



## DIAGNOSTICS FOR NEGLECTED TROPICAL DISEASES

Defining the best tools through target product profiles

## About PATH

PATH is the leader in global health innovation. An international nonprofit organization, we save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health.

### **PATH**

#### **MAILING ADDRESS**

PO Box 900922  
Seattle, WA 98109  
USA

#### **ADDRESS**

2201 Westlake Avenue  
Suite 200  
Seattle, WA, 98121  
USA

TEL: +1.206.285.3500

FAX: +1.206.285.6619

[www.path.org](http://www.path.org)

#### **For more information, contact:**

PATH Diagnostics Program

[sites.path.org/dx](http://sites.path.org/dx)

Email: [dxinfo@path.org](mailto:dxinfo@path.org)

## Acknowledgments

### **Financial support**

Support for this report was provided by the Bill & Melinda Gates Foundation and the United Kingdom Department for International Development.

### **PATH Authors**

Dunia Faulx\*, Helen L. Storey\*, Marjorie A. Murray, Jason L. Cantera, Kenneth R. Hawkins, Brandon Troy Leader, Kerry L. Gallo, Tala de los Santos.

\*equal contributors

### **Suggested citation**

PATH. *Diagnostics for neglected tropical diseases: Defining the best tools through target product profiles*. Seattle: PATH; 2015.

Copyright © 2015, PATH. All rights reserved.

The material in this document may be freely used for educational or noncommercial purposes, provided that the material is accompanied by an acknowledgment line.

Cover photo: PATH/Doune Porter

# **DIAGNOSTICS FOR NEGLECTED TROPICAL DISEASES**

Defining the best tools through target product profiles

## Executive summary

Neglected tropical diseases (NTDs) caused by bacteria, viruses, worms, and other parasites afflict 1.4 billion of the world's poorest people, trapping them in a cycle of poor health, disability, and poverty. The World Health Organization (WHO) has targeted a group of these diseases for control, elimination, or eradication, and many institutions that support global health and international development, including PATH, have joined the effort. A pressing need for programs addressing NTDs is the availability of high-quality, low-cost diagnostic tools deployable in low-resource settings. Tools that enable rapid and accurate detection of these diseases will become increasingly important for monitoring progress as levels of infection are reduced through disease-control efforts. Appropriate diagnostic tools also are needed to conduct surveillance for disease re-emergence after presumed elimination.

PATH's Diagnostics Program works to identify and develop innovative, high-impact, low-cost diagnostic tools to meet the needs of users in low-resource settings. We are working with a broad range of partners—industry, end-users, academic researchers, nongovernmental development organizations, national NTD programs, policymakers, and donors worldwide—to identify areas where the introduction and scale-up of new diagnostic tools for NTDs will have the greatest impact, to evaluate potential technologies, and to focus on the most promising solutions.

A crucial early step in the research and design phase of product development for diagnostic tools is defining their essential features, so that researchers and manufacturers can develop the best solutions. This is the purpose of a target product profile (TPP)—a strategic document that defines key characteristics of a product. TPPs must contain sufficient detail to allow developers to understand the attributes a successful tool must have—not only the technical requirements, but also those that allow its use in a defined setting. A TPP includes descriptions of design features, the types of specimens needed for diagnostic measurements, and performance characteristics such as clinical sensitivity and specificity.

PATH has constructed TPPs for diagnostic tools for three NTDs—schistosomiasis, soil-transmitted helminthiasis (STH), and blinding trachoma. We began this process with a review of the scientific literature and progressed through discussions with experts and other members of the NTD community, assessment of current technologies, mapping of in-country surveillance programs, and identification of biological markers and platforms. Each TPP was refined through an iterative process, with rounds of research, review by experts, and revision until consensus was reached.

