Report of the sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup

Virtual meeting
19–21 December 2022

World Health Organization
Report of the sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup

Virtual meeting
19–21 December 2022
6. Stop MDA threshold study updates ................................................................. 21
   6.1 United Republic of Tanzania ........................................................................... 21
   6.2 Ghana sites 1 and 2 .......................................................................................... 21
   6.3 Malawi ............................................................................................................. 22
   6.4 Summary of discussions .................................................................................. 22
   6.5 Recommendations ......................................................................................... 23

7. Post-treatment surveillance: Ethiopia’s experience ........................................ 24
   7.1 Description of focus and recent results ........................................................... 24
   7.2 Summary of discussions ................................................................................ 25
   7.3 Recommendations ......................................................................................... 25

8. Onchocerciasis-associated epilepsy ................................................................. 26
   8.1 Update and perspectives ................................................................................ 26
   8.2 Summary of discussions ................................................................................ 26
   8.3 Recommendations ......................................................................................... 27

9. Development of a prophylactic onchocerciasis vaccine ................................ 28
   9.1 Onchocerciasis vaccine .................................................................................. 28
   9.2 Summary of discussions ................................................................................ 28
   9.3 Recommendations ......................................................................................... 28

References ........................................................................................................... 29

Annex 1. Agenda .................................................................................................... 30

Annex 2. List of participants ................................................................................ 32

Annex 3. NTD Modelling Consortium consensus position statement on
onchocerciasis elimination ...................................................................................... 34

Report of the sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup: virtual
meeting, 19–21 December 2022
Abbreviations and acronyms

- AP: alkaline phosphatase
- CDC: United States Centers for Disease Control and Prevention
- CDTi: community-directed treatment with ivermectin
- COR-NTD: Coalition for Operational Research on NTDs
- COVID-19: coronavirus disease
- DBS: dried blood spots
- DTAG: Diagnostic Technical Advisory Group for Neglected Tropical Diseases
- ELISA: enzyme-linked immunosorbent assay
- MDA: mass drug administration
- MDGH: Medicines Development for Global Health
- NTD: neglected tropical disease
- NOEC: National Onchocerciasis Elimination Committee
- OCP: Onchocerciasis Control Programme in West Africa
- OEM: onchocerciasis elimination mapping
- OEPA: Onchocerciasis Elimination Program for the Americas
- OTS: Onchocerciasis Technical Subgroup
- Ov: Onchocerca volvulus
- PATH: Program for Appropriate Technology in Health
- PCR: polymerase chain reaction
- qPCR: quantitative real-time PCR
- QA: quality assurance
- QC: quality control
- RCT: randomized controlled trial
- RDT: rapid diagnostic test
- SD: Standard Diagnostics
- TAS: transmission assessment survey
- UOEEAC: Uganda Onchocerciasis Elimination Expert Advisory Committee
- WHO: World Health Organization
Executive summary

The sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup (OTS) was held virtually on 19−21 December 2022. The main outcomes of the meeting are summarized below. Nine sessions were held. The meeting agenda is included as Annex 1 and the participants are listed in Annex 2. A consensus position statement on onchocerciasis elimination prepared by the NTD Modelling Consortium is provided in Annex 3. A separate Web Annex contains the report of a systematic review on moxidectin for the treatment of onchocerciasis prepared by the Noguchi Memorial Institute for Medical Research.

1. Diagnostics

The available serological tests do not meet the current WHO target product profile for onchocerciasis diagnostics. Adequate quality assurance and quality control procedures are critical for the proper interpretation of diagnostic test results, particularly in programmatic settings. The inclusion of an appropriate internal extraction, recovery and amplification control is essential for confidence in individual sample results. According to the presenters in settings where skin snips are collected, dried blood spots (DBS) should also be collected to assess the relationship between skin snip microfilariae and Ov16 positivity. Countries should capitalize, where possible, on capacity already built as part of the COVID-19 response and other new or ongoing laboratory initiatives. As new diagnostics are introduced, plans for country access must be formalized during the development and validation process.

Recommendations

WHO is advised to work with the Diagnostic Technical Advisory Group for Neglected Tropical Diseases (DTAG) to develop the necessary test validation, quality assurance and quality control processes for serological and molecular diagnostics and to provide criteria for validation of diagnostic tests for programmatic use and validation of test performance within individual laboratories. The new blackfly qPCR protocols and their accompanying quality assurance and quality control procedures are recommended to be piloted for implementation in laboratories in countries where onchocerciasis is endemic. It is recommended that WHO explore mechanisms for producing the reagents and supplies for qPCR, Ov16 rapid diagnostic test (RDT) and buffer as well as for ELISA diagnostics within Africa to help ease supply chain issues; such consideration should be part of the process of developing new tests.

1.1 Quality assurance and quality control

To WHO

- Consult with the DTAG to provide standardized guidance for quality assurance and quality control processes.
- Consult with the DTAG to provide the criteria for validation of diagnostic tests for programmatic use and validation of test performance within individual laboratories.
- Make these guidance documents, and support for their implementation, available to countries and facilitate reporting on these processes.
To Member States

- In settings where skin snips are collected, programmes are recommended to also collect DBS to assess the relationship between skin snip microfilariae and Ov16 serology.

1.2 Blackfly qPCR

To WHO

- Owing the importance of high-quality diagnostic tools to achieve and sustain the elimination of onchocerciasis, WHO and DTAG are encouraged to work together to shepherd the development and validation of the new tools critically needed by programmes.
- Given the promising results of blackfly qPCR, in terms of its ability to detect infective flies, to reduce the complexity of the testing process and to provide results with less personnel time, OTS recommends that WHO anticipate the development of a new WHO guideline.
- Work with the onchocerciasis subgroup of DTAG to develop preferred product characteristics for the reagents needed for molecular testing for onchocerciasis, both in blackflies and in humans, recognizing the importance of standardizing the performance of PCR assays.
- Facilitate the strengthening of laboratory capacity for these tools and other diagnostics through the DTAG initiative on building laboratory capacity.

To diagnostic developers

- Continued work on a new qPCR should ensure that the protocols developed can be feasibly implemented in laboratories of endemic countries (paying particular attention to challenges in procurement of reagents and maintenance of equipment) and should examine whether the entomological criterion for stopping mass drug administration needs to be adjusted to reflect the analytic sensitivity/performance of the new test(s).

To Member States

- The new blackfly qPCR protocols and their accompanying quality assurance and quality control procedures are recommended to be piloted for implementation in laboratories in endemic countries.
- National programmes should also capitalize, where possible, on capacity already built as part of the COVID-19 response and other new or ongoing laboratory initiatives in their respective countries.

1.3 Procurement challenges

To WHO

- Explore mechanisms for the production of the reagents and supplies needed for qPCR, Ov16 RDT and buffer as well as for ELISA diagnostics within Africa to help ease supply chain issues; such consideration should be part of the process of developing new tests.
- It is imperative that countries have access to the necessary equipment, reagents and supplies needed to carry out the diagnostics required for programmatic action. As new diagnostics are introduced, plans for country access must be formalized during the development and validation process.

2. Onchocerciasis modelling updates

The discussions were on the modelling comparison of distribution between ivermectin and moxidectin. There was also a presentation on the systematic review of papers to identify factors associated with elimination of transmission, close to elimination and ongoing transmission.
Recommendations

OTS recommends that WHO encourage programmes to investigate the extent of systematic non-participation in MDA during coverage surveys and other evaluations and to endeavor to learn from other neglected tropical disease programmes (e.g. lymphatic filariasis elimination programmes) with experience investigating this issue.

To WHO

- Encourage programmes to investigate the extent of systematic non-participation in MDA during coverage surveys and other evaluations.
- Endeavour to learn from other neglected tropical disease programmes (e.g. lymphatic filariasis elimination programmes) with experience investigating this issue.

To Member States

- Given the importance of understanding the impact of systematic non-participation on the probability of a programme achieving elimination of transmission, programmes should explore ways to capture this information during routine programmatic MDA activities (such as, pilot testing the use of biometric tools to track participation year-to-year).

3. Moxidectin

The results of a moxidectin paediatric pharmacokinetic and safety study to support identification of a dose for treatment of children aged 4–11 years, considered with all relevant safety data and to support simplicity of dose administration in the field settings, yielded recommended doses of 8 mg (4 x 2 mg tablets) for children aged 8–11 years and 4 mg (2 x 2 mg) for children aged 4–7 years. Data from ongoing clinical studies have so far indicated no serious adverse events assessed as related to treatment with moxidectin. Additional safety data for loiasis and lymphatic filariasis co-infection are forthcoming. Medicines Development for Global Health (MDGH) is proactively planning pilot implementation projects with moxidectin that would include treatment of all children aged 4 years and older. OTS was supportive of this approach, with the recommendation that safety data from paediatric participants in ongoing trials be reviewed and communicated to countries before pilot projects began.

Recommendations

OTS recommends that pilot projects be targeted in meso/hyper-endemic areas with good baseline ivermectin MDA coverage where existing programmatic infrastructure could be used to support the rollout. These settings should be non-endemic for lymphatic filariasis and loiasis until further safety data are available and strong pharmacovigilance systems are in place. Pilot projects in hypo-endemic settings were also recommended. The planning process for funding moxidectin and making the medicine available to countries should start now, rather than after pilot projects have been completed. It is recommended that WHO work with MDGH and experts to develop a prioritized list of use cases for moxidectin so that countries can identify appropriate settings and start to plan for moxidectin use.

To WHO

- Work with Medicines Development for Global Health (MDGH) and experts to develop a prioritized list of data-driven use cases for moxidectin (e.g. hot spots where ongoing transmission is due to high transmission potential and not poor programme coverage; hypo-endemic areas; mobile populations) so that countries can identify appropriate settings and start to plan for moxidectin use.
OTS agrees with MDGH’s plan to collect information of the cost of starting and maintaining moxidectin MDA and to study the acceptability of the medication in populations who have become accustomed to receiving ivermectin.

Does the Committee support this proposed approach for progressing moxidectin pilot field projects, treating all aged 4 years and older?

1. Conducting additional pilot studies of moxidectin in the context of routine onchocerciasis elimination programmes is important and would generate valuable data for countries looking to add moxidectin as an additional tool for achievement of the WHO road map elimination targets.

2. The Committee supports moving forward with the planning of the pilot studies. Safety data from paediatric participants (children aged 4–11 years) in the ongoing trial in the Democratic Republic of the Congo should be reviewed before making a final go/no-go decision to include children in this age group in the planned pilot studies of community-based moxidectin MDA, noting that there are fewer children in this site than in the Côte d’Ivoire site where data will not yet be available.

3. WHO, MDGH and partners are recommended not to wait until the end of the next series of pilot studies to start discussions related to making moxidectin available for programme use and the importation process; these discussions will take time and the feasibility of moxidectin as a programmatic tool is dependent upon their resolution.

Are there any areas or area selection criteria that the Committee recommends be considered for undertaking such pilot field projects?

1. OTS agrees with the inclusion criteria specified in the briefing document for the sixth meeting of the OTS for the community-based MDA pilot, which would focus on piloting in meso/hyper-endemic areas with good baseline ivermectin MDA coverage. These areas should be non-endemic for loiasis until additional safety data are available. Areas co-endemic for lymphatic filariasis should not have an active treatment programme (requiring co-administration of albendazole) at the same time as undertaking a pilot project with moxidectin.

2. It would be beneficial to also conduct a pilot project in a hypo-endemic area, recognizing that this may require additional funding and implementation support.

3. Countries with strong pharmacovigilance should be targeted for pilots. WHO should support MDGH to identify these areas and engage its pharmacovigilance unit to help strengthen the relevant country surveillance systems.

4. If funding permits and safety data are available from *Loa loa* safety trials, pilot projects should also be considered in onchocerciasis meso-/hyper-endemic settings co-endemic with loiasis that have been treated with ivermectin for a number of years and where effective systems for detection and management of loiasis-related adverse events are in place.

4. National onchocerciasis elimination committees: country updates

Discussions focused on how national onchocerciasis elimination committees (NOECs) could be supported to harmonize ways of working, share best practices and ensure that rich data and discussions from these experts meetings are not lost.

