAS was failed.

In this example, there is more than a 5% chance that as few as 22 antigenaemia-positive children would be found by chance. Therefore, if the decision were made to stop MDA, there is more than a 5% chance that it would be the wrong decision. To pass the TAS, the chance of making this wrong decision must be 5% or lower.

- Question: An EU passed the first TAS (TAS1) and the second TAS (TAS2), but the prevalence increased from 0.6% to 1.1%. Should we be worried about recrudescence?
 - Answer: Even if the prevalence remains the same between TAS1 and TAS2, point estimates are expected to be different by chance. The sample sizes in the TAS are too

¹⁵ Integrated NTD database. Geneva, World Health Organization, 2015 (http://www.who.int/neglected_diseases/data/ntddatabase/en/, accessed 19 March 2015).

small to have enough power to show whether this is a significant difference. It could be useful to use data from continuing surveillance to see whether this trend is confirmed or to explore whether the positive results have come from the same part of an EU in both years.

- Question: An EU passed TAS1 with a prevalence of 1.2% and failed TAS2 with a prevalence of 1.4%. What should be done?
 - Answer: In this scenario, the issue is not the small difference in prevalence between TAS1 and TAS2. The issue is that both are very close to the cut-off value and in a range where there is a substantial risk of failing the TAS. Yet, the TAS is a decision-making tool and whenever there are more antigen-positive cases than the critical cut-off, two additional rounds of MDA are warranted. To have a high chance of passing the repeat TAS, the additional rounds of MDA need to have very good coverage.
- Question: Three of 13 positive children in our last TAS were from the same school, and 7 were from the same subdistrict. What should be done about this potential hot spot?
 - Answer: Since the survey design is not based on a probability proportional to size, the prevalence rates in schools or subdistricts should be compared not the number of cases. However, whether an EU passes the TAS depends on the average prevalence, so there is nothing inconsistent about there being clusters that have a prevalence above the threshold. Our assumption is that if the average prevalence is low enough, transmission will cease in areas that have a prevalence above the threshold. Although there may be areas with continued transmission, there is no consensus about whether these areas should be investigated, how they should be investigated, and whether MDA should be used in these areas.
- Question: Could a programme skip TAS2 and redirect these resources towards other efforts?
 - Answer: Currently the validation of elimination requires three TASs to be passed. The main purpose of TAS2 is to rule out a recrudescence of transmission. If future experience shows that recrudescence is rare, the GPELF may consider making TAS2 optional if a national programme has implemented continuing surveillance.

Dr Deming also summarized the role of the TAS in the post-MDA scenario. The TAS is useful for validating the elimination of LF as a public-health problem and it is sufficient if all parts of a country have either (i) been determined to be non-endemic or (ii) passed TAS 1, 2 and 3, thus showing that transmission has been kept low for 5 years to 6 years. If the validation process moves towards verifying the interruption of transmission, the TAS is still useful for providing evidence since finding no antigenaemic-positive or antibody-positive children in the third TAS adds considerable weight to the conclusion that transmission has been stopped in formerly endemic areas. But the TAS results alone are unlikely to be sufficient because low-level transmission could be continuing in areas defined as non-endemic. Furthermore, when the cluster sample design is used, a TAS might miss areas in large EUs where transmission is continuing. Finally, even if no positive children are found by the survey, the upper 95% confidence interval is above 0%. If the process becomes more stringent and moves to verify the elimination of transmission, the role of the TAS becomes more marginal because it does not assess whether there are reservoirs of infection among adults. Adding adults to TAS2 and TAS3 could provide important data, but more useful data would come from continuing surveillance of adults to show that prevalence has dropped to 0 and stayed there for years.

6.2.1 Discussion: interpreting results of the TAS

In order to address the proposed WHO standardized processes of elimination, the group discussed the fact that verifying interruption of transmission might require showing evidence of no infection in vectors. Even if the GPELF will be classified under validating elimination as a public-health problem, the group agreed that the research community should work to provide evidence for interruption of transmission. Critical areas that should be addressed by research include (i) using risk assessments to determine what evidence is needed; (ii) ascertaining the implications of hot spots and the movement of people in border areas; (iii) determining how to operationalize xenomonitoring and document the relationship between the results of xenomonitoring and serological results in children; and (iv) assessing the effect of albendazole given through STH programmes on LF in children. Also emphasized by participants were the importance of tracking TAS results to determine the percentage of those surveys that are passed or failed, and the importance of tracking trends in results among TAS1, TAS2 and TAS3 at the global level.

6.3 Comprehensive surveillance in Sri Lanka

Dr Weil presented detailed results from operational research in Sri Lanka assessing post-MDA surveillance¹⁶. In Sri Lanka, LF is caused by *W. bancrofti* transmitted by *Culex* mosquitoes; 10 000 000 people were originally considered to be at risk in 8 districts. Initially, Sri Lanka's national programme employed a test-and-treat strategy but switched to MDA using diethylcarbamazine (DEC) alone from 1999 to 2001; from 2002 to 2006, the programme used DEC plus albendazole. MDA was delivered using directly observed treatment. Coverage averaged 68% with DEC alone and more than 80% with DEC plus albendazole; however, independent assessments of coverage found that some districts had lower coverage. Some districts, such as Galle, had higher infection rates along the coast, with lower prevalence in inland areas at higher elevations. TASs were implemented in 2012 and 2013 in 11 EUs, and all passed with a range of 0–7 positive cases (critical cut-off value, 18). Given the non-uniform risk in the Galle district, it was divided into 2 EUs, and Galle 1 had 7 positive cases.

Comprehensive surveillance was implemented in 8 districts during 2011–2013. The results suggested that provisional end-point criteria should be tailored specifically to areas where *Culex* was present. These criteria included a community antigenaemia rate of less than 2%, an antibody rate in children of less than 2% as measured by the presence of antibody to Bm14, and a filarial DNA rate in mosquitoes of less than 0.25%. To collect community data, surveys were done in at least 2 sentinel sites in each EU, taking 500 ICT and blood-film samples from randomly selected households in an area of 15 000–30 000 people. To assess antibodies in children, school surveys were done, taking 350 samples at each site from children aged 6–8 years. To collect data on vectors, quantitative real-time PCR testing was done on 200 pools of 20 blood-fed or gravid mosquitoes collected at each sentinel site.

Using the antigenaemia criteria, only one area failed, but others had confidence intervals that included the provisional end-point criteria. The study found that testing for antibodies and testing mosquitoes were superior to using a TAS to detect residual LF or a resurgence of infection since 1.5% of mosquitoes tested were infected with some stage of larvae. However, rates of antibody presence and mosquito infectivity were similar, and occurred in areas where the TAS had detected positive children.

The national programme was unclear about how to respond to these results. MDA could have been restarted, but microfilaraemia rates were less than 1% (the criteria for starting). In high-risk areas, everyone could be tested and those who were positive could be treated to try to cover systematic noncompliance. The programme considered promoting bednet use, which had a protective effect but was not significant in multivariate analysis, but this was considered difficult to implement at scale. The programme decided to engage in watchful waiting, and saw decreases in rates of antigenaemia and infections in mosquitoes between 2008 and 2011. In 2014, the survey was repeated in the 6 areas with the highest prevalence; it will be repeated again in 2015. However, the Galle district has decided to implement MDA at the subdistrict level along the coast, so follow-up data will not be collected there. Surveillance also is planned in non-endemic areas bordering endemic areas.