For each of the three diseases, we created TPPs for two use cases: first, for monitoring mass drug administration (MDA) in communities, to help with decisions on when to reduce or stop treatment; and second, for post-elimination surveillance, to determine if a disease has re-emerged. The biomarker—the biological molecule assayed in the diagnostic tool—is either an antigen or a nucleic acid that is a component of the parasite, found in human body fluids and indicating active infection. For re-emergence, the biomarker is a human antibody to the parasite, indicating either current or past infection. In addition to information on how these TPPs were constructed, this report includes summary tables compiled from the original TPPs (see Annex). Full versions of all originals are freely available at [sites.path.org/dx/ntd/resources/](https://sites.path.org/dx/ntd/resources/).

# Introduction

## Neglected tropical diseases

Many diseases caused by bacteria, viruses, worms, and other parasites are endemic in tropical regions, where they inflict a crushing burden on the world's poorest people. Some of these illnesses, such as malaria, are well known, but others that also are widespread have received less attention and investment, and have been declared NTDs. WHO has targeted 17 of these for control, elimination, or eradication (Sidebar: Neglected tropical diseases and their infectious agents). Cumulatively, they are endemic in 149 countries, causing disability, stigmatization, pain, and suffering for 1.4 billion people across sub-Saharan Africa, Asia, and Central and South America.<sup>2</sup> Women and children are especially vulnerable, frequently suffering from several NTDs simultaneously and experiencing lifelong health consequences. NTDs contribute to a cycle of poverty: people become too ill or disabled to work or attend school, which results in detrimental effects not only on their health and livelihoods, but on those of their families and communities.

## Diagnostic tools

The fight to control and eventually eliminate NTDs requires not only effective treatment regimens, but also diagnostic tools to monitor progress and to facilitate decisions for interventions such as community-wide MDA (Sidebar, Mass drug administration of preventive chemotherapy). Current tools for many of these diseases are adequate for mapping disease distribution, but tools that offer better performance for sensitivity and specificity and are appropriate for use in low-resource settings—low-cost, easy-to-use, robust—will be needed as the disease burden is reduced.

### NEGLECTED TROPICAL DISEASES AND THEIR INFECTIOUS AGENTS<sup>1</sup>

#### Protozoa

Chagas disease  
Human African trypanosomiasis (sleeping sickness)  
Leishmaniasis

#### Bacteria

Buruli ulcer  
Leprosy (Hansen's disease)  
Blinding trachoma\*  
Endemic treponematoses (yaws)

#### Helminths

Cysticercosis/Taeniasis  
Dracunculiasis (Guinea worm disease)  
Echinococcosis  
Foodborne trematodiasis  
Lymphatic filariasis  
Onchocerciasis (river blindness)  
Schistosomiasis\*  
Soil-transmitted helminthiases\*

#### Viruses

Dengue  
Rabies

\*Diseases that are the subject of this report.

## Target product profiles

One of the crucial early steps in the research and design phase of product development for new diagnostic tools is defining their essential features, so that researchers and manufacturers can create the best solutions. This is the purpose of a TPP—a strategic document that defines key characteristics of a product and that is completed early in the product development chain (Figure 1). A well-designed TPP provides a structure that informs production of a new tool and maximizes the probability that it will include all fundamental technical features

Figure 1. The product development chain. Target product profiles are prepared during the research and design phase.



and operational requirements to meet the intended use in a defined setting.

PATH is working with a broad range of partners, including industry, end-users, academic researchers, nongovernmental development organizations, national NTD programs, policymakers, and donors to create TPPs for new diagnostic tools for NTDs. This document describes the need for new diagnostic tools for NTDs and the process that PATH uses to develop TPPs. We then discuss how TPPs for improved diagnostic tools for three diseases—schistosomiasis, soil-transmitted helminthiases (STH), and blinding trachoma—were developed. Finally, summaries of the full versions of the TPPs are presented (see Annex).