Recommendations

WHO is encouraged to engage with the chairs of the NOECs to develop a system for sharing best practices across countries for issues of concern to country onchocerciasis programs and to seek funding in order to convene a meeting to share lessons learned across the African region. A formalized communication mechanism between the OTS and the NOECs would help ensure that priority concerns are addressed.
To WHO

- Engage with the chairs of the NOECs at regional and/or subregional levels to devise a system for sharing best practices across countries for issues of concern to national onchocerciasis elimination programmes (e.g. treatment of refugee and mobile populations and cross-border issues). OTS recommends that WHO seek funding in order to convene a meeting of NOEC chairs to share lessons learnt across the African Region.

- Consider the establishment of subregional groups that include NOEC chairs and national programme leadership to allow more rapid and sustainable sharing of knowledge among national committees in West, East, Central and South African regions.

- Devise a system, with the input of the chairs, for sharing national onchocerciasis elimination plans and the annual reports generated by the NOECs in a standardized manner. These NOEC reports, with country permission, might then be shared with WHO and more broadly with other NOECs and onchocerciasis elimination programmes in the region.

- Create a repository for annual reports from the NOECs.

- Continue to encourage NOECs to be established as described in WHO guidelines: the committee should be independent from the national programme and comprise national and international experts, in accordance with practice in some countries in Africa. This committee can be embedded in any existing national committee for NTD activities or onchocerciasis-specific matters. NOECs should strive to be independent bodies.

- Formalize a communication mechanism between OTS and NOECs to help ensure that priority concerns are addressed.

5. Monitoring and evaluation

The experts discussed which improvements in RDTs would be beneficial to the programmes in Benin and the United Republic of Tanzania. The Committee suggests that short-term solutions need to be found so that programmes are not penalized by long lags in procuring diagnostics and can make decisions in a timely manner.

Recommendation

WHO is encouraged to work with manufacturers and suppliers to improve the logistics process and facilitate access to RDTs and reagents and to develop guidance for using RDT on DBS for routine M&E and that the SD Ov16 RDT on DBS be used as the primary tool for routine monitoring and evaluation.

To WHO

- Work with manufacturers and suppliers to improve the logistics process and facilitate access to RDTs and reagents.

- Develop guidance (or gather best practices) for using RDT on DBS for routine monitoring and evaluation; OTS recommends using SD Ov16 RDT on DBS as the primary tool for routine monitoring and evaluation.

6. Stop MDA threshold study updates

Ongoing operational research and modelling studies are evaluating whether the serological threshold of < 0.1% (at the upper confidence limit) in children aged < 10 years for stopping MDA can be increased to a level that would be more technically feasible to measure while remaining a reliable indicator that elimination has been reached. The WHO-recommended serological threshold of < 0.1% (at the upper
Executive summary

confidence limit) in children aged < 10 years for stopping MDA has not changed yet until results from these studies show convincing evidence.

- Ongoing operational research and modelling studies are evaluating whether the serological threshold can be increased to a level that would be more technically feasible to measure while remaining a reliable indicator that elimination has been reached. OTS appreciates the updates on the progress so far with this work, and it looks forward to future updates as data become available.

- OTS would like to clarify that the WHO-recommended serological threshold of < 0.1% (at the upper confidence limit) in children aged < 10 years for stopping MDA has not changed. Such a change would require issuance of new guidelines. Ongoing operational research and modelling studies are evaluating whether this serological threshold can be increased to a level that would be more technically feasible to measure while remaining a reliable indicator that elimination has been reached.

7. Post-treatment surveillance: Ethiopia’s experience

So far Ethiopia has considered vector control to supplement and support MDA on several occasions. The surveillance effort of the national programme has been encouraging, but further investigation is needed to understand human migration patterns around the positive sites and whether moving to vector control may be a potential solution. OTS would appreciate feedback on Ethiopia’s progress towards elimination and its experience with the WHO algorithm for positive entomological findings during post-transmission surveillance.

Recommendation

OTS recommends that WHO follow the data generated as the various planned studies described in the presentation unfold.

To WHO

- The Ethiopian programme shared its experience with the identification of infective flies during post-treatment surveillance. OTS appreciates the programme’s willingness to share its experience and findings. OTS recommends that WHO follow the data generated as the various planned studies described in the presentation unfold.

- OTS highlighted that the programme is following the algorithm for how to respond to positive entomological findings after stopping MDA that is described in WHO guidelines and would appreciate feedback on the results of Ethiopia’s studies.

8. Onchocerciasis-associated epilepsy

Several recent studies have generated convincing evidence of the link between onchocerciasis and epilepsy. There is currently no formal recommendation from WHO for programmes on the topic of onchocerciasis-associated epilepsy.

Recommendation

OTS recommends that WHO organize a meeting with various experts and the WHO seizure and epilepsy group to formalize recommendations on onchocerciasis-associated epilepsy and develop guidance that can be used both as an advocacy tool and for programmatic action.

There is mounting evidence of the association between onchocerciasis and epilepsy, but a thorough analysis of the data and development of programmatic recommendations based on the data were beyond the scope of the current meeting of the OTS.
To WHO

Organize a standalone meeting with the goal of formally evaluating the available data and preparing guidance that can be used for programmatic action and advocacy. It is recommended that the meeting involves neurologists and the WHO seizure and epilepsy group, as well as onchocerciasis experts.

9. Development of a prophylactic onchocerciasis vaccine

An effective and safe vaccine against onchocerciasis could be used in combination with drug therapy to induce additional immunity. Immunoprophylaxis will not interfere with natural immunity.

No recommendation was made by OTS6.
Introduction

The sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup (OTS) was held virtually on 19–21 December 2022. The nine sessions of the meeting are reported sequentially below. The agenda is provided in Annex 1 and the participants are listed in Annex 2.
1. Diagnostics

Recap of ELISA/RDT comparisons (by Paul Cantey)

The WHO guidelines for stopping mass drug administration (MDA) (1) and the OTS-recommended programmatic guidance for onchocerciasis elimination mapping (OEM) (2) require measuring Ov16 seroprevalence between 0.1% for the former and 2% for the latter (i.e. depending on the use case). This makes it very challenging to develop appropriate diagnostics, as the specificity for both the mapping and the stopping use cases is 99.8%. ¹

The OTS on several occasions has reviewed publications and unpublished data relevant to the Onchocerciasis Elimination Program for the Americas (OEPA), the United States Centers for Disease Control and Prevention (CDC) and Standard Diagnostics (SD) Bioline enzyme-linked immunosorbent assays (ELISAs) as well as the SD Bioline rapid diagnostic test (RDT). These comparisons have been challenging because different methods were used to evaluate specificity and sensitivity, different sample types (i.e. whole blood, serum and plasma) were used, and different specimen panels for both positive controls and potential cross-reactants were used. All of the ELISAs evaluated have some issues with cross-reactivity to dried blood spots (DBS) collected from individuals infected with a parasitic infection outside of known endemic countries (e.g. Haiti and the Philippines). In some comparisons, test performance varied across study sites. The conclusion was that no test met the WHO target product profile for either use case, though it appears that the RDT could probably be optimized for use in mapping. Further analysis that examined not only sensitivity and specificity but also reproducibility, time to results, ease of use, test availability/ease of importation and cost, came to a similar conclusion.

Key messages were that the performance characteristics of the current RDT were inadequate, the sensitivity of the OEPA version of the alkaline phosphatase (AP) ELISA was low, the performance of the AP ELISA was variable and made it difficult to standardize the test across laboratories, and the specificity of the SD ELISA was inadequate for decision-making. At the time, it was recommended that optimization of existing tools be accelerated and that programmes should collect and store DBS for potential re-analysis, if needed, when new tools became available.

The presenter suggested that the onchocerciasis community needed access to a standardized, transparent validation process that incorporated not only test sensitivity and specificity but also other comments of test performance, similar to those used for diagnostic tests in clinical laboratories. An example included recommendations from the College of American Pathologists, which assists diagnostic clinical laboratories in the United States of America (USA). The validation process could include determination of analytic sensitivity and specificity, analytic precision, analytic interferences, reportable range and reference intervals. All this information should be recorded and shared with WHO and the relevant NOEC. It was noted also that revalidation was required whenever any change was made to the test standard operating procedures or equipment used to perform the test to ensure that the change did not have unanticipated negative effects on test performance. Individual laboratories would need also to validate the performance of the test(s) in their laboratory. Fortunately, the DTAG has been designated to develop a standardized process;

¹ NB. The WHO target product profile for the stopping use case assumed that the threshold for stopping would eventually change to 1%; note also that the threshold for stopping MDA remains 0.1%.
the OTS could take advantage of the expertise of this group. It would be expected, moving forward, that all new diagnostics undergo a standardized validation process designed for programmatic uses of tests and use standardized quality assurance and quality control processes. The programmatic use validation process will need to take into account other test parameters, such as cost and logistics. Although the currently available serological tests are not ideal, entomological surveys with molecular analysis remain important to compensate for some of the weaknesses (though entomological capacity in some programmes remains weak). The currently available molecular tests need to have QA/QC standards put in place. Finally, it was suggested to begin to think in terms of multiple tests or a confirmatory test as a means for solving some of our current challenges, rather than depending on a single test.

1.1 Quality assurance and quality control

1.1.1 CDC approach: ELISA and RDT (by Scott Elder)

In previous OTS meetings, guidance for ELISA work has stipulated that an Ov16-based ELISA be used, but not a specific protocol. OTS also recommended QA (quality assurance) and QC (quality control) measures be instituted, but did not provide details. This presentation detailed what QA/QC the United States Centers for Disease Control and Prevention (CDC) has put in place for the AP ELISA and RDT, as well as the experience in implementing this procedure successfully in the United Republic of Tanzania, and unsuccessfully in Ghana. While implementing this procedure in Ghana, the quality control measures indicated that the AP ELISA testing failed. This resulted in a pause in testing to troubleshoot technical issues with the assay. The experience in trying to implement this assay in other laboratories highlights the need to implement standardized QA/QC for ELISAs and other diagnostic tests across all laboratories performing testing for onchocerciasis. The presenter recommended that OTS recommend that WHO undertake outlining specific guidance for QA/QC on onchocerciasis diagnostic tools.

1.1.2 WHO Collaborating Centre approach: ELISA (by Thomas Unnasch)

Internal quality control of the OEPA ELISA relies upon the inclusion of an internal standard curve and blank wells on each plate. The standard curve is constructed using serial dilutions of a commercially available humanized monoclonal antibody developed by PATH and sold by BioRad. For a plate to pass QC it has to meet a number of criteria based upon the OD values seen in the standard curve. External quality assurance for the ELISA includes confirmatory testing in a reference laboratory using, if possible, Escherichia coli as an antigen to verify the quality of the stored DBS and external verification of the quality of the results by examination of the raw data. Challenges facing the QA/QC of the ELISA include the inability to fully break down the assay steps to localize problems and the lack of a homologous independent confirmatory assay.

1.1.3 Uganda onchocerciasis laboratory experience, 2007–2022 (by David Oguttu)

The presentation shared the experience of a laboratory dedicated to onchocerciasis elimination evaluations, and highlighted contributions, challenges and milestones the country has made towards elimination of the disease based on Ov16 and O-150 PCR analyses. It showed important quality assurance and control practices in Ov16 and O-150 sample processing.

From 1992 to 2006, annual mass treatment of communities with ivermectin achieved important reductions of O. volvulus prevalence in endemic foci of Uganda. In 2007, a national onchocerciasis elimination policy was launched and semi-annual mass treatment and vector control were adopted as key interventions. The Uganda onchocerciasis elimination Expert elimination advisory committee (UOE5EAC) was formed to guide the country in adhering to WHO guidelines along the elimination journey. Due to reduced prevalence of O. volvulus in the human population, the traditional skin snip microscopy and nodule palpation were
unsuitable in providing reliable data to support decisions on interrupting transmission and stopping MDA. The molecular laboratory was established in 2007 with support of The Carter Center. Staff were trained to carry out countrywide assessments of foci progress towards onchocerciasis elimination using Ov16 ELISA on children aged below 10 years and O-150 polymerase chain reaction (PCR) analysis of vectors and skin snips as recommended by WHO guidelines. The laboratory implements epidemiological and entomological evaluations recommended by UOEEAC every year. Our results provide essential data reviewed by the expert committee to make decisions on the status of onchocerciasis transmission in each focus. Over the many years of uninterrupted operation, the team has experience to share with other programmes on the importance of molecular laboratories in neglected tropical disease (NTD) elimination evaluations, initial problems to be anticipated and solutions, ensuring quality results, how to cope with situations of unexpected results and improve to work better.