7. Processes of validation, verification and certification of elimination

7.1 Background

Dr King presented information about the current processes for validation, verification and certification of elimination for NTDs. The 2014 the Strategic and Technical Advisory Group for Neglected Tropical Diseases (NTD-STAG) recommended that WHO should establish principles and processes for validation, verification and certification of elimination, and standard operating procedures will be submitted to the NTD-STAG in 2015 for endorsement. WHO has decided that those diseases targeted for elimination as a public-health problem, such

¹⁶ Rao RU et al. A comprehensive assessment of lymphatic filariasis in Sri Lanka six years after cessation of mass drug administration. *PLoS Negl Trop Dis*, 2014, 8(11):e3281.

as LF and blinding trachoma, will need to provide evidence of transmission levels and morbidity through a validation process. Those diseases that have been targeted for elimination, such as onchocerciasis in the Region of the Americas, will need to provide evidence of the interruption of transmission through a verification process, which may include an external evaluation by an independent team. WHO will use the disease-specific targets in the NTD roadmap, which for LF is a prevalence of infection that is lower than the target threshold in all endemic areas.¹⁷ The proposed indicator is prevalence as defined for the various species and vector complexes in the 2011 TAS manual. Thus, to validate the elimination of LF as a public-health problem, a national programme must show a sustained prevalence below the relevant thresholds along with a defined level of case-detection, as well as making available the recommended basic package of care for managing morbidity.

7.1.1 Discussion: background

The group asked whether there was a process for diseases to move from one category to another – for example, from validation to verification. Dr Engels clarified that the standard operating procedures, which need to be endorsed by WHO’s legal department, will match the 2020 targets. A disease could be moved from one category to another if sufficient evidence was produced by the successes of a national programme and by research results. As the GPELF gets closer to 2020, the next target for LF then could be set depending on evidence about the interruption of transmission. Countries could submit an addendum to their dossiers that includes new evidence that would move them from the category of validation of elimination of LF as public-health problem to the category of verification of elimination (that is, the interruption of transmission).

The group voiced concern that this could cause confusion at the country level, since national programmes and donors have understood since the inception of the GPELF that interruption of transmission is the goal. Any change would have specific implications if further evidence needed to be collected years after national programmes thought that validation signalled the end of their programmes. Dr Engels responded that if a complete dossier exists that contains data from sustained surveillance, the necessary steps to move towards verification could be followed.

7.2 Elimination criteria: morbidity

Dr LeAnne Fox summarized recommendations from a recent consultation on MMDP for LF. World Health Assembly resolution 50.29, adopted in 1997, included the goal of reducing human suffering caused by LF clinical disease.¹⁸ Based on this, WHO has presented the aims of the MMDP component of the GPELF as (i) ensuring full geographical coverage of MMDP in all areas where LF is endemic, (ii) ensuring access to basic recommended care for all people with lymphoedema and hydrocele in areas where LF is endemic, (iii) reducing the frequency and intensity of episodes of adenolymphangitis (ADL), and (iv) reducing the number of new cases of LF to background levels. The minimum package of care for MMDP for LF includes treating episodes of ADL; preventing episodes of ADL and the progression of lymphoedema; providing access to surgery for hydrocele; and providing antifilarial medicines to destroy any remaining worms and microfilariae, either by MDA or through individual treatment.

The consultation debated what type of data on MMDP should be required for the dossier, while keeping in mind what would be acceptable to – and feasible for – WHO’s Member States. The meeting recommended that the geographical scope of requirements for such data should be areas where LF is endemic, and the requirements should focus on the availability of services from the programme’s perspective. Focusing on the availability of services – instead of on access to services, which involves collecting data from a patient’s perspective – is congruent with the goals of WHO’s NTD roadmap, is feasible for country programmes, and does not require the annual reporting of data that will not be used for validation. Based on research that looked at how reducing the incidence of ADL and implementing hydrocelectomies improve patients’ quality of life, the requirements assume that providing MMDP services will decrease morbidity and this will in turn

¹⁷ *Sustaining the drive to overcome the global impact of neglected tropical diseases: second WHO report on neglected tropical diseases*. Geneva, World Health Organization, 2013 (WHO/HTM/NTD2013.1) (also available at http://www.who.int/neglected_diseases/9789241564540/en/).

¹⁸ *Resolution WHA 50.29: Elimination of lymphatic filariasis as a public health problem*. Geneva, World Health Organization, 1997 (also available at http://www.who.int/neglected_diseases/mediacentre/WHA_50.29_Eng.pdf).

reduce and prevent disability. However, in order to assess whether services are being used and the quality of these services, it was proposed that 10% of targeted health facilities be directly inspected.

One indicator proposed to be included in the dossier is the number of lymphoedema patients and hydrocele patients by IU. These data can be collected anytime during the programme, and a menu of options for assessing the burden (such as population-based surveys, monitoring and evaluation activities, MDA population registration, a listing of cases) will be available to national programmes as part of the MMDP toolkit for LF, which is being prepared. The dossier should also include the number of facilities providing care for lymphoedema or hydrocele, by IU (with a minimum of one per each IU with a known burden of clinical cases). These data should be collected using a questionnaire that is completed by health facilities within an IU within 2 years of submitting the dossier, but programmes may also collect these data earlier in order to monitor progress. The dossier should also include the number of facilities that have been surveyed to assess the quality of care for patients with lymphoedema and hydrocele (to include a minimum of 10% of facilities in areas with a known burden). This survey should be completed within 2 years of the dossier being submitted; a tool to be used for direct inspection will be finalized and pilot-tested in 2015. The findings of the direct inspections will be used to validate the questionnaire data, but no measure of the level of quality has been proposed as a criteria.

7.2.1 Discussion: morbidity

The group discussed the differences in measuring the availability of services, access to services and their utilization, and clarified that assessing availability was the most feasible option for national programmes to implement; however, countries should be encouraged to assess access if it is feasible to do so. In particular, national LF programmes should try to coordinate with other health surveys – such as WHO’s Model Disability Survey¹⁹ or WHO’s Service Availability and Readiness Assessment tool²⁰ – which can measure availability or access, or both. Participants recommended that these proposed indicators should be presented at upcoming meetings of programme managers and the GAELF to obtain additional input from countries.

7.3 Elimination criteria: transmission

Dr Ottesen presented a framework for elimination criteria and encouraged the meeting to remember that the GPELF can still focus on interrupting transmission even though the aim will be referred to as validating elimination as a public-health problem in the new harmonized process for NTDs.

The definition of elimination is the reduction to 0 of the incidence of infection in a defined geographical area, while the definition of eradication is the reduction to 0 of the incidence of infection in all geographical areas. The essential elements that make an infection eradicable are not necessarily biological, but are, first, the tools that are used – that is, effective interventions to eliminate the infection – and, second, the availability of effective diagnostics to ensure that the infection has been eliminated and will not return.

In the past, LF has been eliminated through various strategies, including doing nothing (secular decline due to improved economic and living standards), implementing vector-control measures (Solomon Islands), or delivering selective treatment (Japan) or mass treatment (China). Success has been confirmed through long-term follow up of prevalence in human populations. However, the GPELF needs better and faster options for collecting evidence of elimination, including effective diagnostic tools and sampling approaches. Graphs were presented from two areas in Brazil, with data from the 1960s through the 1990s. The graphs showed that the prevalence of LF did not fall immediately after the introduction of selective treatment or MDA but fell slowly after every round, and no new infections were found after 3–5 years.

