Report of the 1st Meeting of the WHO Onchocerciasis Technical Advisory Subgroup

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I. Abbreviations

ALB	albendazole
AP	alkaline phosphatase
ATP	annual transmission potential
CDC	United States Centers for Disease Control and Prevention
CI	confidence interval
DBS	dried blood spots
DfID	United Kingdom's Department for International Development
DRC	Democratic Republic of Congo
ELISA	enzyme-linked immunosorbent Assay
EMRO	Eastern Mediterranean Regional Office
ESPEN	Expanded Special Project for the Elimination of Neglected Tropical Diseases
EU	evaluation unit
FMOH	Federal Ministry of Health
FTS	Filariasis Test Strip
HRP	horseradish peroxidase
iTAS	Integrated transmission assessment survey
IVM	ivermectin
LF	lymphatic filariasis
LGA	local government area
MDA	mass drug administration
M&E	monitoring and evaluation
Mf	microfilariae
MOH	Ministry of Health
NIH	United States National Institutes of Health
NOEC	national onchocerciasis expert committee
NTDSC	Neglected Tropical Diseases Support Center
OD	optical density
OEPA	Onchocerciasis Elimination Program for the Americas
OTS	Onchocerciasis Technical Advisory Subgroup
PCR	polymerase chain reaction
PPES	probability proportional to estimated size
Pre-TAS	Pre-Transmission Assessment Survey
PSU	primary sampling unit
PTS	post-treatment surveillance
QA	quality assurance
QC	quality control
RDT	rapid diagnostic test
REMO	Rapid epidemiological mapping of onchocerciasis
SD	Standard Diagnostics
SSU	secondary sampling unit
TAS	Transmission Assessment Survey
TFGH	Task Force for Global Health
TZ	Transmission zone

UL	upper-limit
UOEEAC	Uganda Onchocerciasis Elimination Expert Advisory Committee
USAID	United States Agency for International Development
WHO	World Health Organization

II. Executive Summary

The WHO Onchocerciasis Technical Advisory Subgroup (OTS) was established in order to provide advice to WHO in accordance with the terms of reference developed for the subgroup. The objectives of the 1st meeting were to review current strategies and provide recommendations on potential common strategies or components of common strategies for onchocerciasis elimination mapping, for determining when a stop-MDA evaluation should be performed, for performing stop-MDA evaluations, and to identify key research and operational questions that need to be answered to develop the evidence-base to support strategies for the above mentioned programmatic activities. The key conclusions and recommendations of the OTS are described below. Please note that many of the recommendations are provisional and thus may change over time as new evidence emerges. Evidence that emerges after the meeting will not be reflected in this report. Some lessons will have to be learned while programmes continue to strive to eliminate the transmission of onchocerciasis. Recommendations are based on consensus unless otherwise noted. When consensus could not be reached, operational research questions were defined that should provide the evidence required to obtain a consensus in the future.

1. Serology for onchocerciasis. The OTS recognized the need to standardize Ov16 serology and encouraged the continued collaboration between PATH and the US CDC to evaluate the various formats. Although two versions of the ELISA (one alkaline phosphatase-based and one horseradish peroxidase-based) were selected for continued comparisons, the data presented were insufficient for the OTS to determine that any particular ELISA could not be used for programmatic decisions. Once sufficient data are available that describe the performance of the ELISAs in a variety of epidemiological contexts and in multiple laboratories and once those data are reviewed by OTS, it is expected that the OTS will designate one ELISA as the one for which WHO should support a quality assurance programme. Concerns remain about the sensitivity of the Ov-16 rapid diagnostic test (monoplex or biplex), particularly in low prevalence settings. Because of these concerns, the OTS recommended that dried blood spots be collected when Ov-16 rapid diagnostic tests are used for elimination mapping. If transmission not detected by the rapid test, ELISA would be required to confirm this. If transmission is detected by the rapid test, ELISA would not be required. Rapid test results cannot be used to decide to stop mass drug administration. Finally, development of a new test that could be used to exclude infection in an individual is a priority.

2. Entomology, Vector Monitoring and Control. The OTS recognized that there is an undersupply of the entomology technicians that would be required to perform the various entomological surveys required by the WHO guidelines for stopping mass drug administration and verifying the elimination of human onchocerciasis. It thought efforts should be made to increase country entomological capacity and that the WHO entomological manuals should be updated as appropriate. Updates on progress with traps for black flies and new low-cost techniques for limited vector control were presented. Continue work on both was encouraged, with requests to focus on how to calculate annual transmission potentials when using fly traps and to try the low-cost vector control technique, which consists of training community members to reduce vector habitat, outside Uganda.