### 1.1.4 Summary of discussions

The discussions focused on standard processes for QA/QC and validation of new and existing tests. Current WHO guidelines recommend doing a confirmatory skin snip PCR if there are less than 10 Ov16-positive children in a stop MDA study. There is a need for a homologous independent confirmatory assay. This is common practice in other areas, such as with arboreal assays developed by CDC which all rely on a first line followed by a confirmatory test. It would help reach the level of specificity necessary to detect rare events. WHO laboratory networks for other diseases exist and it might be helpful for OTS to consider lessons learnt from these networks, including their approach to quality management, QA and QC. There are logistical issues such as the difficulty obtaining RDTs or reagents. It might be helpful to develop an agreement with the providers of diagnostics/reagents for a formal process in Africa to ease the logistics issues.

### 1.1.5 Recommendations

**To WHO**

- Consult with the DTAG to provide standardized guidance for quality assurance and quality control processes.
- Consult with the DTAG to provide the criteria for validation of diagnostic tests for programmatic use and validation of test performance within individual laboratories.
- Make these guidance documents, and support for their implementation, available to countries and facilitate reporting on these processes.

**To Member States**

- In settings where skin snips are collected, programmes are recommended to also collect DBS to assess the relationship between skin snip microfilariae and Ov16 serology.

### 1.2 Blackfly qPCR

#### 1.2.1 Development of a new assay and standard operating procedures (by Steve Williams)

Global elimination of onchocerciasis is a challenge that will take tremendous effort by many agencies for many years to accomplish. The presented study aimed to make one aspect of that challenge more efficient by introducing a new qPCR assay and standard operating procedures for the molecular detection of *O. volvulus* in pools of blackfly heads. In this multi-laboratory collaborative study, researchers compared four different qPCR assays and six different, shelf-stable PCR polymerase/master mixes in order to develop
updated procedures for screening pooled blackflies. The new qPCR assay was demonstrated to provide the best combination of species-specificity, sensitivity, simplicity and cost–effectiveness and requires only 4.2 hours of labour to screen 9000 fly heads. This comparative study demonstrated that the new OvND5 qPCR assay using the HFP DNA polymerase/master mix gave the best combination of all of these attributes in testing pooled blackfly heads for *O. volvulus* (see Table 1 for results of a Cameroon field study (3); note an MDA in the region marked Day 0).

### Table 1. Cameroon field study results

<table>
<thead>
<tr>
<th>Positive detection of <em>Onchocerca volvulus</em> DNA</th>
<th>This study</th>
<th>Abong et al. (2021)*</th>
<th>This study</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH O150 and OvND5 assays</td>
<td></td>
<td>O-150 LAMP</td>
<td>OvActin qPCR</td>
</tr>
<tr>
<td>Day 0</td>
<td>15/15 (100%)</td>
<td>5/15 (33%)</td>
<td>4/15 (26.7%)</td>
</tr>
<tr>
<td>Day 30</td>
<td>16/17 (94%)</td>
<td>7/17 (41.2%)</td>
<td>4/17 (23.5%)</td>
</tr>
<tr>
<td>Day 90</td>
<td>22/30 (73%)</td>
<td>8/30 (26.7%)</td>
<td>11/30 (36.7%)</td>
</tr>
<tr>
<td>Day 180</td>
<td>10/14 (71%)</td>
<td>4/14 (28.6%)</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>Day 270</td>
<td>34/53 (64%)</td>
<td>23/53 (43.4%)</td>
<td>20/53 (37.7%)</td>
</tr>
<tr>
<td><strong>Positive pools</strong></td>
<td>97/129 (75%)</td>
<td>47/129 (36.4%)</td>
<td>43/129 (33.3%)</td>
</tr>
</tbody>
</table>

* See reference (3).

OvND5 and NIH O150 assays were concordant on 125 of the 129 samples (97%). All O-150 PCR-ELISA positive results were also positive with OvND5 and NIH O150 assays. There was one false positive with the O-150 PCR-ELISA and one with the OvActin qPCR.

This OvND5 qPCR assay with all reagents delivered at ambient temperature to local laboratories will minimize logistical challenges while avoiding the high costs of cold chain shipping and potentially expensive losses when delays occur, freezers break down or power is interrupted. In addition, a qPCR assay done in sealed microtiter plates has the advantage of greatly reducing the chances of sample-to-sample or general laboratory contamination, since the concentrated PCR amplification products are never opened in the laboratory. This optimized and standardized OvND5 qPCR protocol for the monitoring of *O. volvulus* in vector blackflies in endemic countries will contribute to more timely processing of samples, more reliable results and reduced delays in programmatic decision-making. Using these newly developed procedures, a network of laboratories will be trained to use the new methodology and will be able to handle the significant load of blackfly molecular xenomonitoring. The currently used O-150 PCR-ELISA methodology has been very important to *Onchocerca* elimination efforts, but to deal with the large backlog of blackfly pools it is important to modernize and update to a more efficient method that will be critical to the success of onchocerciasis elimination programmes. Standard operating procedures have been prepared, and with these standardized approaches and stable reagents now available, the network of laboratories supporting molecular xenomonitoring to detect the presence of onchocerciasis in communities can be enlarged as needed to provide those responsible for eliminating onchocerciasis with the reliable data needed to aid in MDA decision-making and post-MDA surveillance.

### 1.2.2 Quality assurance for PCR/qPCR (by Nils Pilotte)

While capable of providing increased sensitivity and specificity of detection, nucleic acid amplification tests require proper quality assurance (QA) and quality control (QC) measures in order to ensure the accuracy of results obtained during testing. Proper QA ensures that there is confidence in testing results, and includes procedures such as training, qualification, results monitoring and periodic proficiency assessment. QC focuses on the validity of individual test results and ensures that data used for programmatic decision-making are valid and of the highest possible quality. In this brief presentation, the proposed QA/QC...
measures for use with the OvND5-targeting qPCR were discussed, with an emphasis on training and post-training requirements and the importance of an effective and appropriate internal extraction, recovery and amplification control. An understanding of these procedures is critical to the interpretation of experimental results and the use of such results for programmatic decision-making processes.

1.2.3 Summary of discussions

The committee agreed that the results of the studies were very promising. The discussion centered around the need for external laboratory evaluations of the new OvND5 real-time qPCR protocol and comparisons with the conventional assays, including the O150 ELISA PCR. The presenter noted that existing work has shown that users can be easily trained to work with the new protocol successfully, but that this has not taken place in national laboratories where common challenges may arise. The presenter also stated that there are conversations ongoing with the The Task Force for Global Health about training African laboratories conducting field comparison studies, with the first planned for Mali in early 2023. It was suggested that countries should be encouraged to share their experiences with the new protocol, and that country learnings be captured in a standardized way so that comparisons can be clearly made across sites.

The committee formally recommended that WHO encourage the planning of additional field studies to compare the new OvND5 qPCR protocol with conventional entomological laboratory approaches.

There was also discussion regarding the entomological threshold for stopping decisions, and whether this would need to be reevaluated given the apparent increased sensitivity of the OvND5 qPCR. There is a possibility that the OvND5 would yield a higher percentage of pools than the O-150 PCR, which could cause confusion in a setting where the stopping threshold was met with the O150 PCR but not the OvND5, for example. There are ongoing efforts to assess the performance of the OvND5 assay. It was noted that the assay may be picking up residual DNA in the thorax of the flies from degraded microfilaria, which could be one cause for the increased sensitivity. Going forward it will be necessary to investigate this carefully and potentially adjust some of the cut-offs for positivity in the assay. The question about recalibration of the assay will become clearer once data are available from operational research studies in African laboratory settings. The presenter recommended that a group of experts be convened – as was done during the planning of the presented studies – to discuss the potential need to recalibrate the assay and questions around the thresholds for stopping. Finally, it was noted that the role of the DTAG on this topic is yet to be determined. The committee recommended that WHO investigate whether a target product profile for PCR (which was not done previously) is needed, or whether it is sufficient to adhere to forthcoming recommendations from the DTAG for validation criteria of new diagnostics.

1.2.4 Recommendations

To WHO

- Noting the importance of high quality diagnostic tools to achieve and sustain the elimination of onchocerciasis, WHO and DTAG are encouraged to work together to shepherd the development and validation of the new tools critically needed by programmes.
- Given the promising results of blackfly qPCR, in terms of its ability to detect infective flies, to reduce the complexity of the testing process and to provide results with less personnel time, OTS recommends that WHO anticipate the development of a new WHO guideline.
- Work with the onchocerciasis subgroup of DTAG to develop preferred product characteristics for the reagents needed for molecular testing for onchocerciasis, both in blackflies and in humans, recognizing the importance of standardizing the performance of PCR assays.
- Facilitate the strengthening of laboratory capacity for these tools and other diagnostics through the DTAG initiative on building laboratory capacity.
To diagnostic developers

- Continued work on development of a new qPCR should ensure that the protocols developed can be feasibly implemented in endemic-country laboratories (paying particular attention to challenges in procurement of reagents and maintenance of equipment) and should examine whether the entomological criterion for stopping MDA needs to be adjusted to reflect the analytic sensitivity/performance of the new test(s).

To Member States

- The new blackfly qPCR protocols and their accompanying quality assurance and quality control procedures are recommended to be piloted for implementation in laboratories in endemic countries.
- National programmes should also capitalize, where possible, on capacity already built as part of the COVID-19 response and other new or ongoing laboratory initiatives in their respective countries.

1.3 Procurement challenges

1.3.1 Ov16 RDT and SD ELISA (by Penny Smith)

An initial working group of procurers for the Abbott Ov16 RDT, and potentially the SD ELISA, has been convened to explore a relationship with Abbott on their OV diagnostic products, to ensure all procurers receive the same pricing and production timing as they do under the FTS long-term agreement. The initial understanding is that Abbott’s RDT and SD ELISA co-development agreement with PATH ends this month; Abbott has initiated discussions with PATH on extending the agreement, but no further information is available currently. Abbott would like to see US$ 1 million in total OV procurements each year to keep their OV diagnostics in production, including at least 10 000 RDT kits per year. In anticipation of a discussion with Abbott about establishing a long-term agreement, the working group is developing a forecasting table for RDT and ELISA, looking at 3–5 years, to be available in Q1 of 2023.

1.3.2 LoaScope update (by Lee Hundley)

The LoaScope, a handheld mobile device used to measure Loa loa microfilaria in whole blood, has to date been used only for operational research purposes in a few settings. A new version of the LoaScope that improves upon the previous designs has been developed and requires validation in the field before it can be used for larger scale mapping studies. Supply chain issues during the course of the COVID-19 pandemic delayed production of the first 10 devices for more than a year. The devices have recently been assembled and are being shipped to Cameroon where the field validation will take place under the supervision of Dr Joseph Kamgno and his team at the Centre for Research on Filariasis and Other Tropical Diseases (CRFilMT). Additional devices are currently being manufactured and will be used in Loa–Onchocerca mapping operational research studies supported by the Coalition for Operational Research on Neglected Tropical Diseases (COR-NTD), tentatively planned to begin in late 2023.

1.3.3 Summary of discussions

Following the presentations there was a brief discussion on procurement challenges related to the SD Bioline Ov16 from Abbott. It was noted by several members that there have been challenges acquiring the tests in a timely manner, and that there is confusion about whom to contact to purchase tests. Some believed that RDT orders have to go directly through Abbott (rather than SD Bioline), while others have worked with an SD Bioline in-country procurer to secure tests within a given country. The consensus was that greater emphasis needs to be placed on ensuring that countries have access to diagnostics required for programmatic activities, ideally directly from the manufacturer. For new diagnostics, plans for country access should be determined during the development and validation process. Particular emphasis was
placed on ensuring access to the SD Bioline Ov16 RDT, as it is currently recommended for several key programmatic decisions.

1.3.4 Recommendations

To WHO

- Explore mechanisms for producing the reagents and supplies needed for the qPCR, Ov16 RDT and buffer as well as for ELISA diagnostics within Africa to help ease supply chain issues; such consideration should be part of the process of development of new tests.
- It is imperative that countries have access to the necessary equipment, reagents and supplies needed to carry out the diagnostics required for programmatic action. As new diagnostics are introduced, plans for country access must be formalized during the development and validation process.
2. Onchocerciasis modelling updates

2.1 NTD Modelling Consortium
(by Graham Medley and Mutono Nyamai)

The NTD Modelling Consortium presented a consensus statement on the current modelling evidence for onchocerciasis (Annex 3). The statement focuses on the questions of expected duration until elimination and the potential role of moxidectin. Time to elimination cannot be predicted exactly, but indicative times can be calculated for different circumstances, for example the median time to elimination is about 15 years for settings with moderate endemicity and current treatment programmes. The consensus is that use of moxidectin will reduce the time to elimination by ¼ – ½ depending on setting. The use of multiple models allows the uncertainties in underlying decisions to be better defined.