Experimental studies in 21 villages in China carried out interventions (including administering DEC, and providing DEC-fortified salt and bednets) that lowered the prevalence of microfilaraemia, and were stopped at different levels of prevalence before surveillance was implemented. These studies found that when the prevalence of microfilaraemia was reduced to less than 1.7% in areas where *W. bancrofti* was present, and to

¹⁹ The Model Disability Survey is available at <http://www.who.int/disabilities/data/mds/en/>.

²⁰ The Service Availability and Readiness Assessment tool is available at http://www.who.int/healthinfo/systems/sara_introduction/en/.

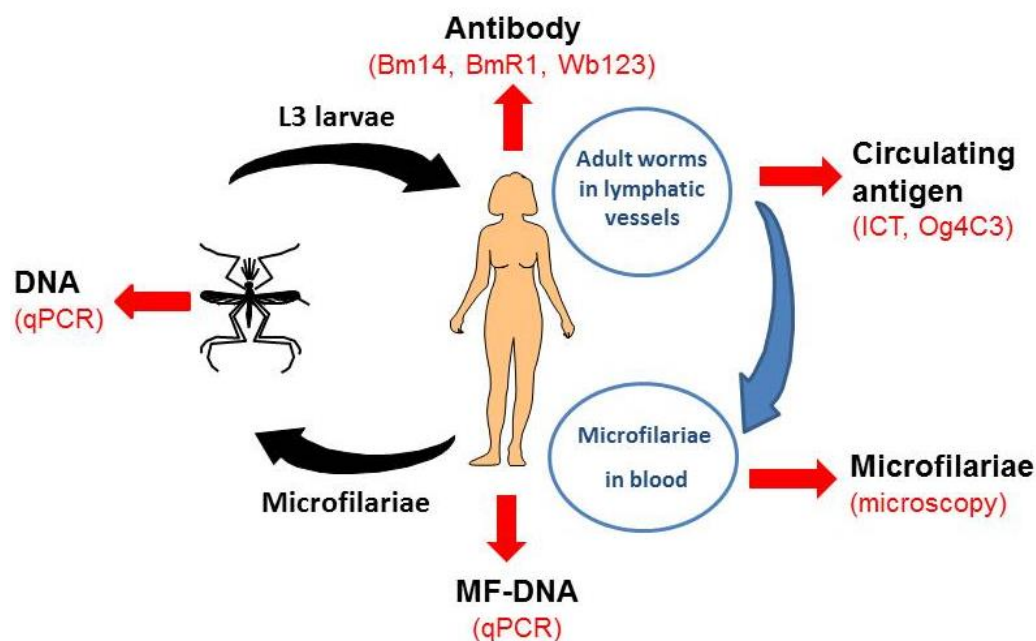
less than 1.5% in areas where *Brugia* spp. were present, there was no resurgence and microfilaraemia was gone 9 years after interventions were stopped. This basic strategy of elimination – stopping MDA when the prevalence of microfilaraemia is less than 1% – was then used throughout all of the endemic provinces in China. In the post-MDA phase (that is, after basic elimination had been achieved as measured by a prevalence of microfilaraemia of less than 1%), microfilaraemia rates were seen to fall progressively to 0% in approximately 7 years, as determined by random sampling of sites in endemic provinces.

In order to measure the incidence of infection (to achieve elimination), three things must be defined. First, the population must be defined: samples from young children give the fastest, clearest answer since they start at 0 incidence. Second, the sampling strategy must be defined: the TAS is statistically robust, but it is not known for certain whether the thresholds are low enough. Third, the tool must be defined in terms of sensitivity: the ICT is better than blood films, but an antibody tool is needed to measure exposure or the potential for infection.

The GPELF’s current strategy is based on the Chinese model and the threshold of less than 1% microfilaraemia. Sentinel-site and spot-check assessments prior to a TAS look at the prevalence of LF in the entire population after MDA. To be eligible to implement a TAS, results from these sites must be less than 1% microfilaraemia or less than 2% antigenaemia. The strategy then adds the TAS, which is a measure of incidence. Finally, the strategy relies on surveillance (by repeating the TAS or using other tools) to prove the correctness of the approach and to identify whether the target parameters and tools need to be modified.

The GPELF’s strategic plan has the goal of interrupting LF transmission, which is a critical step in the process of elimination.²¹ However, transmission is not seen directly. Instead, evidence of transmission is seen: by measuring antibodies, circulating antigen or microfilariae in humans; or by measuring DNA in humans or vectors (Figure 2). Currently, the programme does not have evidence as to which of these markers of transmission in vectors or humans is most effective.

Figure 2. Targets of potential tools to assess transmission



²¹ Progress report 2000-2009 and strategic plan 2010-2020 of the global programme to eliminate lymphatic filariasis: halfway towards eliminating lymphatic filariasis. Geneva, World Health Organization, 2010 (WHO/HTM/NTD/PCT/2010.6) (also available at http://www.searo.who.int/entity/vector_borne_tropical_diseases/topics/lymphatic_filariasis/LFREP.pdf).

7.3.1 Discussion: transmission

The group agreed that including adults in post-MDA surveillance methods might be as important as the current focus on children. In terms of vector monitoring, the group emphasized that it is not necessary to eliminate all infections in either humans or mosquitoes in order to interrupt transmission, since even finding third-stage larvae (L3) in a mosquito does not mean that it will be transmitted to a human, reproduce and produce microfilariae.

7.4 Developing a template for the dossier used to document elimination

Ms Brady presented the draft template for a dossier that may be used to document the elimination of LF. The template is a reference to help national programmes summarize the minimum information needed in a dossier that documents elimination of LF as a public-health problem and that can be submitted to WHO for validation. The template will standardize the presentation of information to ensure that the required information is provided at the beginning of the process, thus making it easier to review the dossiers and to reduce the need for clarifications. The template is based on previous WHO guidance, including chapter 9 of the 2011 WHO TAS manual. The draft template was pilot-tested in Bangladesh and the Philippines, and then modified. The current proposed template results from this experience, as well as from further harmonization with the data summary tables from the WHO TAS Eligibility and Planning Form, the WHO Joint Reporting Form and the PC Epidemiological Data Reporting Form.²²

The template consists of two parts: a narrative section providing an overall description of the programme and an annex in a Microsoft Excel file that is used to present supporting data. The information to be included in the narrative sections and the supporting data are described briefly in *Table 4*. Countries are requested to provide data from each IU.

The next steps in assessing the draft were to collect comments from meeting participants, with the aim of finalizing the template so that it can be submitted to the NTD-STAG Working Group on Monitoring and Evaluation, and then to the NTD-STAG in April 2015 as part of the standard operating procedures for the process of assessing elimination.

7.4.1 Discussion: dossier template

The group agreed that the proposed template would be useful for giving national programmes an idea of which data it is necessary to collect and how their data should be organized, as well as for helping RPRGs know what information is important when reviewing a dossier. Making such a template available to programmes now – with the recommendation that they begin developing a preliminary version of their dossier – will help them begin to organize their data, reach out to lower levels of the health-care system to fill any gaps in the data, and uncover potential issues. However, the group raised concerns that national programmes need to understand what the reward will be for completing the dossier and how the dossier will be judged – that is, what criteria will be assessed to determine whether a country passes and elimination has been validated? Finally, countries will need technical and financial support to complete the dossier, and countries might need to rely on WHO for some data especially if there has been a high turnover of staff in their programme.

²² All of the forms for the Joint Application Package can be found at http://www.who.int/neglected_diseases/preventive_chemotherapy/reporting/en/.

