Diagnostic test for surveillance of lymphatic filariasis

TARGET PRODUCT PROFILE

World Health Organization

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ISBN 978-92-4-001864-8 (electronic version)
ISBN 978-92-4-001865-5 (print version)

Suggested citation. Diagnostic test for surveillance of lymphatic filariasis: target product profile. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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Acknowledgements

This WHO target product profile (TPP) was developed under the direction of the Department of Control of Neglected Tropical Diseases following standard WHO guidance for TPP development. Special thanks are due to the NTD Diagnostics Technical Advisory Group Lymphatic Filariasis Sub-Group members Marco Biamonte, Katherine Gass, Achim Hoerauf, Rahmah Noordin, Sammy Njenga, Kapa Ramaiah, Reda Ramzy, Gary Weil, Steven Williams and Kimberly Won (Chair). We thank Christopher Hanna for contributing a structured framework for this TPP and for facilitating initial discussions on needs and landscape analysis. We thank Camilla Ducker and Ashley Souza for organizational support to Sub-Group meetings; Patrick Lammie (Chair) and members of the NTD Diagnostics Technical Advisory Group for guidance; and members of the NTD community and general public who provided feedback on draft versions of the TPP. WHO staff members Daniel Argaw Dagne, Jonathan King, Ronaldo Scholte and Anthony Solomon gave support and input to the TPP development process.

Funding support for the development of this TPP was provided by the Bill & Melinda Gates Foundation and the United States Agency for International Development.

Background

Lymphatic filariasis (LF) is a mosquito-borne parasitic infection that is endemic in 72 countries. Adult worms live in the host lymphatic system for years causing lymphatic dysfunction.

LF is caused by parasitic worms; *Wuchereria bancrofti*, *Brugia malayi*, or *Brugia timori*. *W. bancrofti* is found in nearly all LF endemic countries and *Brugia* spp are found only in limited areas of a few countries across South-east Asia. The adult worms cause lymphangiectasia, leading to swelling of legs (lymphoedema), scrotum (hydrocele) and other parts of the body. LF is a major cause of disability and is responsible for at least 1.6 million Disability Adjusted Life Years (DALYs) each year (*1*), resulting in productivity loss at the individual and national level.

Public Health Response

WHA 50.29 called for the elimination of LF as a public health problem. An estimated 51.4 million people were infected with LF as of 2018 (*2*), a significant reduction since WHO launched the Global Programme to Eliminate Lymphatic Filariasis (GPELF). GPELF aims to interrupt transmission and prevent new disease through the WHO recommended strategy of mass drug administration (MDA). All but 3 of the 72 endemic countries have established national LF elimination programmes and implemented MDA (*3*). Currently, 23 of 72 endemic countries have reduced infection levels below target thresholds and no longer require MDA nationally. WHO has acknowledged 17 of these 23 countries for meeting the criteria for achieving elimination of LF as a public health problem.

As more national programmes see success and begin to stop MDA, the importance of monitoring for resurgence through surveillance activities increases. As defined in the new NTD Road Map, all LF endemic countries should be implementing post-MDA or post-validation surveillance by 2030 (*3*).

Available Diagnostic Tools

WHO recommends repeating the transmission assessment survey (TAS) twice in 2 to 3-year intervals after MDA has stopped (*4*). Successful results in both surveys i.e. passing TAS, indicates incident infection remains below target thresholds over all endemic geographical areas and meets the epidemiological criteria for elimination as a public health problem. While the TAS is useful for stop-MDA decisions, it is not powered to measure reductions in prevalence or incidence over time or to be a sensitive measure of recrudescence in transmission potential.

This limitation of the TAS for surveillance is compounded by limitations of the available diagnostics. WHO recommends the Alere Filariasis Test Strip (FTS) for all areas endemic for *W. bancrofti* and Brugia Rapid Test for all areas endemic for *Brugia* spp. The FTS which measures circulating filarial antigen (CFA) is used in all steps of the GPELF strategy. However, CFA takes 12 months or more to appear after infection and persists several years after adult worms can no longer reproduce or have died. New diagnostics targeting analytes which represent recent exposure are needed to inform LF post-MDA and post-elimination surveillance and response activities.

Other diagnostic tools available for LF have been reviewed and include antibody-based ELISA formats and antibody-based point of care rapid diagnostic tests specific to *W. bancrofti* and *Brugia* spp. WHO has not recommended these diagnostic tests because the tests have not met required performance characteristics.

Development of the TPP

The WHO Department of Control of Neglected Tropical Diseases (NTD) manages a diverse portfolio of twenty diseases, each with its own unique epidemiological and diagnostic challenges. It was decided by the Strategic and Technical Advisory Group (STAG), the principal advisory group to WHO for the control of NTDs, that a single WHO working group would help ensure that a unified approach could be used to identify and prioritize diagnostic needs, and to inform WHO strategies and guidance on the subject.

The first meeting of the Diagnostic Technical Advisory Group (DTAG), an advisory group to Department of Control of Neglected Tropical Diseases, was held in Geneva, Switzerland, on 30 and 31 October 2019. DTAG members discussed priorities for the year ahead as well as how to manage the complexity of supporting the diagnostics agenda across the entirety of the WHO NTD portfolio (5). One of the recommendations was that there should be a diagnostic disease specific group to support the GPELF noting the diagnostic gaps in settings co-endemic with loiasis, areas implementing triple-therapy MDA and areas under post-treatment or post-elimination surveillance (*5*).

A DTAG sub-group of LF technical experts, end users and other stakeholders was formed and met 29th April 2020 virtually. The sub-group identified the need for improved diagnostics for surveillance, a need previously highlighted by WPRO during its meeting on NTD post-elimination surveillance in the Western Pacific (*6*). The need for feasible diagnostic formats and new biomarkers was reiterated by WHO expert panel members during a WHO expert consultation to establish the post-2020 targets for GPELF.

The DTAG sub-group drafted the TPP for this specific use case and WHO posted the draft TPP for public comment. Comments received were discussed with the DTAG sub-group and revisions were made where warranted.

Purpose of the TPP

The purpose of this TPP is to communicate the minimum and ideal characteristics desired to meet the need for discriminating low levels of risk for transmission, i.e. targeted prevalence thresholds in the surveyed areas. An in vitro diagnostic test is needed for the detection of analyte(s) specific to *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori* to aid in the surveillance of defined geographic areas as to whether infection and/or transmission potential has increased (recrudescence) or decreased (elimination of transmission).