To understand factors underlying achievement of elimination of transmission and reported risk of infection resurgence, a systematic review and meta-analysis of onchocerciasis studies in Africa was conducted, assessing onchocerciasis transmission status after at least 10 years of ivermectin mass drug administration (MDA) with or without vector control. Of the 2960 studies identified through database searches, 63 studies covering 231 foci were included in the systematic review. Based on the WHO 2016 (1) and African Programme for Onchocerciasis Control (APOC) 2010 (2) guidelines, 20 (8%), 64 (28%) and 147 (64%) of the foci were classified as having achieved elimination of transmission (EOT), close to elimination or with ongoing transmission, respectively. Meta-regression analysis showed systematic non-adherence of > 5%, forested ecological areas (compared with savannah) and holoendemic status at baseline (compared with hypo-endemic status) were associated with less likelihood of achieving EOT. At least 10 years of continuous ivermectin treatment reaching 80% or more of the eligible population, and 14 years or more of ivermectin treatment in the West and East African region (compared with Central Africa) were associated with increased likelihood of EOT. None of the five foci that had achieved EOT and conducted post-transmission surveillance had reported resurgence of infection. The study highlights the importance of improving therapeutic coverage, reducing systematic non-adherence and requirement for long-term interventions to achieve EOT, especially in areas with high baseline endemicity.

2.2 Summary of discussions

The discussions were on the modelling comparison of distribution between ivermectin and moxidectin. Coverage might be improved with the new medicine which would decrease time to elimination and motivate the community. However it could also be the opposite, with issues of moxidectin acceptance in the field, which would decrease coverage. Clear WHO recommendations encouraging countries to use moxidectin would be helpful. Climate change could affect the vectors and their distribution, and extreme weather events could disrupt MDA delivery.

2.3 Recommendations

To WHO

- Encourage programmes to investigate the extent of systematic non-participation in MDA during coverage surveys and other evaluations.
Endeavour to learn from other NTD programmes (e.g. lymphatic filariasis elimination programmes) with experience investigating this issue.

To Member States

- Given the importance of understanding systematic the impact of non-participation on the probability of a programme achieving elimination of transmission, programmes should explore ways to capture this information during routine programmatic MDA activities (such as, pilot testing the use of biometric tools to track participation year-to-year).
3. Moxidectin

3.1 Systematic review (by Dziedzom de Souza)

The elimination of transmission of onchocerciasis requires new approaches to address existing challenges, including the need for new and effective treatments. The current medicine (ivermectin) only temporarily stops the adult female worm from producing microfilariae. In some settings, resistance to ivermectin has also been reported following years of treatment. A new medicine (moxidectin) has been developed and shown to be a safe and effective alternative to ivermectin, with various trials ongoing. To assess the safety and efficacy of using moxidectin to treat entire populations in areas endemic for onchocerciasis, a systematic review was conducted, the report of which is included in a separate Web Annex to this document.

To assess the efficacy, different databases were searched for randomized controlled trials (RCTs) assessing the impact of single treatments of ivermectin and moxidectin in onchocerciasis and other helminth populations. Publications on pharmacokinetic studies were also included for safety assessments. The data from these studies were extracted, analysed and presented in Forest plots and tables. The certainty of the evidence, for the outcomes of interest, was assessed only for the included RCTs, using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach. Only PICO (Population, Intervention, Comparator, Outcome) question 1 and annual treatment with moxidectin could be effectively addressed in this review. Two RCTs in individuals aged 12 years and older were included in the review. In these studies, the overall outcome of 8 mg moxidectin was significant compared with 150 mg/kg ivermectin at 6 and 12 months. In both studies the proportion of undetectable skin microfilaria density (SmfD) rose gradually until the 6 months assessment period in the moxidectin group. Beyond 6 months, the proportion of the population with undetectable SmfD started declining. In the ivermectin group the duration of clearance was 1 or 2 months post-treatment. Pooled analysis from the two RCTs showed increased odds in skin microfilaria clearance post-treatment in the moxidectin group compared with the ivermectin group (odds ratio [OR]: 2.81; 95% confidence interval [CI]: 0.95–4.68; medium quality of evidence). The safety profile was similar between both treatments and was insignificant. Pooled analysis from the two RCTs showed that there was no significant difference in the occurrence of adverse events among community members post-treatment between the moxidectin and ivermectin groups (OR: 0.43; 95% CI: -1.64 to 2.5; medium quality of evidence). The evidence supports the use of moxidectin for the control of onchocerciasis in endemic populations. However, no added impact of moxidectin was observed in Strongyloides stercoralis, Trichuris trichiura, Schistosoma haematobium and S. mansoni and other helminth populations. Other clinical trials are ongoing, the data from which could help strengthen the evidence and address other PICO questions. The available data provide evidence to initiate a formal review by a guideline development group and systematic review team established by WHO, towards the recommendation of the use of moxidectin for the mass treatment of onchocerciasis in endemic populations.

3.2 Results of a paediatric pharmacokinetic and safety study and proposed dose selection (by Sally Kinrade)

The outcomes of a moxidectin paediatric pharmacokinetic and safety study (MDGH-MOX-1006) to support identification of a dose for treatment of children aged 4–11 years for onchocerciasis were presented. The purpose of this single dose study was to determine a dose of moxidectin for use in children aged 4–11 years that achieves exposures in the range observed in adults administered a dose of 8 mg and provide information on which to base dosing recommendations. Thirty-six Ghanaian children aged 4–17 years
completed the study. Moxidectin dose administration was a single dose of 8 mg (cohort I; 12 to 17 years), 6 or 8 mg (cohort II; 8 to 11 years), and 4 mg (cohort III; 4 to 7 years).

Fig. 1 shows the mean concentration-time profiles for cohorts I, II and III presented together with those obtained previously in *O. volvulus* infected adults after an 8 mg dose as well as those obtained in uninfected adults receiving a 36 mg moxidectin dose (the highest dose evaluated in healthy adults and which did not raise any safety concerns).

![Figure 1](image)

The pharmacokinetic analysis of all available pharmacokinetic data in conjunction with all relevant safety data and to support simplicity of dose administration in the field settings has resulted in proposed selection of the following doses for children to achieve exposures comparable to those for which efficacy and safety have been shown in ≥ 12-year-old individuals:

- 8 mg (4 x 2 mg tablets) for children aged 8−11 years (the dose approved by the United States Food and Drug Administration for use in individuals aged ≥ 12 years); and
- 4 mg (2 x 2 mg tablets) for children aged 4−7 years.

### 3.3 Update of ongoing clinical studies in onchocerciasis (by Sally Kinrade)

An update on progress with the repeat dose efficacy and safety study (MDGH-MOX-3001) in people with high levels of onchocerciasis skin microfilariae and large single-dose safety study (MDGH-MOX-3002) in people with and without detectable infection living in endemic communities, comparing treatment with moxidectin or ivermectin, was also presented. To date, 263 of a reduced target of 320 participants have been enrolled to study 3001. More than 5200 participants aged ≥ 12 years are enrolled in study 3002. These studies are being enrolled concurrently in the Democratic Republic of the Congo. A second site for study 3002 will commence in early 2023 in Côte d’Ivoire to achieve a total enrolment of approximately 12 500 (10 000 to receive moxidectin). Both studies are progressing well, with no serious adverse events assessed as related to treatment with moxidectin or ivermectin reported to date. Amendment to study
Moxidectin treatment in all relevant age groups.

3.4 Key outputs on moxidectin use cases from the COR-NTD annual meeting breakout discussion (by Lee Hundley)

This year’s annual meeting of COR-NTD featured a breakout session titled “Moxidectin—a new tool for accelerating onchocerciasis elimination?” The session featured several speakers who highlighted the existing evidence and ongoing field studies, the status of WHO guidance development, and countries’ experiences with considering moxidectin as a possible solution in their elimination efforts. The session also included three breakout discussions on the topics of country concerns, evidence needed by WHO to issue formal guidance, and identifying where moxidectin would add the most value.

The session highlighted the need to formally identify the use case (or use cases) for moxidectin and determine precisely where moxidectin will add the most value, in addition to establishing the business case. There is also a need to quantify the number of people that could benefit from moxidectin in areas that are deemed to be suitable for its introduction.

The breakout discussions yielded several suggestions for possible use cases, including:

- high transmission hot spots, or highly hyper-endemic areas;
- untreated endemic areas;
- implementation units where biting rates are increasing;
- insecure areas; and
- areas with high seasonality of transmission.

It was noted that moxidectin would be most appropriate in areas where relatively few rounds of MDA have been conducted in order to minimize the disruption of introducing a new treatment. Where treatment has been delivered, it was also noted that moxidectin would be best suited in settings where programmes have achieved effective coverage.

3.5 Planned process for implementing pilot field projects with moxidectin (by Sally Kinrade)

Although OTSS considered in December 2021 a proposal to commence pilot implementation projects with moxidectin, these have been slow to proceed. MDGH is now planning to take a proactive approach to identify interested countries with suitable locations for implementation of such pilot field projects. MDGH outlined the objectives for these projects (including to generate data on feasibility and acceptability of implementing moxidectin and test information and training materials), the proposed parameters for area selection, how MDGH will partner countries and support such projects with supply of moxidectin, provision of regulatory documentation, content for training materials and development of social research tools. The OTS was asked to consider the proposed approach and was requested to offer feedback on the plan in order to assist countries in their consideration of moving forward to implement moxidectin in defined areas through pilot field projects. MDGH anticipates that site identification and planning for the projects will be undertaken in 2023, with implementation commencing in 2024.

3.6 Summary of discussions

It was noted that so far there had not been any adverse events related to the 36 mg dose in adults, so there are no particular concerns for adverse events among children taking higher doses of 8 mg in upcoming
trials. A question was posed regarding whether moxidectin could be pilot tested in areas co-endemic for *Loa loa* or lymphatic filariasis. The presenters indicated that safety data are still being collected for both infections, so for the time being co-endemic areas will have to be avoided. Particular caution will need to be taken in areas highly endemic for *Loa loa*, as there is a concern that moxidectin could have adverse effects similar to ivermectin among patients with high burdens of *Loa* microfilariae. There was discussion about the added value of administering moxidectin biannually and its impact on suppressing microfilariae, and whether there would be a differential response in low prevalence settings. Existing data suggest that a repeated dose every 6 months would be ideal for suppression, but there may be settings where every 12 months is sufficient, particularly in areas with low burden of disease. Ongoing studies will provide more data on the benefits of 6-month versus annual treatment. It was also noted that the 2022 paper by Bakajika and colleagues (4) provides some insight on the subject of differential impact in hypo- versus meso-/hyper-endemic settings.

The question of a cost analysis was raised. The presenters anticipate that overall the cost will theoretically be lower than ivermectin given the fewer number of rounds required to reach elimination. From a programmatic perspective the costs would be similar to those for ivermectin. The medicine itself cannot be donated by Medicines Development for Global Health (MDGH) on its own behalf (it can be given at cost or additional cost), so work will be needed to identify ways to make it widely available in the field, which will take some time. If the medicine could not be donated, then programmatic costs would increase.

There was a discussion about potential use cases for moxidectin. It was agreed that moxidectin would be valuable in hot spots where endemicity was driven by high transmission potential rather than poor treatment coverage. Hypo-endemic areas were also discussed as a possible use case, with the caveat that many of these areas are co-endemic for loiasis, and that there remains a question of whether annual moxidectin would be sufficient to achieve elimination in hypo-endemic areas where twice yearly treatment may be hard to justify. Untreated areas, where moxidectin could have a positive impact on skin manifestations, and mobile populations were also identified as possible use cases. It was stressed that high treatment coverage will be critical for the introduction of moxidectin.