Table 4. Outline of the proposed template for the lymphatic filariasis (LF) dossier to be used to document elimination^a

Section	Narrative	Data annex
1	General description of the context in the country and required overview of the LF programme)	Sheet 1. Population
2	Description of methods used to delineate endemicity of LF, and resulting maps.	Sheet 2. Mapping
3	Interventions used to stop the spread of infection (includes information about MDA and other interventions implemented)	Sheet 3. MDA
4	Epidemiological monitoring and evaluation of interventions (required sections include information on assessments of sentinel sites and spot-check sites, and surveys conducted to determine whether MDA should be stopped)	Sheet 4.1 M&E Sheet 4.2 TAS
5	Surveillance (includes cross-sectional surveys, including TAS2 and TAS3, and commitment to sustain surveillance activities post validation)	Sheet 5. TAS surveillance
6	Morbidity management and disability prevention (includes data on clinical cases and the availability of treatment)	Sheet 6. Morbidity
7	Special issues (will vary by country)	For narrative sections 7–10, no data are required to be provided in the annex
8	Resources and partnerships (optional description of human and financial resources utilised and any partners supporting the programme within the country)	
9	Bibliography	
10	Abbreviations	

MDA, mass drug administration; TAS, transmission-assessment survey.

^a Additional detail about each section can be found in the text.

It was recommended that a section on funding milestones and budgets should be added to the template because these have an impact on what kind of data are collected during the programme. It was suggested that feedback be requested from other national programmes so that the template can be finalized and presented at the meeting of the NTD-STAG Working Group on Monitoring and Evaluation in February 2015. Meeting participants also were asked to send specific recommendations for changes to the narrative form or the Excel tables to WHO.

8. Meeting conclusions and recommendations

8.1 Objective 1: strategies to delineate endemicity and determine when to initiate MDA

8.1.1 Lack of baseline data from sentinel sites

- The group recommended that a lack of baseline data from sentinel sites should not delay the start of MDA. Although the group acknowledged the usefulness of having baseline data on microfilaraemia to monitor the progress of MDA, it recommended that the baseline collection of data from sentinel sites should be optional in areas in which data on microfilaraemia or antigenaemia have been obtained from mapping surveys. Where time or resources are lacking to collect baseline data from sentinel sites, countries may substitute mapping data for baseline data on microfilaraemia or antigenaemia.

8.1.2 Uncertainties about endemicity

- In IUs originally classified as endemic based on mapping surveys but then found through baseline surveys at sentinel sites to have less than 1% microfilaraemia or antigenaemia, the group recommended that programmes should either start MDA or use a more statistically robust survey protocol to re-evaluate endemicity.
 - These IUs should not be reclassified as non-endemic based only on data from sentinel sites or on additional data from spot-check sites.
- In IUs where MDA has not started due to low endemicity (1–2%) found during mapping and where no baseline data from sentinel sites have yet been collected, the group recommended that programmes should either start MDA or use a more statistically robust survey protocol to re-evaluate endemicity.
- The group agreed that in unmapped areas, programmes should continue to follow the current mapping protocol – that is, guidance from WHO’s Regional Office for Africa or the 2011 TAS manual.^{23,24}
- The group acknowledged that there is a need to validate mapping protocols for large urban areas.

8.1.3 Loiasis areas

- Given that ICTs are known to be cross-reactive in patients with high loads of *Loa loa* microfilariae, the group strongly recommended the rapid development of other tools to measure LF in areas where loiasis is coendemic.
- In IUs where loiasis is coendemic with LF and that have been determined by ICT to have communities with 1% or higher LF microfilaraemia or antigenaemia, the group recommended that programmes proceed with twice annual albendazole MDA together with vector-control interventions while operational research is implemented to determine how best to measure LF in loiasis areas suspected to be coendemic with LF.
- In unmapped areas, operational research should include the collection of additional specimens for supplemental assays in addition to using ICTs.
 - A district-level list of potentially coendemic districts should be developed for each country where loiasis is endemic to identify any specific needs for additional specimens and laboratory processing.
- Although the GPELF does not have a specific target for the coverage of vector-control interventions in areas where loiasis is coendemic, the group encouraged LF programmes to work with malaria programmes to scale-up and report vector-control coverage and bednet use in these areas.

²³ *Operational guidelines for rapid mapping of bancroftian filariasis in Africa*. Geneva, World Health Organization, 2000 (WHO/CDS/CPE/CEE2000.9) (also available at http://whqlibdoc.who.int/hq/2000/WHO_CDS_CPE_CEE_2000.9.pdf).

²⁴ *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>, accessed 28 August 2014).

8.2 Objective 2: programmatic use of the new Alere Filariasis Test Strip

- The group endorsed the FTS for *W. bancrofti* antigen, subject to the concerns expressed below. The group recommended that the new test should be included in WHO's internal procurement catalogue of approved devices after concerns have been addressed by the manufacturer.
- The group strongly recommended documenting the operational challenges in performing the FTS in the field and including these challenges in a report to the manufacturer.
 - Major operational challenges include the flimsiness of the test strip, the need to secure the strip to something, and the lack of space to write the time and results.
- WHO should insist that the manufacturer:
 - without increasing costs should make structural changes to the FTS to overcome the issues identified as affecting the test's performance, and
 - allow end-users to vet design changes before the test moves to the production phase.
- The group recommended that the manufacturer should provide a quantitative measure of the test's sensitivity using a measured quantity of purified antigen with each lot of the FTS.
- The group recommended that the manufacturer should provide a positive control with each order so that countries can perform quality-control testing.
- The group recommended that the manufacturer should continue to produce the ICT until the end of 2015 in order to allow country programmes to train technicians in the use of the new test, establish a new centralized procurement process, and forecast their needs for the FTS. In the interim, countries can use either the ICT or FTS for surveys.
- The group urged WHO to quickly disseminate updated guidance and training materials on using the FTS during TAS trainings, at GAELF and RPRG meetings, and through other fora.
 - The group recognized the importance of training staff working in country programmes, as well as WHO's regional and country staff, and making RPRG members aware about the use of the FTS.
- The group recommended that WHO should coordinate with endemic countries and with organizations procuring diagnostic tests in order to forecast needs and ensure appropriate coverage for each country, especially during the transition from one test to the other.
 - WHO should update global forecasts for both the ICT and the FTS every 6 months and make this information publicly available.
 - WHO should work with the consortium of partners to coordinate the procurement and supply of diagnostic tests to countries in need.
- The group recommended using the same critical cut-offs for the TAS, regardless of whether the ICT or the FTS is used. The increased sensitivity of the FTS is acceptable given that the ultimate goal of the GPELF is to interrupt transmission.
- The group recommended that countries consult WHO when an EU has used the ICT and passed the TAS to determine whether to stop MDA but has failed the post-MDA surveillance TAS using the FTS.

8.3 Objective 3: documenting targets for the achievement of elimination

- The group noted the benefit of having the draft dossier template to document the achievement of LF elimination as a public-health problem, and recommended soliciting input from additional countries before it is finalized.

8.4 General recommendations

- The group urged that WHO should lead a meeting in 2015 to share methods for conducting operational research, and results from and opportunities related to post-MDA surveillance.
- The group recommended that after the FTS is finalized by the manufacturer, WHO should lead the development of new training materials for the new test and implement regional TAS training in 2015.

9. Closure of the meeting

Dr Lammie closed the meeting by making four key points.