## Global efforts to combat neglected tropical diseases

In 2012, WHO released a global roadmap to accelerate work to control, eliminate, or eradicate 17 NTDs by 2020,<sup>1</sup> noting that despite the complexity of these diseases, the targets are achievable. Shortly after the release of this plan, 20 public and private institutions that support global health and international development—including pharmaceutical companies, donors, governments of endemic countries, nonprofit organizations, and others—joined the efforts to reach the 2020 goals for 10 of the 17 diseases, in a document known as the London Declaration on Neglected Tropical Diseases.<sup>3</sup> This group of partners is known as Uniting to Combat NTDs, and its efforts are coordinated by a stakeholders' working group that includes, among others, the following organizations: United States Agency for International Development (USAID), Department for International Development (DFID), the Global Network for Neglected Tropical Diseases, GlaxoSmithKline, the World Bank, and the Bill & Melinda Gates Foundation. Many more organizations have become signatories to the London Declaration, including PATH.

The pharmaceutical sector has contributed significantly to the control of these diseases by donating preventive chemotherapy (PCT) drugs necessary for treating some NTDs. Since the launch of the London Declaration in 2012, over 5.5 billion tablets have been donated.<sup>4</sup> However, the lack of effective diagnostic tools has been recognized as an obstacle for programs using PCT: as treatments

### MASS DRUG ADMINISTRATION OF PREVENTIVE CHEMOTHERAPY<sup>1</sup>

For some NTDs, the primary strategy for achieving the WHO roadmap targets is through MDA of preventive chemotherapy (PCT)—the regular and coordinated administration of safe, single-dose medicines on a large scale. This community-wide therapy is given regardless of individual disease status, to reduce and control infections. The following are designated as PCT diseases:

Lymphatic filariasis

Onchocerciasis

Foodborne trematode infections

Schistosomiasis\*

Soil-transmitted helminthiases\*

Blinding trachoma\*

The goal is to reduce infection in communities through a combination of MDA and prevention efforts, to the point that the diseases do not re-emerge once MDA programs are scaled back or stopped.

\*Diseases that are the subject of this report.

are scaled up, better diagnostic tools will be essential to inform and direct community MDA programs and take measure of their effects over time.

## Need for improved diagnostic tools

According to the 2014 report on progress to realize the London Declaration commitments,<sup>5</sup> leaders in research and development must continue to build on progress and develop new tools to address critical gaps. High-quality, sensitive, low-cost diagnostic tools that enable rapid and accurate detection of infections will become increasingly important as levels of infection are reduced through successful MDA and other disease-control efforts. New diagnostic tools are also needed to conduct surveillance for re-emergence after diseases have been declared eliminated and MDA has been discontinued. PATH, the Drugs for Neglected Diseases Initiative, the Foundation for Innovative New Diagnostics, and Medicines Development for Global Health are among the groups working to develop new drugs, diagnostic tools, and vaccines for NTDs.

## PATH'S ROLE IN IMPROVING DIAGNOSTIC TOOLS FOR THREE NTDs

PATH's Diagnostics Program aims to make appropriate diagnostic technologies available, broadly accessible, and integrated within health systems in low-resource settings. We work across the full spectrum of diagnostics technology development and introduction to orchestrate the design, development, and early introduction of new diagnostic solutions, and to position new tools for successful scale-up. We have expertise in the areas of needs assessments; research and development; commercialization and market dynamics; and product introduction and market development.

PATH is working with partners in the NTD community to spur development of high-impact tools needed to achieve control or elimination of NTDs targeted in the London Declaration. Among our activities are conducting a comprehensive search for existing platform technologies and biological markers; undertaking technical due diligence to select among candidate technologies; and providing product development expertise to advance selected diagnostic technologies. In the future, efforts will be directed at other NTDs targeted in the London Declaration, in addition to the three highlighted in this report and described below.