Following the presentation on pilot field projects, the discussion centered on two questions posed by the presenters to the OTS. The first was whether the committee supports the proposed approach for progressing moxidectin pilot field projects, treating all children aged 4 years and older. It was clarified that the aim of the pilots was to assess feasibility, acceptability and safety. The intent is not to assess population-level impact, though MDGH is open to working with countries that are interested in pursuing impact assessments. Members agreed that the pilots should move forward, and also recommended that safety data in children from the ongoing study in the Democratic Republic of the Congo be reviewed and shared with potential pilot sites to assuage country concerns about safety among children. It was noted that the process of ultimately getting moxidectin to the field as a viable treatment option will be lengthy, and that conversations about how to make the medicine available to countries and navigate the importation and regulatory approval processes should begin now, rather than waiting until pilot projects are complete. The importance of working with countries with strong pharmacovigilance was also stressed, and the OTS recommended that WHO support MDGH in identifying these countries and engage its pharmacovigilance unit to strengthen the relevant national systems.

The second question posed to the OTS was whether there are any areas or area selection criteria that the committee recommends be considered for undertaking the pilot field projects. As with the previous discussion around use cases, it was agreed that hot spots or hyper-endemic areas would be ideal, particularly in settings where programmes had funding and infrastructure to support the roll-out. Hypo-endemic areas were also recommended, with the recognition that these settings may require external funding and additional support. Initial pilot sites should be non-endemic for both loiasis and lymphatic filariasis, but co-endemic areas (particularly co-endemic loiasis) should be considered once safety data are available. Mobile populations were noted as a priority group once more, but it was agreed that this may not be technically feasible for the initial pilot studies.
3.7 Recommendations

To WHO

- Work with MDGH and experts to develop a prioritized list of data-driven use cases for moxidectin (e.g. hot spots where ongoing transmission is due to high transmission potential and not poor programme coverage; hypo-endemic areas; mobile populations) so that countries can identify appropriate settings and start to plan for moxidectin use.

- OTS agrees with MDGH’s plan to collect information of the cost of starting and maintaining moxidectin MDA and to study the acceptability of the medication in populations who have become accustomed to receiving ivermectin.

- Does the committee support this proposed approach for progressing moxidectin pilot field projects, treating all aged 4 years and older?

  1. Conducting additional pilots of moxidectin in the context of routine onchocerciasis elimination programmes is important and would generate valuable data for countries looking to add moxidectin as an additional tool for achievement of the WHO road map elimination targets (5).

  2. The committee supports moving forward with the planning of the pilot projects. Safety data from paediatric participants (children aged 4–11 years) in the ongoing trial in the Democratic Republic of the Congo should be reviewed before making a final go/no-go decision for inclusion of children in this age group in its planned pilot studies of community-based moxidectin MDA, noting that there are fewer children in the site in the Democratic Republic of the Congo than in the Côte d’Ivoire site where data will not yet be available.

  3. WHO, MDGH and partners are recommended not to wait until the end of the next series of pilots to start discussions related to making moxidectin available for programmatic use and the importation process; these discussions will take time and the feasibility of moxidectin as a programmatic tool is dependent upon their resolution.

- Are there any areas or area selection criteria that the committee recommends be considered for undertaking such pilot field projects?

  1. OTS agrees with the inclusion criteria specified in the briefing document for the sixth meeting of the OTS for the community-based MDA pilot, which would focus on piloting in meso/hyper-endemic areas with good baseline ivermectin MDA coverage. These areas should be non-endemic for loiasis until additional safety data are available. Areas co-endemic for lymphatic filariasis should not have an active treatment programme (requiring co-administration of albendazole) at the same time as undertaking a pilot project with moxidectin.

  2. Countries with strong pharmacovigilance should be targeted for pilot projects. OTS recommends that WHO support MDGH in identifying these areas and to engage its pharmacovigilance unit to help strengthen the relevant national surveillance systems.

  3. If funding permits and safety data are available from *Loa loa* safety trials, pilot projects should also be considered in onchocerciasis meso-/hyper-endemic settings co-endemic with loiasis that have been treated with ivermectin for a number of years and have effective systems to detect and manage loiasis-related adverse events.
4. National onchocerciasis elimination committees: country updates

4.1 Nigeria (by Bertram Nwoke)
The Nigerian NOEC was inaugurated in 2015 with the following terms of reference: (i) provide technical advice on onchocerciasis elimination to the Federal Ministry of Health; (ii) support the Government of Nigeria to develop a national guideline and road map for onchocerciasis elimination in Nigeria; (iii) assess where and when breakpoints have been reached and recommend to the Honourable Minister of Health the localities where ivermectin treatment can be safely stopped; and (iv) support the government in the preparation of the country’s dossier for verification of Nigeria as having interrupted transmission of onchocerciasis infection nationwide.

The NOEC of Nigeria has produced impressive results over the past seven years (2015–2022): 1. Brought to focus the map of Nigeria showing the pre-control onchocercal nodule rate; 2. Collated the available recent and historic onchocerciasis epidemiological and entomological data in 2015; 3. Created tables for each transmission status and indicated the implementation strategies to achieve interruption/elimination of onchocerciasis; 4. Developed a map of Nigeria showing transmission status colour code by States based on historical epidemiological and entomological data; 5. Produced the National Guidelines for elimination of onchocerciasis in line with WHO guidelines to create a road map to eliminate onchocerciasis; 6. Produced the nationwide provisional sample sites to guide the epidemiological and entomological evaluation for the elimination of onchocerciasis; 7. Undertook onchocerciasis elimination mapping (OEM) in all the transmission zones and reclassified the transmission zones in view of emerging results; 8. Undertook operational research to assess the prevalence of Loa loa infection and risk of central nervous system events, especially in ivermectin-naive transmission zones; 9. Assessed where and when breakpoints have been reached and recommend to the Honourable Minister of Health the localities where ivermectin treatment can be safely stopped.

Onchocerciasis has been eliminated in two States and transmission interrupted in four States, and a total of 10.2 million people from 58 local government areas are no longer in need of MDA for onchocerciasis. A strategic plan and activities to align with the 2020–2030 plan to end onchocerciasis in order to attain the Sustainable Development Goals has been established.

4.2 Uganda (by Thomas Unnasch)
The Uganda Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) was formed in 2008 following Uganda’s 2007 commitment to eliminate onchocerciasis. The first such committee in Africa, it was modelled on the Program Coordinating Committee and Interamerican Conference on Onchocerciasis of the Onchocerciasis Elimination Program for the Americas. The UOEEAC serves as an advisory body to the Uganda Ministry of Health, which has the final decision on the programmatic recommendations made by the UOEEAC. The committee is composed primarily of Ugandans, with a small number of external experts also serving as members. The UOEEAC meets once a year in Kampala, in a meeting that includes invitees from the Ministry of Health, the local elimination teams and representatives from the Democratic Republic of the Congo and South Sudan. The primary tools the UOEEAC uses to visualize the progress towards
elimination are the onchocerciasis flag and the onchocerciasis map, which colour code foci based upon current transmission status. Currently, these show great progress towards elimination, with transmission suppressed, interrupted or eliminated in all 17 foci in the country.

The UOEEAC has played an important role in guiding the effort to eliminate onchocerciasis from Uganda. It has developed recommendations that have been implemented by the Ministry of Health on ways to verify elimination in foci where vector control has eliminated the blackfly population, how to approach verification of elimination of onchocerciasis in foci co-endemic with lymphatic filariasis, and has facilitated collaborations with the elimination programmes in the Democratic Republic of the Congo and South Sudan. The committee continues to advise the Ministry of Health on ways to address challenges facing the programme, including cross-border issues, refugees and formulating plans for monitoring for potential resurgence in the post-elimination era.

4.3 Côte d’Ivoire (by Hugues N’Gassa)

The NOEC was created in January 2018 by a ministerial decree and is made up of a president, a vice-president, a general secretariat and members (entomologists, epidemiologists and members of the programme and then a WHO representative). The committee meets once a year and, whenever needed, an extraordinary session is convened by the president with themes proposed by the programme. The decision-making process is as follows: the national NTD programme organizes a thematic meeting. Data relating to the theme are presented. The NOEC analyses the data relating to the theme and makes recommendations which are taken into account by the responsible Ministry of Health. The following is a summary of recommendations provided at the last NOEC meeting:

- Maintain treatment in endemic districts with required coverage rates (100% geographical coverage and at least 65% therapeutic coverage).
- Update the mapping of breeding sites throughout the country.
- Conduct OEM in districts that were not eligible for treatment.
- Integrate epidemiological assessments of onchocerciasis during transmission assessment surveys (TAS) for lymphatic filariasis in all districts.
- Review onchocerciasis control from 1955 to date and use the results to produce publications.
- Recruit a consultant to develop the onchocerciasis elimination plan.
- Organize a validation workshop for the onchocerciasis elimination plan.
- Disseminate the onchocerciasis elimination plan within 6 months.
- Advocate with WHO to make Ov16 tests and biplexes available to the country for OEM.

4.4 Summary of discussions

In this session, NOEC working procedures and best practices were discussed. Countries are implementing the WHO 2016 guidelines and translating them into the national context. Discussions focused on how NOECs could be supported to harmonize way of working, share best practices and ensure that rich data and discussions from these expert meetings are not lost. There is no one-size-fits-all approach given that each country has a unique situation and knows its situation best. Countries that are not as far along in their elimination efforts can benefit from reviewing the results of other countries. The suggestion is to standardize the way information is reported and shared from these committees. This will be particularly relevant for other countries in the same region that may be able to learn from what is taking place in the region. Creating a simple format for reporting could help facilitate this. WHO should help strengthen regional networks. Key areas of concern are cross-border issues and how to treat refugee populations. These and other concerns should be discussed by NOECs jointly and lessons learnt should be summarized in standardized reports.
supported by WHO. WHO, with the support of OTS, should provide recommendations (not a mandate) to countries on how NOECs should be established and maintained, and what the minimum reporting outputs of the NOEC meetings should be. A publication featuring the proceedings and recommendations of NOEC meetings will be useful and facilitate sharing of experiences among countries.

4.5 Recommendations

To WHO

- Engage with the chairs of the NOECs at regional and/or subregional levels to develop a system for sharing best practices across countries for issues of concern to national onchocerciasis programmes (e.g. treatment of refugee and mobile populations and cross-border issues). OTS recommends that WHO seek funding in order to convene a meeting of NOEC chairs to share lessons learnt across the African Region.
- Consider establishing subregional groups that include NOEC chairs and national programme leadership to allow more rapid and sustainable sharing of knowledge among country committees in West, East, Central and South African regions.
- Develop a system, with the input of the chairs, for sharing national onchocerciasis elimination plans and the annual reports generated by the NOECs in a standardized manner. These NOEC reports, with country permission, might then be shared with WHO and, more broadly, with other NOECs and onchocerciasis programmes in the Region.
- Create a repository for annual reports from the NOECs.
- Continue to encourage NOECs to be established as described in WHO guidelines: the committee should be independent from the national programme and comprise national and international experts, in accordance with practice in some countries in Africa. This committee can be embedded in any existing national committee for NTD activities or onchocerciasis-specific matters. NOECs should strive to be independent bodies.
- Formalize a communication mechanism between the OTS and the NOECs to help ensure that priority concerns are addressed.
5. Monitoring and evaluation

5.1 Use of Ov16 RDT in onchocerciasis elimination mapping in the United Republic of Tanzania (by Clara Jones)

The United Republic of Tanzania conducted OEM countrywide by implementing a district-by-district exclusion process. The process identified 15 districts which either bordered known onchocerciasis-endemic areas under MDA where transmission is ongoing or had environmental features conducive for blackflies. The programme conducted river prospection for breeding sites and selected five first-line villages for blood sample collection in the districts. The diagnostic tool used was Ov16 RDT. Out of the 15 districts, eight districts were to conduct TAS; therefore OEM was integrated with TAS. The integrated survey was conducted in two steps: the first step was a community-based survey and the second step was a school-based survey. Step one involved collection of DBS from adults aged 20 years and older from first-line villages. A total of 100 individuals were tested from each village. A threshold of 5% positivity was set whereby above the threshold onchocerciasis MDA was warranted and below the threshold the second step, which included analysing DBS from children aged 6–9 years sampled from 30 clusters, was warranted. The programme also conducted OEM in four districts by testing individuals aged 20 years and older from 25 villages per district (five purposely selected and 20 randomly selected). The findings indicated that there is a likelihood of exposure in these four districts; therefore, the programme will collect DBS from children aged 5–9 years to establish if there is ongoing transmission. The positive cases were detected from both first-line villages and randomly selected villages. Based on these findings, four districts will conduct stage 2 of OEM (testing children aged 5–9 years) and one district will start MDA in 2023.