1. Recent studies have found that ICTs have cross-reactivity in loiasis-endemic areas. This problem will continue with the new FTS because it is based on the same reagents as are used in the ICT.
2. The ICT and the FTS are similar in terms of technical performance, and the FTS can be recommended for programmatic use without making changes to current programmatic guidelines. However, the current design of the FTS poses problems for teams in the field, so WHO should compile specific comments and forward them to the manufacturer to allow for quick corrections.
3. Additional input is needed from countries before the dossier template for validating the elimination of LF as a public-health problem can be finalized.
4. In order to move the elimination process for LF towards verification of the interruption of transmission, the GPELF needs more insight into surveillance strategies. Therefore, the meeting recommended that WHO should hold a consultation to determine interim recommendations for countries, and this could be coordinated with recommendations for post-treatment surveillance of onchocerciasis.

Dr King reminded the group that the recommendations and algorithms will help programmes overcome the barriers to scaling-up MDA that are related to uncertainties in mapping, and will encourage countries to finish mapping. He appreciated the group's consensus on changing the diagnostic test. He asked the group to give further detailed feedback on the dossier template so that it can be finalized quickly.

Dr Engels reminded the group about the complexity of taking disease-specific challenges and putting them into a broad, integrated perspective. Additionally, the group is responsible for addressing these complexities and providing simple and consistent advice to countries to help them implement successful programmes.

Annex 1. List of participants

Participants

Professor Moses J Bockarie

Director, Centre for Neglected Tropical Diseases
Liverpool School of Tropical Medicine
Pembroke Place, Liverpool L3 5QA, England
E-mail: moses.bockarie@liv.ac.uk

Ms Molly Brady

NTD Technical Adviser, ENVISION, RTI International
701 13th St NW, Suite 750, Washington, DC 20005, USA
E-mail: mbrady@rti.org

Dr Jane Y Carter

Technical Director, Clinical and Diagnostics, AMREF Health Africa
PO Box 30125, 00100 GPO, Nairobi, KENYA
E-mail: jane.carter@amref.org

Dr Michael Deming

8420 Via Mallorca, Unit 205, Mailbox CBU 1, No. 11, La Jolla, CA 92037, USA
E-mail: demingms@yahoo.com

Dr Peter Fischer

Associate Professor, Division of Infectious Diseases, Washington University School of Medicine
Molecular Helminthology and DOLF Project, R 4182A,
4444 Forest Parkway, St Louis, MO 63110, USA
E-mail: Pufischer@dom.wustl.edu

Dr LeAnne Fox

Medical Doctor, Centers for Disease Control and Prevention,
Centers for Global Health
Division of Parasitic Diseases
1600 Clifton Road, MS A-06, Atlanta, GA 30333, USA
E-mail: lfox@cdc.gov;

Dr Leda Hernandez

Division Chief, Infectious Disease Office, National Center for Disease Prevention and Control
Philippines Department of Health
Manila, Philippines
E-mail: dr_ledamher@yahoo.com

Dr Louise Kelly-Hope

Project Manager, Centre for Neglected Tropical Diseases
Liverpool School of Tropical Medicine
Pembroke Place, Liverpool L3 5QA, England
E-mail: Louise.Kelly-Hope@lstm.ac.uk

Dr K Krishnamoorthy

Vector Control Research Centre, Indian Council of Medical Research
Indira Nagar, Pondicherry 605006, India
E-mail: drkgkmurthy@gmail.com

Dr Patrick Lammie

NTD Support Center, Task Force for Global Health
325 Swanton Way, Decatur, GA 30030, USA
E-mail: plammie@taskforce.org / pjl1@cdc.gov

Dr Colleen Lau

Senior Research Fellow, WHO Collaborating Centre for Children's Health and the Environment Queensland
Children's Medical Research Institute
University of Queensland
PO Box 2726, New Farm, QLD 4005, Australia
E-mail: colleen.lau@uq.edu.au

Dr Upendo Mwingira

Coordinator NTD,
Neglected Tropical Disease Control Programme
Ministry of Health and Social Welfare
PO BOX 9083 Dar es Salaam, United Republic of Tanzania
E-mail: umwingira@yahoo.com

Gregory S Noland, PhD

Epidemiologist, Health Programs, The Carter Center
453 Freedom Parkway, Atlanta, GA 30307, USA
E-mail: gnoland@emory.edu

Dr Eric Ottesen

Director, ENVISION Program, RTI International
701 13th St NW, Suite 750, Washington, DC 20005, USA
E-mail: eottesen@rti.org

Maria Rebollo, MD, MPH

Program Director, NTD Support Center, Task Force for Global Health
325 Swanton Way, Decatur, Georgia 30030, USA
E-mail: mrebollo@taskforce.org; mariazyl@hotmail.com

Dr Yao Sodahlon

Senior Associate Director, Mectizan Donation Program
c/o The USA Embassy in Cameroon, Avenue Rosa Parks, PO Box 817, Yaounde, Cameroon
E-mail: Ysodahlon@TASKFORCE.ORG

Dr Pradeep K Srivastava

Joint Director, National Vector Borne Disease Control Programme
Ministry of Health and Family Welfare
22 Shamnath Marg, Delhi 110054, India
E-mail: pkmalaria@yahoo.co.in

Dr Gary Weil

Professor, Division of Infectious Diseases, Washington University School of Medicine
660 South Euclid Ave, Campus Box 8051, St Louis, MO 63110, USA
E-mail: GWEIL@dom.wustl.edu

Ms Kimberly Won

Health Scientist, Centers for Disease Control and Prevention,
Centers for Global Health
Division of Parasitic Diseases
1600 Clifton Road, MS A-06, Atlanta, GA 30333, USA
E-mail: kfw7@cdc.gov

Observers

Dr Mark Bradley

Director Global De-worming, Global Health Programs, GlaxoSmithKline
980 Great West Road, Brentford, Middlesex TW8 9GS, England
E-mail: mark.h.bradley@gsk.com

Dr Angela Weaver

United States Agency for International Development
15A Keating Street, Black Rock, VIC 3191, Australia
E-mail: aweaver@usaid.gov

WHO Secretariat

Dr Dirk Engels

Director, Department of Neglected Tropical Diseases
World Health Organization, Geneva, Switzerland
E-mail: engelsd@who.int

Dr Denis Daumerie

Coordinator, Department of Neglected Tropical Diseases
World Health Organization, Geneva, Switzerland
E-mail: daumeried@who.int

Dr Jonathan King

Scientist, Department of Neglected Tropical Diseases
World Health Organization, Geneva, Switzerland
E-mail: kingj@who.int

Dr Anthony Solomon

Medical Officer, Department of Neglected Tropical Diseases
World Health Organization, Geneva, Switzerland
E-mail: solomona@who.int

Dr Aya Yajima

Technical Officer, Department of Neglected Tropical Diseases
World Health Organization, Geneva, Switzerland
E-mail: yajimaa@who.int

Dr Ramaiah Kapa

Technical Officer, Malaria, Other Vectorborne and Parasitic Diseases Unit
World Health Organization, Regional Office for the Western Pacific
E-mail: kapad@wpro@who.int

Unable to attend

Mr Lincoln Gankpala

Senior Technician, Liberia Institute for Biomedical Research
PO Box 10-1012, 1000 Monrovia 10, Liberia
E-mail: lincolngankpala@yahoo.com