### Schistosomiasis

Schistosomiasis is caused by several species of parasitic worms that live part of their life cycle in freshwater snails and release larvae into lakes and streams. These larval forms penetrate the skin of people who wade into contaminated water to fish, wash clothes, or play; and after several days, the parasite makes its way to the liver to feed on red blood cells. When the worms reach maturity, they lay eggs—hundreds or thousands a day—and most of these become trapped in veins, the liver, and other organs. Then, the body's vigorous immune response becomes a problem, causing abdominal pain, diarrhea, fever, fatigue, genital sores, and enlargement of liver and spleen. Long-term symptoms include chronic bladder infection, intestinal polyps, and increased blood pressure in the vessels of the lung and liver. Children with schistosomiasis suffer from malnutrition and stunted growth, and adults with some forms of schistosomiasis may be more vulnerable to sexually transmitted infections such as HIV. In 2013, 261 million people in 52 countries were estimated as requiring preventive treatment for schistosomiasis.<sup>4</sup> Schistosomiasis is treated by MDA with the drug praziquantel. The goals set by WHO for schistosomiasis are disease control and regional elimination, to be achieved by a recommended national coverage rate of 75 percent with praziquantel.

### Soil-transmitted helminthiasis

STH is an infection by parasites called helminths, also known as intestinal worms. The main species that infect humans are roundworm, whipworm, and hookworm, which complete part of their life cycle in the soil. When an infected person's feces contaminate the environment, helminth eggs and larvae enter the soil. Other people become infected when they accidentally ingest contaminated soil containing eggs or, in the case of hookworm infection, walk on the ground with bare feet, which allows the larvae to enter through the skin. The worms feed on host tissues, including blood, which leads to a loss of iron and protein. Heavy infections can cause a range of symptoms including diarrhea and abdominal pain, general malaise and weakness, and impaired cognitive and physical development. Hookworms cause chronic intestinal blood loss that can result in anemia. WHO estimates that as many as 2 billion people<sup>4</sup> around the world are infected, and the effects on children are especially devastating—they are physically, nutritionally, and cognitively impaired. STH is treated by MDA with anthelmintic drugs such as albendazole and mebendazole. WHO has set the goal of disease control for STH through PCT coverage of 75 percent of at-risk preschool- and school-age children.

### Blinding trachoma

Blinding trachoma is the leading cause of infectious blindness worldwide. The disease is caused by the bacterium *Chlamydia trachomatis*, with infections usually beginning in infancy or childhood. If left untreated, years of repeated infection cause the eyelid to persistently turn inward and the eyelashes to rub on the eyeball, resulting in intense pain and scarring of the cornea, which ultimately leads to irreversible blindness. The infection is spread through contact with discharge from the eyes of an infected person or contact with eye-seeking flies that transfer the bacteria. Approximately 2.2 million people worldwide suffer from visual impairment due to trachoma, and 1.2 million of these are irreversibly blind.<sup>4</sup> Treatment consists of facial cleanliness and MDA with antibiotics such as azithromycin. The goal set by WHO for blinding trachoma is global elimination, through a comprehensive strategy that includes MDA, surgical intervention, and hygiene and environmental improvements.



PATH/Doune Porter

# To support NTD control programs and continue moving toward elimination, we need more sensitive diagnostic tools that are field friendly to ensure use in endemic settings.

## Current diagnostic tools for schistosomiasis, STH, and blinding trachoma

Control programs based on MDA have four designated stages: mapping disease prevalence, monitoring the impact of MDA interventions, making decisions to reduce or stop MDA, and performing surveillance after elimination has been certified (Figure 2). The current diagnostic tools for schistosomiasis and STH address the first stage by using methods that count the number of parasite eggs excreted in urine or stool. The main strength of this type of tool is extensive validation and familiarity worldwide. Requiring a microscope and a good light source, the technology allows use at some lower infrastructure levels. The major limitations are the need for a trained microscopist and the low sensitivity for detecting infections that have a low burden of infectious agents, which diminishes usefulness in later disease control stages. To support control programs and continue moving toward elimination, we need more sensitive diagnostic tools for STH and schistosomiasis for the reduction decision phase. The tools need to be field-friendly, to ensure use in endemic settings.