Some of the challenges with Ov16 RDT procurement include: having a single supplier, which makes it difficult to acquire it in the market in a short timespan; the short shelf-life of the kits, which is usually 12 months; delays in clearing the consignment once in country, which poses a risk as kits may expire before they can be used; and the uncertain sensitivity and specificity of the diagnostic tool, which arises from no independent evaluation studies having been done in similar epidemiological settings.

5.2 RDTs for routine monitoring and evaluation in Benin (by N’Deye Marie Bassabi Alladj)

The fight against onchocerciasis in Benin has gone through several phases since the closure of the Onchocerciasis Control Programme in West Africa (OCP) and APOC. New diagnostic impact assessment methods including Ov16 have been adopted by Benin. Since the endorsement of the London Declaration on Neglected Tropical Diseases in 2012, Benin, with the financial and technical support of partners, has resumed epidemiological assessments in the context of this fight. From 2013 to 2015, the epidemiological evaluation was carried out by skin biopsy followed by the migration survey of these positive cases from 2013 to 2015, which revealed that all positive people, including children aged under 10 years, have not spent long stays outside the assessment area. In 2017, based on the recommendation of the committee of experts for the elimination of onchocerciasis, the evaluation of seroprevalence with Ov16 was carried out in 60 villages, which made it possible to examine 2780 children with a very high seroprevalence (i.e. 226 cases). Unfortunately, the positive cases had not been confirmed by ELISA. In 2020, an epidemiological evaluation was carried out in 107 villages out of 10 685 children with Ov16 RDTs under laboratory conditions. During this evaluation, 10% of the samples including all positive cases were confirmed by ELISA. The process of
transporting reagents for carrying out laboratory analyses constitutes a real challenge for public health programmes in view of the experience of Benin.

5.3 Summary of discussions

In the United Republic of Tanzania, there were some areas with very few positive cases in the first-line villages; most of which came from the second-line/randomly selected villages. The random sample seems to suggest that restricting MDA to first-line villages is risky, even if they still give a good signal. Benin did not make a decision on the programmatic side because after 2 years they are still waiting for confirmation on ELISA results. The experts discussed which improvements in RDTs would be beneficial to both programmes. The committee suggests that short-term solutions need to be found so that programmes are not penalized by long lags in procuring diagnostics and can make decisions in a timely manner. It is encouraged that RDT on DBS be used as the primary tool for routine monitoring and evaluation.

5.4 Recommendations

To WHO

- Work with manufacturers and suppliers to improve the logistics process and facilitate access to RDTs and reagents.
- Prepare guidance (or gather best practices) for using RDT on DBS for routine monitoring and evaluation; OTS recommends using SD Ov16 RDT on DBS as the primary tool for routine monitoring and evaluation.
6. Stop MDA threshold study updates

6.1 United Republic of Tanzania (by Akili Kalinga)

The WHO guidelines (1) recommend that MDA should be stopped if it is demonstrated that the Ov16 ELISA seroprevalence in children aged below 10 years is < 0.1% (at the 95% upper confidence limit). However, 0.1% is hard to measure in many settings in endemic countries. Recent modelling has suggested further investigation of the use of > 0.1%, and preferably < 2%, which might be sufficient to determine stopping MDA. Therefore, this study aims to evaluate whether MDA can be safely stopped at a serological threshold of > 0.1%. The study was done in three phases: phase 1 was completed in 2021 and involved full Ov16 evaluation in 20 randomly selected villages to determine seroprevalence of < 2%. An entomological study was simultaneously conducted in the same focus by collecting blackflies for O-150 PCR methods to detect infectivity rate that will guide the decision on the seroprevalence study. The seroprevalence threshold of < 2% was achieved and MDA was stopped in the area. Due to supply chain difficulties and travel restrictions, we were unable to provide complete phase 1 results before starting phase 2 in 2022. The study results had met the serological criteria (seroprevalence of 1.1%) for stopping MDA (< 2%). However, the entomological results were unclear because the number of positive pools of blackflies was significantly higher than that obtained during a previous (2015–2016) study in the same study area. In the researchers’ opinion, possibly an infected population of blackflies has migrated into Tukuyu focus from another transmission zone. Alternatively, possibly blackfly samples were contaminated in the laboratory, for which a molecular evaluation is ongoing to determine whether the samples were contaminated. For the time being the researchers agreed with the national NTD control programme to delay MDA in the study areas to understand the above scenario by collecting more blackflies for further analysis (6).

6.2 Ghana sites 1 and 2 (by Joseph Opare)

Onchocerciasis is endemic in 138 districts in Ghana and these districts have been treated with ivermectin for more than 20 years. An assessment in 2017 indicated that the prevalence of the disease has decreased drastically to < 0.1% in many endemic areas and there is a need to stop treatment for onchocerciasis in these areas. The WHO guidelines (1) require demonstration of < 0.1% seroprevalence of Ov16 antibody using ELISA in children aged 5–9 years. Additionally, less than 1/2000 blackflies can have evidence of infectivity as determined by PCR of the head of the flies. One in 1000 people is hard to achieve and a seroprevalence of < 2% might be sufficient to determine stopping MDA as suggested by modellers. This will save money and resources if MDAs are stopped and money is diverted for other health projects. A three-phased project has been set up in four onchocerciasis-endemic districts in northern Ghana to evaluate whether MDA can be safely stopped at a serological threshold higher than that currently recommended by WHO.

The study will determine Ov16 antibody seroprevalence by ELISA among children aged 5–9 years at baseline and conclusion of the study, conduct annual serological and blackfly evaluations to detect any reappearance of the parasite in the study area after stopping MDA in the period between baseline and conclusion studies, and determine baseline and final seroprevalence of Ov16 by RDT. The study commenced in August 2022 with data collection. A total of 2749 participants from 66 communities were enrolled in the study, of whom 2721 (99.0%) had a blood specimen collected and no adverse events were noted during the collection. Blackfly collection was started in October 2022 in eight vector collection sites. As of 16 December, 3428 blackflies have been collected. Blackfly collection was delayed due to changes in the vector’s breeding habits, and collections have been lower than expected due to this year’s rainfall patterns and pollution.
from mining. Five out of the eight sites have been closed due to blackflies no longer being present. If any of the closed sites become productive at a later time, then they may be reopened. Plans for 2023 include testing Ov16 ELISA and Ov16 RDT, of blood specimens collected and the completion of blackfly collection and analysis with O-150 PCR. The study will move to phase II if the threshold is met.

A similar study has been set up in two transmission zones, namely the Pra/Offin and Dayi/Asukawkaw transmission zones in Ghana. The study uses a sampling design that takes variation in pre-control endemicity levels into account. All villages outside the identified high-risk foci and in the remaining space in the transmission zones were considered as one low-risk evaluation area. There is a purposive sampling approach in the high-risk focus to select the communities with similar high pre-control endemicity values and a stratified random sampling spatially to select children from the low-risk evaluation areas in communities separated about 50 km from each other for the two zones. The fly-catching is ongoing in selected fly-catching areas, and training on the serological survey has just been done. Data collection begins on 19 December 2022 until the end of the year.

6.3 Malawi (by Laston Sitima)

Malawi conducted a stop MDA survey that has two study components: entomology and epidemiology. The study involved collecting *Simulium damnosum* flies, the vectors responsible for transmitting onchocerciasis, skin snips and DBS. The study was conducted in two districts (Neno and Thyolo) in the Southern Region of the country. Both districts have typical tropical savannah climate and have been under MDA, uninterrupted since 1997, with 100% geographical coverage and > 80% therapeutic coverage achieved in both districts. Thyolo district attained the entomologic rate recommended to stop MDA in 2017 while Neno district attained the entomological rate recommended for stopping MDA in 2020. The previous entomological surveys in both districts were conducted as part of larger evaluation units, which is why we did new entomological surveys as part of the stop MDA project. The epidemiological samples collection was implemented in 35 villages selected in each of the two districts. Five villages were purposely selected while 30 villages were randomly selected. The entomological study was conducted in five villages in each district. During the entire period of sample collection, a total of 4507 DBS, 4460 skin snips and 60 338 flies were collected (Table 2). Skin snips and the flies will undergo PCR analysis at the University of Malawi while the DBS will be analysed with RDT at the national reference laboratory of the Community Health Science Unit (CHSU), Ministry of Health.

<table>
<thead>
<tr>
<th>District</th>
<th>DBS collected</th>
<th>Skin snips collected</th>
<th>Flies collected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyolo</td>
<td>2313</td>
<td>2242</td>
<td>40 634</td>
</tr>
<tr>
<td>Neno</td>
<td>2194</td>
<td>2218</td>
<td>19 704</td>
</tr>
<tr>
<td>Total</td>
<td>4507</td>
<td>4460</td>
<td>60 338</td>
</tr>
</tbody>
</table>

6.4 Summary of discussions

There was initially some uncertainty around why a 2% serological threshold was being used for stopping in these settings when the WHO guidelines state that the threshold is < 0.1%. It was clarified that the WHO criteria for stopping remains < 0.1%, and that a new threshold would require a new guideline. The 2% threshold was determined using modelling and is being used in carefully planned study settings only. The purpose of the studies is to validate that a new serological threshold would be reasonable. It was also clarified that, for the purposes of the studies, the WHO-endorsed entomological threshold would still have to be met in order to stop MDA in these settings. If the entomological threshold is met along with the study serological threshold of 2%, then they will stop MDA and use subsequent entomology and serology to ensure that the decision is correct.
6.5 Recommendations

- Ongoing operational research and modelling studies are evaluating whether the serological threshold can be increased to a level that would be more technically feasible to measure while remaining a reliable indicator that elimination has been reached. OTS appreciates the updates on the progress so far with this work, and it looks forward to future updates as data become available.

- OTS wishes to clarify that the WHO-recommended serological threshold of < 0.1% in children for stopping MDA has not changed. Such a change would require issuance of new guidelines. Ongoing operational research and modelling studies are evaluating whether this serological threshold can be increased to a level that would be more technically feasible to measure while remaining a reliable indicator that elimination has been reached.
7. Post-treatment surveillance: Ethiopia’s experience

7.1 Description of focus and recent results (by Rory Post)

The Galabat-Metema cross-border transmission zone is shared between Sudan (Galabat sub-focus) and north-west Ethiopia (Metema sub-focus). It is surrounded by a buffer zone which is considered to be free of onchocerciasis. About 20 km south of the Metema sub-focus lies the Metekel transmission zone. To the north, transmission was recorded in 1981 centered on the River Tekezé (which forms the border between Ethiopia and Eritrea), although more recent surveys indicate that this may have disappeared; OEM is planned to confirm this (when the security situation allows). In the Galabat sub-focus, baseline rates of transmission were fairly low. Annual MDA began in 2007 (with biannual treatments during 2011–2014) and ceased in 2017 after a successful stop MDA survey. A new survey (similar to a post-transmission surveillance assessment) in 2022 indicated that there had been no recrudescence of transmission, but the sub-focus will remain in post-transmission surveillance until the Metema sub-focus is also ready to move into post-elimination surveillance.

The Metema sub-focus started annual MDA in different areas in 2003 and 2008, which increased to biannual MDA everywhere in 2016. A stop MDA survey in 2014–2015 found all children examined to be Ov16 negative (after a small number were confirmed by skin-snip PCR), and 6/7 vector collection points were pool-screening negative except for two pools, both from Wudi Gemzu. The extent of this hot spot of transmission was delineated by intensive Ov16 mapping, and MDA was stopped outside the hot spot in 2017. MDA coverage surveys within the hot spot revealed geographical and therapeutic issues in some areas, which were mostly related to hard-to-reach and unstable migratory populations. MDA was increased to four times a year (to accelerate progress towards elimination and to protect the surrounding regions for post-transmission surveillance in Galabat and Metema sub-foci. A programme of health education was introduced along with enhanced supervision and timing of MDA to take into account patterns of migration.

A recent entomological survey in the hot spot (in 2022 after 13 rounds of four times a year MDA) found 0/5956 infective vectors in pools from four sites, which might indicate suppression of transmission, but MDA was not interrupted during the survey. The same survey (equivalent to a post-transmission surveillance assessment) from six sites in the post-transmission surveillance area of Metema found S. damnosum sensu lato to be scarce (only 1068 were captured, compared with 5211 anthropophilic S. bovis), and there were three positive pools of S. damnosum s.l. (from three dispersed sites), strongly indicating that transmission had not been suppressed or that it had recrudesced, effectively failing PTS.