Dr Patricia Graves

Coordinator, WHO Collaborating Centre for LF, STH and other NTDs
School of Public Health, Tropical Medicine and Rehabilitation Sciences, James Cook University
PO Box 6811, Cairns QLD 4870, Australia
E-mail: patricia.graves@jcu.edu.au

Dr Rosanna Peeling

Professor and Chair of Diagnostics Research, Clinical Research Unit, ITD
London School of Hygiene and Tropical Medicine
Keppel St, London WC1E 7HT, England
E-mail: rosanna.peeling@lshtm.ac.uk

Dr Frank Richards

Technical Director, Health Programs, The Carter Center
1 Copenhill, Atlanta, GA 30307, USA
E-mail: frank.richards@emory.edu

Dr Paul Simonsen

Department of Veterinary Disease Biology, Faculty of Health and Medical Sciences
University of Copenhagen
Dyrlægevej 100, Frederiksberg C, Copenhagen, Denmark
E-mail: pesi@sund.ku.dk

Annex 2. Agenda

AGENDA - 27 August 2014		
Time	Subject	Facilitator
09:00 - 09:15	1. Opening session <ul style="list-style-type: none"> - Welcoming remarks - Introduction of the participants - Nomination of the chair and rapporteur - Administrative arrangements 	Coordinator, PCT Dr J King
09:15 – 09:30	2. Purpose and objectives	Dr P Lammie
09:30 – 10:00	3. Background methods to assess LF transmission: mapping, sentinel-site monitoring and TAS	Dr J King
10:00 – 10:30	4. Supplemental guidance for areas where classification of endemicity is uncertain <ul style="list-style-type: none"> - Country experiences <ul style="list-style-type: none"> o Tanzania o Indonesia o Bangladesh 	Dr U Mwingira Ms M Brady Dr R Kapa
10:30 - 11:00	Coffee break	
11:00 – 11:30	- Proposed supplemental methods to classify endemicity (Ethiopia proposal)	Dr M Rebollo
11:30 - 12:00	- Issues in <i>Loa loa</i> coendemic setting	Dr P Fischer
12:00 - 12:30	- Proposed algorithms for decision-making	Dr E Ottesen
12:30 - 13:00	- Discussion and recommendations	Dr P Lammie
13:00 - 14:00	Lunch break	
14:00 - 14:30	5. Comparison of LF antigen tests <ul style="list-style-type: none"> - Filariasis NOW ICT and Filariasis Test Strip 	Ms K Won
14:30 - 15:30	<ul style="list-style-type: none"> - Laboratory comparison of the antigen tests <ul style="list-style-type: none"> o Alere o Washington University o India Council for Medical Research: Vector Control Research Centre 	Dr G Weil Dr K Krishnamoorthy
15:30 – 16:00	Coffee Break	
16:30 - 17:00	- Discussion on diagnostic performance in lab	Dr P Lammie
17:00-17:30	<ul style="list-style-type: none"> - Field comparison of the antigen tests <ul style="list-style-type: none"> o Overview 	Dr J King

AGENDA - 28 August 2014

Time	Subject	Facilitator
09:00 – 11:00	5. Comparison of LF antigen tests (cont) <ul style="list-style-type: none"> - Field comparison of the antigen tests <ul style="list-style-type: none"> ○ Côte d'Ivoire ○ Liberia ○ DRC ○ Indonesia ○ Sri Lanka ○ Malawi 	Mr L Gankpala Dr P Fischer Dr G Weil Professor M Bockarie
11:00 - 11:30	Coffee break	
11:30 - 13:00	<ul style="list-style-type: none"> ○ Nigeria (Carter Center) ○ Haiti ○ Niger ○ Tanzania (TFGH) ○ India (VCRC) 	Dr G Noland Dr P Lammie Dr E Ottesen Dr U Mwingira Dr K Krishnamoorthy
13:00 - 14:00	Lunch break	
14:00 - 15:00	<ul style="list-style-type: none"> - Discussion – Filariasis Test Strip <ul style="list-style-type: none"> ○ Performance characteristics ○ Operational characteristics 	Dr J King
15:00 - 15:30	- Conclusions and recommendations	Chair
15:30 – 16:00	Coffee Break	
16:00 - 16:45	6. Improving the efficiency of implementing and interpreting TAS <ul style="list-style-type: none"> - TAS Eligibility and Reporting Form - Interpretation of results TAS 1-3 	Dr A Yajima Dr M Deming
16:45 - 17:30	- Discussion	Dr E Ottesen

AGENDA - 29 August 2014

Time	Subject	Facilitator
09:00 - 10:30	7. Process of validation, verification and certification of elimination <ul style="list-style-type: none"> - Background - Elimination criteria – morbidity and disability - Elimination criteria – transmission 	Dr J King Dr L Fox Dr E Ottesen
10:30 - 11:00	Coffee break	
11:00 – 11:30	- Documenting the achievement of elimination as a public health problem – development of a standardized dossier template	Ms M Brady
11:30 -12:30	- Discussions	Dr Y Sodahlon
12:30 - 13:30	Lunch break	
13:30 - 14:30	8. Meeting conclusions and recommendations	Dr P Lammie
14:30 - 15:00	9. Closure of the meeting	Director, NTD

Annex 3. Comparison of survey methods recommended for use since the inception of the Global Programme to Eliminate Lymphatic Filariasis

The following tables summarize the methods that have been utilized for monitoring and evaluation in the Global Programme to Eliminate Lymphatic Filariasis (GPELF) since its inception. WHO published global guidelines in 2000, 2005 and 2011. WHO's regional offices have published regionally specific guidance or followed regionally specific approaches. These have been described in the tables where applicable.

Table A3.1. Mapping: methods

	WHO 2000 programme managers' guide ^a	2005 WHO monitoring and evaluation manual ^b	2011 WHO TAS manual ^c
Methods	Lot quality-assurance sampling (LQAS) in grey areas – that is, areas considered to be possibly endemic	Mapping surveys in areas with unknown endemicity	Mapping surveys only in areas considered to be possibly endemic
Sample size	250	Not specified	References different regional approaches, but does not specify sample size
Site selection	Highest-risk areas	Not specified	Highest-risk areas
Age group	Older schoolchildren	Not specified	Adults or older schoolchildren
Diagnostic test	Preferred: antigenaemia measured by ICT; microfilaraemia	Antigenaemia measured by ICT; microfilaraemia	Preferred: antigenaemia measured by ICT; microfilaraemia
Cut-off for endemicity	≥1 positive case	Antigenaemia or microfilaraemia ≥1%	Antigenaemia or microfilaraemia ≥1%
Estimates IU prevalence	No	No	No
Morbidity measured	Yes, through questionnaires	Not specified	Not specified

TAS, transmission-assessment survey; ICT, immunochromatographic test.

^a *Preparing and Implementing a National Plan to Eliminate Lymphatic Filariasis: a guideline for programme managers*. Geneva, World Health Organization, 2000 (also available at http://whqlibdoc.who.int/hq/2000/who_cds_cpe_cee_2000.15.pdf).

^b *Monitoring and epidemiological assessment of the programme to eliminate lymphatic filariasis at implementation unit level*. Geneva, World Health Organization, 2005 (also available at http://whqlibdoc.who.int/hq/2005/WHO_CDS_CPE_CEE_2005.50.pdf?ua=1).

^c *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>).