3. Onchocerciasis Elimination Mapping. Onchocerciasis elimination mapping is the additional mapping of areas that are not receiving MDA for onchocerciasis but in which transmission is possible. This

additional mapping is required in order to identify all areas with ongoing transmission that need to be treated in order to achieve the interruption of transmission of onchocerciasis. Significant time and effort was devoted to reviewing protocols and data relevant to development of an elimination mapping strategy. General consensus was that the initial strategy should be conservative and biased towards finding transmission. If WHO were to raise the provisional threshold for starting MDA, programmes who started MDA using the lower provisional threshold would not be expected to pass a stop-MDA survey in order to stop treatment in areas that used the lower provisional threshold. A process by which programmes exclude districts that do not need elimination mapping is the first step of the process. For the next step, consensus was obtained that a district-based strategy was an acceptable starting point for mapping and that such a strategy would not preclude more precise determination of transmission zones if needed. Programmes could opt to map by sub-district when the context suggests that transmission is unlikely in the entire district. In areas where transmission is likely and 1st-line villages can be identified, a purposive strategy of village selection is recommended. If the purposive strategy does not identify transmission or if 1st-line villages cannot be identified, then a random strategy of village selection is required. Details of the purposive strategy were agreed upon; for the random strategy additional information is needed though its creation is a priority for future meetings. A provisional threshold for starting MDA was set at 2% Ov-16 seropositivity in adults, as this would bias towards identifying transmission until additional data are obtained. Programmes are encouraged to use the Ov-16 RDT for mapping, with the understanding that results above the provision threshold require starting MDA and results below the threshold require confirmation with Ov-16 of dried blood spots collected at the time the RDTs are performed. This recommendation may change as the performance of ELISA and RDT in low prevalence settings is better described.

General Outline of the Elimination Mapping Protocol in Areas Not Treated with Ivermectin

1. Determine areas that may be excluded from mapping.
2. Identify areas where transmission is most likely for the initial elimination mapping and then move out to areas where transmission is less likely
3. Determine the evaluation unit (district or sub-district), this may vary depending on the context of the evaluation
4. Begin with evaluating 3-5 purposively selected 1st-line villages and a minimum of 300 people
    - Use the Ov-16 RDT (countries may opt to use ELISA; either the monoplex or biplex RDT is acceptable)
    - Sample adults ≥ 20 years old
    - If the seroprevalence in a village exceeds 2% then initiate MDA in the evaluation unit
    - If the RDT results are less than the 2% threshold, then they should be confirmed by ELISA
5. If purposive sampling cannot be done or if transmission is not identified by purposive sampling, a random sampling evaluation should be performed
    - Use the Ov-16 RDT (countries may opt to use ELISA; either the monoplex or biplex RDT is acceptable)
    - Sample adults ≥ 20 years old
    - Consensus on the protocol for this was not reached
    - For research purposes, protocols should be designed that enroll people from 30 clusters with an appropriate cluster size to detect an evaluation unit level seroprevalence of 2%

- If the upper bound of the 95% confidence interval of the random sample excludes the tentative threshold of 2%, then MDA is not needed

It should be noted that mapping protocols that are more conservative than those proposed by OTS should be acceptable for decision making at this point in time. For example, if a programme evaluated seroprevalence in children 5-9 years old and found a seroprevalence above the threshold for starting MDA, it would not need to repeat the exercise in adults. However, if seroprevalence in children was below the threshold, mapping in adults would be required.

A number of operational research questions related to onchocerciasis elimination mapping were identified. Some of the key questions are listed here, while all of the questions may be found in the report section of this document. Identification of other environmental factors that exclude the possibility of black fly presence would allow additional districts to be excluded without need for serologic testing. Entomologic studies are needed to help refine the threshold for starting MDA. Studies are needed to determine the minimal number of clusters and minimal cluster size for the random selection of villages component of the mapping strategy.

4. Monitoring and Evaluation. The focus of the discussion of M&E was the creation of a standard approach that would be quick and inexpensive and still provide information to programmes about their progress towards the interruption of transmission. Ideally, routine M&E could also serve as a pre-stop-MDA survey whose results indicate when a programme should proceed with a stop-MDA survey. Citing the experience of many country programmes, the OTS recommended that programmes continue to make use of opportunities to collect M&E information even if they do not align with a defined strategy (e.g. add Ov-16 testing to LF or other NTD evaluations). Routine M&E should continue to use the 1st-line village, using convenience sampling in children aged 5-9 to perform serological evaluations. It was suggested the 100 children in 3 villages per evaluation are would be appropriate. Key operational questions are whether evaluations could be school-based instead of community-based and what the prevalence threshold in the evaluated villages would be that indicate a programme is ready for a stop-MDA survey. It was noted by OTS that coverage surveys and rapid coverage tools can be used in the absence of any diagnostic testing to provide actionable data to programmes. Entomologic M&E was recommended in the WHO guidelines. As it will be important for programmes to know the location of breeding sites, the duration and peak of transmission season, and biting rates, these should be a focus of initial M&E, rather than measuring infectivity of black flies, particularly if the country does not have the laboratory capacity required for poolscreen PCR