The programme has now reduced MDA to twice a year in the hot spot. It has not yet reintroduced MDA into the PTS region, but is following the WHO guidelines (1) to confirm the level of transmission by catching sufficient vectors to calculate the seasonal transmission potential (upper 95% CL), and, if that is confirmed, to carry out an Ov16 survey of children. Simultaneously, the programme is investigating the cause of the failure by: (i) assessing the local populations for migrants who might have brought parasites into the area; (ii) checking the infectivity status of S. damnosum s.l. collected from the buffer zone to see if they might be carrying parasites into the area from some unknown source; (iii) performing OEM in districts of Tigray Region which borders Metema and Galabat; (iv) performing O-150 pool screening of heads of S. bovis, to determine if they might play a role in transmission; (v) using RadSeq genome analysis of S. damnosum s.l.
to see if the flies carrying *O. volvulus* are immigrants from Metekel; and (vi) using RadSeq check to see if there is migration of *S. damnosum* s.l. from Metekel or Metema into Galabat.

### 7.2 Summary of discussions

As disappointing as the positive pools are, it is encouraging to have a system that can detect resurgence. An investigation is planned to understand human migration patterns around the positive sites. This will answer many questions and help determine next steps. So far, Ethiopia has considered vector control to supplement and support MDA on several occasions. The investigations at the moment may indicate that vector control may be a potential solution. More information is needed before going down the road of vector control. Deploying improved tests across Africa would help to obtain as much valuable information as possible.

### 7.3 Recommendations

**To WHO**

- The Ethiopian programme shared its experience with the identification of infective flies during post-treatment surveillance. OTS appreciates the programme’s willingness to share their experience and findings. OTS recommends that WHO follow the data generated as the various planned studies described in the presentation unfold.

- OTS highlighted that the programme is following the algorithm for how to respond to positive entomological findings after stopping MDA that is described in WHO guidelines and would appreciate feedback on the results of Ethiopia’s studies.
8. Onchocerciasis-associated epilepsy

8.1 Update and perspectives (by Sébastian Pion, Cédric Chesnais)

The highest prevalence values of epilepsy worldwide have been reported from communities where onchocerciasis has been hyper-endemic. Retrospective studies have shown that people living with epilepsy showed higher density of *O. volvulus* microfilariae in the skin, and higher numbers of palpable onchocercal nodules than non-epileptic individuals of the same age, gender and village of residence. Yet, the causal relationship between infection with *O. volvulus* and epilepsy has long been a matter of debate. The reason for this is that, to date, nobody has been able to identify the pathogenic mechanisms involved in such a relationship.

A renewed interest in onchocerciasis-associated epilepsy (OAE), including nodding syndrome, has helped generate twice as many scientific articles over the past 5 years as during the previous 80 years. Among those recent studies, some have reported, for the first time, the occurrence of OAE in different provinces of the Democratic Republic of the Congo. The unbearable individual burden of OAE has been thoroughly documented and, at a wider scale, the first global burden assessment of OAE points to substantial estimates, in particular because of the treatment gap for active epilepsy cases.

Progress has also been made in understanding the puzzling OAE condition. Two cohort studies conducted in Cameroon suggest that presenting high grade *O. volvulus* microfilaridermia during childhood resulted in a 10−30-fold increased risk of developing epilepsy several years later in life compared with children presenting no skin microfilariae at the same age. Since a heavy exposure to *O. volvulus* at an early stage of life seems critical to set up the epileptogenic condition, it could explain why the numerous excellent biological and clinical studies on already active cases, therefore older individuals, have led to inconclusive results. This being said, knowing the pathological pathways to explain OAE may not be mandatory to tackle this problem of public health. Indeed, evidence is accumulating that elimination of *O. volvulus* transmission is followed by a significant reduction in incidence of epilepsy. However, action is urgently needed before expecting OAE to fade out with onchocerciasis elimination. Wherever OAE occurs, which is still highly correlated with hyper-endemic onchocerciasis settings, protecting young children from onchocerciasis should be a priority. Providing ivermectin, or other protective antifilarial treatment, to children weighing < 15 kg or < 5 years of age, as well as pregnant women, should be considered. More efforts are also urgently needed to fill the antiepileptic treatment gap.

8.2 Summary of discussions

There was agreement that the findings presented, as well as results of other studies mentioned during the discussion, constitute convincing evidence of the connection between onchocerciasis and epilepsy. It is still to be determined what recommendations WHO is prepared to make in response to OAE, and what questions need to be answered before formal recommendations can be made. OTS recommended that WHO, at the request of the WHO Onchocerciasis Focal Point, organize a meeting involving neurologists, the WHO seizure and epilepsy group and onchocerciasis specialists to formalize recommendations for programmes regarding OAE. It was stressed that efforts to eliminate onchocerciasis should be redoubled, as this would also lead to the elimination of OAE if the connection does in fact exist. There was some discussion about expanding treatment to younger children, possibly with moxidectin, as a means of...
combating OAE. It was noted that there is interest in doing so, but that this would require further research and a new recommendation.

8.3 Recommendations

There is mounting evidence of the association between onchocerciasis and epilepsy, but a thorough analysis of the data and development of programmatic recommendations based on the data were beyond the scope of the current meeting of the OTS.

To WHO

Organize a standalone meeting with the goal of formally evaluating the available data and developing guidance that can be used for programmatic action and advocacy. It is recommended that the meeting involves neurologists and the WHO seizure and epilepsy group, as well as onchocerciasis experts.
9. Development of a prophylactic onchocerciasis vaccine

9.1 Onchocerciasis vaccine (by Sara Lustigman)

TOVA, The Onchocerciasis Vaccine for Africa initiative, has a candidate vaccine ready for clinical development. Dr Lustigman presented the exciting progress that has been made by members of TOVA towards a preventive onchocerciasis vaccine (“TOVAx”) that is now ready for advancement of clinical development.

This group identified the antigens Ov-103 and Ov-RAL-2 as the most promising vaccine candidates and demonstrated that when these antigens are combined into a fusion recombinant protein (Fus-1), the adjuvanted vaccine is better in protecting mice against challenge with infective stage larvae (using the diffusion chamber model). The adjuvanted vaccine also protects significantly against developing adult- and gravid female worms in the Brugia malayi gerbil infection model, and reduces the worm burden and microfilarial loads in calves after 24-months exposure to natural trickle infection with O. ochengi. The TOVAx vaccine is now entering cGMP production and engineering runs are being produced to be used in GLP toxicology testing followed by cGMP manufacture and clinical testing for safety in non-exposed volunteers and in endemic pre-exposed volunteers (Phase I clinical studies, 2023–2025), including evaluation of immunogenicity and the induction of functional protective antibodies. TOVAx will be indicated for children aged 1–5 years and is projected to protect children and young adults (aged < 20 years) from acquiring patent infections and consequent onchocerciasis-associated pathologies, including epilepsy. It is anticipated that newly integrated control strategies, including a prophylactic vaccine such as TOVAx, and macrofilaricidal and microfilaricidal treatments will be more effective in reaching and supporting the WHO elimination of transmission 2030 targets for onchocerciasis in Africa.

9.2 Summary of discussions

An effective and safe vaccine against onchocerciasis could be used in combination with drug therapy to induce additional immunity. Immunoprophylaxis will not interfere with natural immunity.

9.3 Recommendations

☐ None
References


# Annex 1. Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00–14:10</td>
<td>Welcome &amp; introductions</td>
<td>All</td>
</tr>
</tbody>
</table>
| 14:10–15:20   | Diagnostics                           | Paul Cantey, OTS Chair; Chief, Parasitic Diseases Branch, Div. of Parasitic Diseases and Malaria, CDC, USA  
                  |                                      | Scott Elder, Microbiologist, CDC, USA  
                  |                                      | Thomas Unnasch, Distinguished USF Health Professor, USA  
                  |                                      | David Oguttu, NTD Control Programme, Vector Control Division, Ministry Of Health, Uganda |
| 15:30–16:30   | Diagnostics                           | Steve Williams, Gates Professor of Biological Sciences, Smith College, USA  
                  |                                      | Nils Pilotte, Assistant Professor of Biology, Quinnipiac University, USA  
                  |                                      | Penny Smith, Senior NTD Adviser and Lead, Pharmaceutical quality, procurement and supply chain, USAID  
                  |                                      | Lee Hundley, Associate Director of Programs, Task Force for Global Health, USA |
| 16:30–17:00   | Onchocerciasis modelling              | Graham Medley, Principal investigator, NTD Modelling Consortium, London School of Hygiene & Tropical Medicine, UK  
                  |                                      | Mutono Nyamai, Research Scientist, NTD Modelling Consortium, University of Nairobi |
## Day 2: 20 December 2022

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00–15:30</td>
<td>Moxidectin</td>
<td>Dziedzom K. de Souza, Associate Professor, University of Ghana</td>
</tr>
<tr>
<td></td>
<td>~ Systematic review</td>
<td>Sally Kinrade, Vice President, Medicines for Development, Australia</td>
</tr>
<tr>
<td></td>
<td>~ Paediatric studies</td>
<td>Lee Hundley, Associate Director of Programs, Task Force for Global Health, USA</td>
</tr>
<tr>
<td></td>
<td>~ Other studies (dosing studies, cost analysis and modelling)</td>
<td>Sally Kinrade, Vice President, Medicines for Development, Australia</td>
</tr>
<tr>
<td></td>
<td>~ COR-NTD outputs on use cases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion (focus on use cases, study results)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Proposed pilots</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>15:40–17:00</td>
<td>NOEC country presentations</td>
<td>Bertram Nwoke, Chair of NOEC Nigeria, Imo State University, Nigeria</td>
</tr>
<tr>
<td></td>
<td>~ Nigeria</td>
<td>Thomas Unnasch, Chair of the NOEC of Uganda</td>
</tr>
<tr>
<td></td>
<td>~ Uganda</td>
<td>Hugues N’Gassa, Onchocerciasis focal point, Ministry of Health, Côte d’Ivoire</td>
</tr>
<tr>
<td></td>
<td>~ Côte d’Ivoire</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
</tbody>
</table>

## Day 3: 21 December 2022

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00–14:30</td>
<td>M&amp;E</td>
<td>Clara Jones, Onchocerciasis focal point, United Republic of Tanzania</td>
</tr>
<tr>
<td></td>
<td>~ RDTs for mapping</td>
<td>N’Deye Marie Bassabi Alladji, Onchocerciasis focal point, Benin</td>
</tr>
<tr>
<td></td>
<td>~ RDTs for routine M&amp;E</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>14:30–15:15</td>
<td>Stop MDA updates</td>
<td>Akili Kalinga, National Institute for Medical Research, United Republic of Tanzania</td>
</tr>
<tr>
<td></td>
<td>~ United Republic of Tanzania</td>
<td>Joseph Opare, Senior Public Health Specialist, College of Physicians, Ghana</td>
</tr>
<tr>
<td></td>
<td>~ Ghana</td>
<td>Laston Sitima, Onchocerciasis focal point, Malawi</td>
</tr>
<tr>
<td></td>
<td>~ Malawi</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>15:25–15:55</td>
<td>PTS experience in Ethiopia</td>
<td>Rory Post, Chair of NOEC Ethiopia, London School of Hygiene &amp; Tropical Medicine, UK</td>
</tr>
<tr>
<td></td>
<td>~ Description of focus and recent results</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>15:55–16:25</td>
<td>OAE epilepsy morbidity</td>
<td>Sébastien DS Pion, IRD, France</td>
</tr>
<tr>
<td></td>
<td>~ Updates on studies</td>
<td>Cédric Chesnais, IRD, France</td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>16:25–16:45</td>
<td>Onchocerciasis vaccine</td>
<td>Sara Lustigman, Head, Laboratory of Molecular Parasitology, NY Blood Center, USA</td>
</tr>
<tr>
<td></td>
<td>~ Onchocerciasis vaccine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>~ Discussion</td>
<td></td>
</tr>
<tr>
<td>16:55–17:00</td>
<td>Closing remarks</td>
<td>Chair and/or WHO</td>
</tr>
</tbody>
</table>
Annex 2. List of participants

Members
Paul Cantey (Chair), United States Centers for Disease Control and Prevention, Atlanta, United States of America
Katherine Gass, The Task Force for Global Health/Neglected Tropical Diseases Support Center, Decatur, United States of America
Joseph Kamgno, University of Yaoundé, Cameroon
Robert Klein, Universidad del Valle de Guatemala, Guatemala City, Guatemala
Thomson Lakwo, Onchocerciasis Control Programme (retired), Entebbe, Uganda
Upendo Mwingira, National Institute for Medical Research, Dar-Es-Salaam, United Republic of Tanzania
Thomas Unnasch, University of South Florida, Tampa, United States of America
Isam M.A. Zarroug, Federal Ministry of Health, Khartoum, Sudan