Table A3.2. Mapping: approaches used, by WHO region or other area

	African Region	Pacific programme for the Elimination of Lymphatic Filariasis (PacELF)	Region of the Americas (Haiti, Guyana)
Methods	Convenience sampling surveys in grey areas – that is, areas considered to be possibly endemic	Convenience or cluster sampling	School-based surveys (lot quality-assurance sampling)
Sample size	50–100 per village	33–7006 total	50 per school
Site selection	2 high risk villages at least 25 km apart	Random selection or selected for convenience	2–5 schools based on their size, accessibility and risk status
Age group	≥15 years and living in the community for >10 years	Adults	Schoolchildren aged 6–11 years
Diagnostic test	Antigenaemia measured by ICT	Antigenaemia measured by ICT	Antigenaemia measured by ICT
Cut-off for endemicity	>1%	0–1% considered partially endemic; >1% considered endemic	≥1%

ICT, immunochromatographic test.

Table A3.3. Monitoring: methods

	WHO 2000 programme managers' guide ^a	2005 WHO monitoring and evaluation manual ^b	2011 WHO TAS manual ^c
Purpose	Monitor progress; collect baseline data	Monitor impact; collect baseline data; determine eligibility for stopping MDA	Monitor trends in infection; determine eligibility for stopping MDA
Sample size	500	500	300
Site selection	2 sentinel sites plus 2 spot-check sites per 1 000 000 population	2 sentinel sites plus 2 spot-check sites per 1 000 000 population <i>To stop MDA, add 5–10 high-risk sites</i>	At least 1 sentinel site plus 1 spot-check site per 1 000 000 population
Age group	>2 years	Entire population <i>When surveying to determine whether to stop MDA, add testing in children aged 2–4 years</i>	>5 years
Timing	Baseline; before third round of MDA; before fifth round of MDA	Baseline; before third round of MDA; before fifth round of MDA	Baseline; before fourth round of MDA (optional); before sixth round of MDA
Diagnostic test	Microfilaraemia	Microfilaraemia	Microfilaraemia or antigenaemia (ICT)
Morbidity	Clinical assessment	Clinical assessment	Not specified

TAS, transmission-assessment survey; MDA, mass drug administration; ICT, immunochromatographic test.

^a *Preparing and Implementing a National Plan to Eliminate Lymphatic Filariasis: a guideline for programme managers.* Geneva, World Health Organization, 2000 (also available at http://whqlibdoc.who.int/hq/2000/who_cds_cpe_cee_2000.15.pdf).

^b *Monitoring and epidemiological assessment of the programme to eliminate lymphatic filariasis at implementation unit level.* Geneva, World Health Organization, 2005 (also available at http://whqlibdoc.who.int/hq/2005/WHO_CDS_CPE_CEE_2005.50.pdf?ua=1).

^c *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes.* Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>).

Table A3.4. Methods used to determine whether to stop mass drug administration (MDA)

	WHO 2000 programme managers' guide ^a	2005 WHO monitoring and evaluation manual ^b	2011 WHO TAS manual ^c
Methods	Lot quality-assurance sampling (LQAS)	Lot quality-assurance sampling (LQAS)	Prevalence survey with LQAS-like critical cut-off for decision-making
Sample size	3000	300 followed by an additional survey of 3000	≤3080
Site selection	Highest-risk area	Cluster survey in highest-risk areas followed by systematic sample survey in entire IU	Census, systematic or cluster survey in schools or communities
Age group	6–10 years	2–4 years; School entrants	6–7 years
Diagnostic test	Antigenaemia (ICT)	Antigenaemia (ICT)	Antigenaemia (ICT) or antibody using BR
Cut-off for stopping MDA	<0.1% (0 positives)	0 positives	<2% antigenaemia or antibody or <1% antigenaemia for where vector is <i>Aedes</i>

TAS, transmission-assessment survey; IU, implementation unit; ICT, immunochromatographic test; BR, Brugia Rapid test (Reszon Diagnostics International, Selangor, Malaysia).

^a *Preparing and Implementing a National Plan to Eliminate Lymphatic Filariasis: a guideline for programme managers*. Geneva, World Health Organization, 2000 (also available at http://whqlibdoc.who.int/hq/2000/who_cds_cpe_cee_2000.15.pdf).

^b *Monitoring and epidemiological assessment of the programme to eliminate lymphatic filariasis at implementation unit level*. Geneva, World Health Organization, 2005 (also available at http://whqlibdoc.who.int/hq/2005/WHO_CDS_CPE_CEE_2005.50.pdf?ua=1).

^c *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes*. Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>, accessed 28 August 2014).

Table A3.5. Surveillance: methods

	2000 WHO programme managers' guide ^a	2005 WHO monitoring and evaluation manual ^b	2011 WHO TAS manual ^c
Purpose	To identify foci of transmission	To detect new foci; to collect data on trends in infection; to confirm the end of transmission	To detect recurrence of transmission
Methods	Repeat the survey used to determine whether to stop MDA 5 years after MDA has been stopped. Ongoing surveillance: – in the entire country – in population groups such as military or police recruits, blood donors. Microfilaraemia, hydrocele and lymphoedema are reportable events. Look for clinical disease when conducting other surveys.	Repeat the survey used to determine whether to stop MDA 5 years after MDA has been stopped	Repeat TAS at 2–3 years and 4–6 years after stopping MDA. Ongoing surveillance: - in the entire country - in population groups such as military or police recruits, university students, blood donors, hospital inpatients.

TAS, transmission-assessment survey; MDA, mass drug administration.

^a *Preparing and Implementing a National Plan to Eliminate Lymphatic Filariasis: a guideline for programme managers.* Geneva, World Health Organization, 2000 (also available at http://whqlibdoc.who.int/hq/2000/who_cds_cpe_cee_2000.15.pdf).

^b *Monitoring and epidemiological assessment of the programme to eliminate lymphatic filariasis at implementation unit level.* Geneva, World Health Organization, 2005 (also available at http://whqlibdoc.who.int/hq/2005/WHO_CDS_CPE_CEE_2005.50.pdf?ua=1).

^c *Monitoring and epidemiological assessment of mass drug administration for eliminating lymphatic filariasis: a manual for national elimination programmes.* Geneva, World Health Organization, 2011 (also available at <http://apps.who.int/iris/handle/10665/44580>).

Annex 4. Rationale and description of an example decision-making prevalence survey proposed for remapping the endemicity of lymphatic filariasis

1. *Where might remapping be required?*

Some countries face a situation where mapping for lymphatic filariasis (LF) has not led to a decision to scale-up MDA. In some districts evidence of endemicity is contradictory, either between mapping surveys and sentinel sites or between surveys conducted several years apart. Another scenario involves districts where decision makers were not convinced of the need of MDA based on very few positives identified in original mapping. In these cases, remapping may be required.

2. *What survey design is proposed for remapping?*

A cluster-sample (CS) or systematic sample (SS) design that provides a prevalence estimate but uses a critical cut-off value to make a decision on the need for MDA is recommended. This is a similar design as followed in the TAS. School-based surveys are recommended. When there are more than 40 schools in a mapping area (that is, a district), sampling 16 children in each of 30 schools using selection probability proportional to estimated size (PPES) is recommended. Using a SS design is recommended when the number of schools in the district or mapping unit is 40 or fewer. An SS requires smaller sample sizes (320 children compared with 480) but all schools have to be visited.

3. *What is the target age group to be surveyed?*

Older children aged 9–14 years are the recommended target age group. LF infections are acquired in childhood, yet the prevalence of infection among children is often lower than the prevalence among adults. The prevalence of LF in older children is expected to be more similar to the prevalence in adults. Antigenaemia in children is a sign of recent transmission and infection. Children's grade level at school can be used as a proxy for their exact age. Grades should be selected where the majority of children are typically 9 years or older. Once a selection of grades has been made, all children in those grades should be eligible for selection independent of their age.

4. *When should PPES be used?*

Every child in the district should have an equal probability of being selected during mapping. Because schools are different sizes, children in larger schools will have less chance of being selected when randomly selecting from a list of schools. Selection by probability proportional to estimated size (PPES) should be used. Schools with larger populations will have greater chances of being selected proportional to the number of children enrolled in that school, so that each child in the mapping unit has the same probability of being selected. This method also facilitates planning for fieldwork because a predetermined number of individuals (16 children) are tested in each school selected. PPES cannot be used when information about the size of schools (that is, the number of children enrolled in each school) is not available when the survey is designed.

5. *How can geographical representation be improved for selected clusters?*

Randomly selecting schools could result in proportionally more schools in one area being included in the survey than schools in another area. In order to avoid this, the sampling frame (the list of schools) should be ordered by geographical proximity. This can be achieved by providing information from where the school is located (the subdistrict level). Two-stage sampling with PPES in the first stage can be then conducted. Subdistricts can be listed and selected during the first stage, and PPES can be used in the second stage to select schools within the selected subdistricts.

6. *What is the critical cut-off value?*

The critical cut-off value is the maximum number of children who test positive that will ensure with 95% confidence that the endemicity of LF is below the threshold at which MDA would be warranted. The following definitions and critical cut-off values were derived from the TAS design:

- non-endemic, MDA not required - this is where the prevalence of LF is less than 1% (and where the upper limit of the 95% confidence interval does not include 2%); a mapping area is non-endemic when *no more than 3* positive children are identified in the CS survey design; no more than 2 positive children are identified in the SS survey design

- endemic, MDA required – this is where the prevalence of LF antigenaemia is 1% or higher (and the 95% confidence interval includes or is greater than 2%); a mapping area is endemic when *more than 3* positive children are identified in the CS survey design; *more than 2* positive children are identified in the SS survey design

7. *Can the prevalence and confidence intervals be estimated?*

Yes. Using the appropriate statistical software, the prevalence and confidence intervals can be estimated to determine a point prevalence of LF for the age group. That point prevalence in children will be used as a proxy for the prevalence of LF in the district.

8. *What diagnostic tools should be used?*

Antigenaemia as measured by the immunochromatographic test (ICT) or the Filariasis Test Strip (FTS) will be used for mapping.

9. *What is the estimated cost?*

The incremental cost of conducting a survey to determine endemicity is estimated to be US\$ 6000 per district or implementation unit but this may vary across settings.

10. *What information is required to design the survey?*

The information required to design the survey includes the number of schools, the number of children in each grade, and the age of the children in each grade (or at least which is the first grade level that contains a majority of children aged 9 years or older).

Table A4.1. Comparison of cluster sampling and systematic sampling designs in an example decision-making prevalence survey to determine the endemicity of lymphatic filariasis

Requirements	Cluster sampling using probability proportional to size	Systematic sampling
Number of schools	30	All schools in district
Sample size	480	320
Age group	9–14 year olds	9–14 year olds
Design effect	1.5	1
Selection of individuals	15 randomly selected children per school	Sampling interval
Alpha error	0.05	0.05
Power	0.4	0.4
Primary sampling unit	≥40 schools	<40 schools in the mapping area
Data needed prior to survey	Information on the age of children in different grades at school	Information on the age of children in different grades at school
Pros	Commonly accepted sampling approach; no need to calculate sampling interval; exact sample size achieved; all children have an equal probability of being selected	Ensures entire geographical area is represented; smaller total sample size
Cons	Schools with a population larger than the sampling interval are certain to be selected	Using a sampling interval leads to a greater chance of oversampling or undersampling; Need to visit all schools in the district, which is often the most costly and time-consuming aspect
Cost	US\$ 6000 per mapping unit	Varies, cost increases as number of schools increases
Critical cut-off value (decision rule)	>3 positives indicate MDA is required	>2 positives indicate MDA is required
Point prevalence estimate	Can be calculated using statistical software; estimate will have a large confidence interval	Can be calculated using statistical software; estimate will have a large confidence interval

MDA, mass drug administration.

Annex 5. Comparisons of the BinaxNOW Filariasis immunochromatographic test and the Alere Filariasis Test Strip

Table A5.1. Description and results of the 15 comparison studies of the BinaxNOW Filariasis immunochromatographic test (ICT) and the Alere Filariasis Test Strip (FTS)^{a,b,c}

Country	Programme setting	Monitoring and evaluation activities	No. of tests	No. of positives using either test	Prevalence (%)	% overall agreement between ICT and FTS	% agreement among positive tests	% agreement among negative tests	Ratio of positive FTS to positive ICT
Côte d'Ivoire	Pre-MDA	Mapping	837	245	29.3	97.7	92.2	97	1.07
Democratic Republic of the Congo	Pre-MDA	Mapping	187	42	22.5	93.0	69.0	91.8	1.5
Haiti	Post-MDA	Pre-TAS	505	15	3.0	97.4	7.1	97.4	14.0
Indonesia ^d	Post-MDA	Monitoring	881	61	6.9	97.4	62.3	97.3	1.4
Liberia	Pre-MDA	Mapping for CDTI	519	124	23.9	95.4	80.6	94.3	1.2
Malawi 1	Post-MDA	TAS	1680	13	0.8	89.6	0.0	99.1	0.3
Malawi 2	Post-MDA	TAS	1680	1	0.1	99.9		99.9	
Niger	Post-MDA	TAS	2147	41	1.9	99.3	61.0	99.2	0.6
Nigeria	Post-MDA	TAS; surveillance	5895	14	0.2	99.9	50.0	99.9	0.9
Sri Lanka 1	Post-MDA	Surveillance	390	28	7.2	96.2	46.0	96.0	2.2
Sri Lanka 2	Post-MDA	Surveillance	378	16	4.2	97.1	31.3	97.1	3.2
United Republic of Tanzania 1	Pre-MDA	Baseline SS	402	38	9.5	100.0	100.0	100.0	1.0
United Republic of Tanzania 2	Pre-MDA	Baseline SS	436	0	0.0				
United Republic of Tanzania 3 ^e	Post-MDA	TAS; surveillance	1629	62	3.8	96.4	6.4	96.4	15.5
Uganda	Post-MDA	TAS	1566	5	0.3	99.8	40.0	99.8	1.3

MDA, mass drug administration; TAS, transmission-assessment survey; CDTI, community-directed treatment with ivermectin; SS, systematic sample.

^a Both tests are manufactured by Alere, Scarborough, ME, United States.

^b Blank cells indicate that the agreement statistic could not be estimated.

^c All data are unpublished except the study in Liberia by Weil GJ et al. Laboratory and field evaluation of a new rapid test for detecting *Wuchereria bancrofti* antigen in human blood. [American Journal of Tropical Medicine and Hygiene](#), 2013, 89:11–15

^d These data were not presented at the meeting but were made available on 18 September 2014.

^e Samples were collected in EDTA (ethylenediaminetetraacetic acid) tubes; in the study in Sri Lanka this caused frequent false-positive results.

Preventive Chemotherapy and Transmission Control (PCT)
Department of Control of Neglected Tropical Diseases (NTD)
World Health Organization
20, Avenue Appia
1211 Geneva 27, Switzerland

http://www.who.int/neglected_diseases/en