Invited experts
N’Deye Marie Bassabi Alladji, Onchocerciasis focal point, Benin
Cédric Chesnais, Institut de recherche pour le développement, Montpellier, France
Scott Elder, Microbiologist, United States Centers for Disease Control and Prevention, Atlanta, United States of America
María-Gloria Basáñez, Chair in Neglected Tropical Diseases, Imperial College London, United Kingdom of Great Britain and Northern Ireland
Deirdre Hollingsworth, Senior Group Leader, NTD Modelling Consortium, University of Oxford, United Kingdom of Great Britain and Northern Ireland
Lee Hundley (co-rapporteur), Associate Director of Programs, Task Force for Global Health, Decatur, United States of America
Clara Jones, Onchocerciasis focal point, United Republic of Tanzania
Akili Kalinga, National Institute for Medical Research, United Republic of Tanzania
Sally Kinrade, Vice President, Medicines Development for Global Health, Southbank (VIC), Australia
Sara Lustigman, Head, Laboratory of Molecular Parasitology, NY Blood Center, United States of America
Graham Medley, Principal investigator, NTD Modelling Consortium, London School of Hygiene & Tropical Medicine, United Kingdom of Great Britain and Northern Ireland
Hugues N’Gassa, Onchocerciasis focal point, Ministry of Health, Côte d’Ivoire
Bertram Nwoke, Chair, National Onchocerciasis Elimination Committee (Nigeria), Imo State University, Owerri, Nigeria
Mutono Nyamai, Research Scientist, NTD Modelling Consortium, University of Nairobi, Kenya
David Oguttu, Neglected Tropical Disease Control Programme, Vector Control Division, Ministry of Health, Kampala, Uganda
Joseph Opare, Senior Public Health Specialist, Ghana College of Physicians & Surgeons, Accra, Ghana
Nils Piotte, Assistant Professor of Biology, Quinnipiac University, Hamden, United States of America
Sébastien D.S. Pion, Institut de recherche pour le développement, Montpellier, France
Rory Post, Chair, National Onchocerciasis Elimination Committee (Ethiopia), London School of Hygiene & Tropical Medicine, United Kingdom of Great Britain and Northern Ireland

Laston Sitima, Onchocerciasis focal point, Malawi

Penny Smith, Senior Neglected Tropical Disease Adviser and Lead, Pharmaceutical Quality, Procurement and Supply Chain, United States Agency for International Development, Washington, United States of America

Dziedzom K. de Souza, Associate Professor, University of Ghana, Accra, Ghana

Wilma Stolk, Assistant Professor, Department of Public Health, Erasmus Medical Center, Rotterdam, Kingdom of the Netherlands

Andreia Vasconcelos, Scientific Manager, Big Data Institute, University of Oxford, United Kingdom of Great Britain and Northern Ireland

Steve Williams, Gates Professor of Biological Sciences, Smith College, Northampton, United States of America

WHO secretariat

Maria Rebollo Polo, Lead, Global Programme for Onchocerciasis Elimination and Scabies Control, WHO Department of Control of Neglected Tropical Diseases, Geneva, Switzerland

Nadia Rozendaal, Consultant (co-rapporteur)
Annex 3. NTD Modelling Consortium consensus position statement on onchocerciasis elimination

This consensus position statement prepared by the NTD Modelling Consortium (NTDMC) summarizes the modelling evidence presented to the WHO Onchocerciasis Technical Advisory Subgroup (OTS) meeting on 19–21 December 2022. It addresses the current evidence from observation and models regarding the transmission dynamics of onchocerciasis at low prevalence and hence the likelihood of elimination; it is not a summary of all evidence from modelling.

There are two policy questions which are closely related. The first is the timescales of interventions against onchocerciasis that will be required to achieve local/regional elimination of transmission. The second is to inform the business case for deployment of moxidectin, and whether moxidectin will be useful in 5 years from now, i.e. in 2027.

There are two situations in which onchocerciasis occurs at low prevalence which are currently included in the modelled scenarios:

- either prevalence has been historically high and has been driven low by prolonged implementation of interventions,
- or the prevalence has been historically low due to low baseline transmission and has remained so in the absence of interventions.

The former scenario is the focus of current policy decisions, but the latter is linked and important in terms of transmission dynamics.

This consensus statement summarizes the understanding from the modelling rather than from individual models. Model comparison is informative, and highlights uncertainty, which is important for policy-making and decisions.

Policy relevant summary

- Epidemiological models are abstractions of reality that are unable to provide precise numerical predictions or forecasts. Different results from different models highlight inherent uncertainty in the epidemiological and biological processes. Models are neither “right” nor “wrong”, but using multiple models potentially gives greater robustness to evidence.

- Critical aspects of the underlying biology of onchocerciasis are uncertain, particularly relating to dynamics at low prevalence. There are relatively few data from areas of low prevalence.

- The definition of elimination and its ascertainment are dependent on diagnostics and definitions, and time horizon. Achieving elimination is a chance process, so any projection of duration to elimination results in a range of expected times.

- The required duration of current interventions to achieve elimination of transmission in a single village (or larger area) increases with increasing baseline endemicity.
In settings with moderate baseline endemicity (40–59% microfilarial prevalence) elimination within 15 years is a realistic possibility (40–50%) with current interventions. The probability is increased with more frequent mass drug administration (e.g. biannual rather than annual) and lower baseline endemicity.

The probability of achieving elimination within this timescale over a wider geographical area is greatly reduced (because each individual village must have eliminated transmission concurrently).

Moxidectin will accelerate elimination in all settings. The greatest value of moxidectin is in higher endemic settings.

1. There is uncertainty about whether moxidectin is strictly necessary to achieve elimination in settings with high baseline endemicity.
2. There is consensus that the higher the endemicity the more useful moxidectin is in achieving elimination and reducing duration of intervention required.
3. In treatment-naive settings with moderate baseline endemicity, the introduction of moxidectin will likely reduce the duration to elimination of transmission by ⅓–½ compared with ivermectin.
4. In settings where ivermectin is being used but elimination is not yet achieved, switching to moxidectin will likely reduce the remaining time to elimination of transmission by ¼–½ (where it can be achieved).

Models differ in predicted durations required to reach elimination thresholds and elimination of transmission. The differences between the two NTDMC models arise from differences in biological and epidemiological processes and the interactions between them. The model differences reflect true biological uncertainty.

Coverage and adherence are critical processes regardless of the medicine use: moxidectin will not reduce the need for effective delivery programmes. It is possible that interventions will continue to be required because of relatively low coverage and adherence.

Host and vector mobility and interactions between settings/populations are largely unknown but are likely crucial in understanding observed patterns and response to interventions at low prevalence.

The NTDMC will continue to develop the modelling and the understanding that arises from it. However, it is the consensus view that the current differences are fundamentally due to scientific uncertainty.

Scientific evidence

Areas of low prevalence of onchocerciasis are heterogeneous. Some have historically high baseline prevalence which has been driven to low levels by mass ivermectin administration (MDA), vector control and a combination of both, as well as environmental and land-use change. Some areas have low baseline transmission intensity. Some of these areas are currently undergoing onchocerciasis elimination mapping and may not have yet been incorporated into intervention programmes. The future transmission dynamics are highly likely to be different in different populations.

NTDMC has identified four critical drivers for persistent low prevalence of infection:

1. heterogeneities in transmission (within and between populations),
2. heterogeneities in interventions (within and between populations),
3. landscape/network patterns driving interconnectedness of populations,
4. the potential role of immunity.

Heterogeneities in transmission/exposure are characterized by groups of individuals that continue to be infectious to vectors and pose transmission risk to the whole population. Biting rates are not randomly distributed, but clustered within individuals/communities because of differences in occupation, size,
local environment (especially proximity to vector breeding sites), as well as intrinsic behavioural and genetic differences between individual people.

- Heterogeneities in interventions are largely driven by the non-random distribution of chemotherapeutics to the target population, with relatively large proportions of the population seldom or never treated, i.e. low adherence or systematic non-adherence/participation, and with population groups that are not eligible for treatment (children aged under 5 years and pregnant women).

- The landscape and population structure generate heterogeneity at a local scale, but also create more complex patterns of transmission. These are largely as yet unexplored, but given the long infectious period (about 15 years), it is likely that the “who infects whom” interactions by age, sex, place, etc. are complicated. The long infectious period means that transmission patterns are generated across long distances by migration, movement and translocation. Additionally, the vectors are highly mobile.

- The potential role of immunity is not clear, and would interact closely with heterogeneity in exposure. In particular, if immunity has a significant impact on limiting acquisition of patent infections, then reduction in prevalence will reduce immunity (depending on the length of “immunological memory”) creating a self-sustaining, low prevalence stable state.

- The difference between the models arises from the different plausible assumptions included in the models. In particular, the sources/causes of the heterogeneities described above and their interaction with immunity and other processes are likely to be driving the differences in dynamics observed at low prevalence.

- The required duration of current interventions to achieve elimination of transmission in a single village (or larger area) increases with increasing baseline endemicity for two reasons:
  1. There are more worms to kill, which requires more rounds of MDA; and
  2. There is greater propensity for rebound and faster rebound between treatments.

- If low prevalence in a population is maintained by importation of infection (through humans and/or vectors), then sustained elimination is not possible unless prevalence is reduced in the source populations.

- If low prevalence in a population is stable (i.e. generated by transmission patterns) then the probability of elimination is increased by better coverage/adherence and medication (i.e. moxidectin).

- Both models are limited by the population size of hosts modelled: about 400 individuals (for both ONCHOSIM and EPIONCHO-IBM) and their default assumption that the populations are closed, single entities. Consequently, the models capture the precise details of neither human movement (migration, temporary translocation, etc.), nor non-contiguous vector populations overlying human populations.

- A critical question is whether or not the observed low prevalence state is dynamically stable and to what extent continued introduction of infection through host and vector movement contributes to transmission.

**Background and current position**

NDMWC was set up in 2014 with two onchocerciasis model frameworks involved from the outset (ONCHOSIM and EPIONCHO), which had been developed over decades. ONCHOSIM is stochastic individual-based. EPIONCHO was deterministic, but was extended to a stochastic individual-based framework (EPIONCHO-IBM) after 2017. Both models informed the global consultation process for the WHO road map on neglected tropical diseases 2021–2030.²

---

**Future model development**

The NTDMC will continue to develop the models and use the modelling to produce evidence for policy decisions. Our immediate next steps are listed below. Interaction with policy-makers is essential if the modelling evidence is going to be fit for purpose.

- Conduct simultaneous fitting of nested models which will aid understanding of why the two model structures differ in terms of dynamics at low prevalence.
- Conduct systematic review of publications reporting elimination of transmission under different conditions of baseline endemicity, vector species, vector types, coverage and duration of interventions.
- Model frameworks are needed that take into account within-area spatial heterogeneity, for example multiple-village models.

**Suggestions for future studies**

Data are always more important than models: models are to a large extent analysis tools that turn data into policy-relevant information. Below NTDMC identifies several areas of potential study that could reduce the biological and epidemiological uncertainty. These are not fully developed and are not in any order of priority.

- Transmission patterns are potentially informed by particular genetic patterns, e.g. degree of inbreeding, relatedness of infections. Developing genetic studies could provide data which inform on transmission patterns, especially at low prevalence.
- A key uncertainty is the potential operation of immunity and its effect, which could wane as prevalence falls and allow a faster rebound. This would mean that low prevalence could be reached but would be unlikely to lead to elimination. This requires longitudinal (i.e. same individuals over time) measurement of epidemiological and immunological parameters.
- If fly numbers have reduced dramatically over the course of the programme, then forward projections of models based on baseline prevalence will overestimate the timelines to elimination. Climate change is likely to be playing a key role in fluctuations in prevalence. Longitudinal estimates of vector abundance would be informative.
- There are no data as yet of the impact of moxidectin MDA programmes and their epidemiological impact from field trials. When they become available they will be used to develop the modelling.
Report of the sixth meeting of the WHO Onchocerciasis Technical Advisory Subgroup

Virtual meeting
19–21 December 2022

World Health Organization
Avenue Appia 20
1211 Geneva
Switzerland