For blinding trachoma, current diagnosis is based on a physical examination of the inside of the eyelids and, as with the tools for schistosomiasis and STH, this tool is most appropriate for mapping. However, the clinical grading process is difficult to learn and conduct reliably, even for skilled health workers, because of variability in clinical signs, and these signs do not always indicate

active infection. Low levels of infection will become more common after multiple rounds of MDA, so more sensitive and specific diagnostic tools should be used to monitor the impact of MDA and to inform stopping decisions.

More sensitive tools for all three diseases will enable programs to assess quickly and accurately the points in time when levels of infection are low enough to reduce or stop mass treatment. These decisions are critical for preventing overtreatment as well as monitoring for re-emergence of disease. Defining the features necessary for these new tools is the goal of TPPs.

## Target product profiles

### Constructing a target product profile

A TPP is a strategic document that lists the desirable characteristics of any product, as a first step toward development of the product. TPPs must contain sufficient detail to allow developers and key stakeholders to understand the attributes a tool must have to be successful—not only the technical requirements, but also those that allow its use in a defined setting; for example, in a health care post in a tropical low-resource area.

The intended use of a product—here, a diagnostic tool for an NTD—is one aspect of its “**use case**,” which defines how and where it will be deployed and what interventions it will enable (Sidebar, Use case). In addition to describing the use case, a TPP includes information about design features such as instrument complexity, time to results, and shelf life; the type of specimens that must be collected for examination; and performance characteristics of the tool, such as clinical sensitivity and specificity. A TPP describes “**acceptable**” levels or values for these attributes and typically also includes “**ideal**” values that would make a tool more attractive; thus, there are two descriptions for each attribute. For example, an acceptable diagnostic tool might provide results in 24 hours, while an ideal one would take 15 minutes.

Ultimately, trade-offs between acceptable and ideal values will be necessary, and supporting information gathered during the TPP research process can help with these decisions. Research tools such as **conjoint analysis** can help with particularly difficult choices. In this type of analysis, potential users of the product





PATH/Dunia Faulx

**The SD BIOLINE Onchocerciasis IgG4 rapid test, the first in a suite of new diagnostics for NTDs supported by PATH.**

are asked to choose among various combinations of product characteristics, allowing researchers to find the “breakpoints” where trade-offs can satisfy stakeholders.

In addition to lists of acceptable and ideal attributes, TPPs contain explanations that support the decision to include each attribute, with citations of the scientific literature and other sources used to justify decisions. TPPs are further refined through an iterative process, with rounds of research, review by experts, and revision, until consensus is reached. These are considered “living” documents, to be reviewed at specific stage gates in the product development process and updated as research brings new knowledge to the field.

## Creating target product profiles for neglected tropical diseases

In developing TPPs for diagnostic tools for the three diseases discussed in this report, PATH first conducted a **review of the scientific literature** to understand how tools are used in surveillance programs. We identified the use cases for the diagnostic tools, and discussed these with disease and diagnostic subject-matter experts, both internally at PATH and with the broader NTD community. Once consensus was reached on the use cases, we assessed the availability of diagnostic tools and mapped this information onto the use cases to pinpoint technology gaps.

Next, we went deeper into defining the needs for new technologies, conducting **extensive interviews** with international experts and stakeholders, including those in NTD-endemic countries. These discussions revealed

limitations in available technologies and constraints imposed on tools by the way disease-surveillance programs work to find and diagnose people with these diseases. To better understand and characterize how surveillance testing is conducted, we constructed **process maps**, which are flow charts commonly used to understand a set of actions that make up a process. We used these maps to understand each step for diagnosing someone with a disease in communities of interest; for example, to see how a stool sample from a child is obtained and diagnosed during a surveillance program for STH (Figure 3).

Once we understood both the desirable use cases and had a working process map, we looked at available technologies for diagnostic tooling in more detail—not only relevant technologies already in use or available on the market, but also current and emerging biomarkers, platforms, and ancillary technologies reported by researchers or other experts in the field. Feedback and comments allowed iterative changes to the TPPs, and further refinement was achieved with targeted literature reviews and semi-quantitative stakeholder surveys.

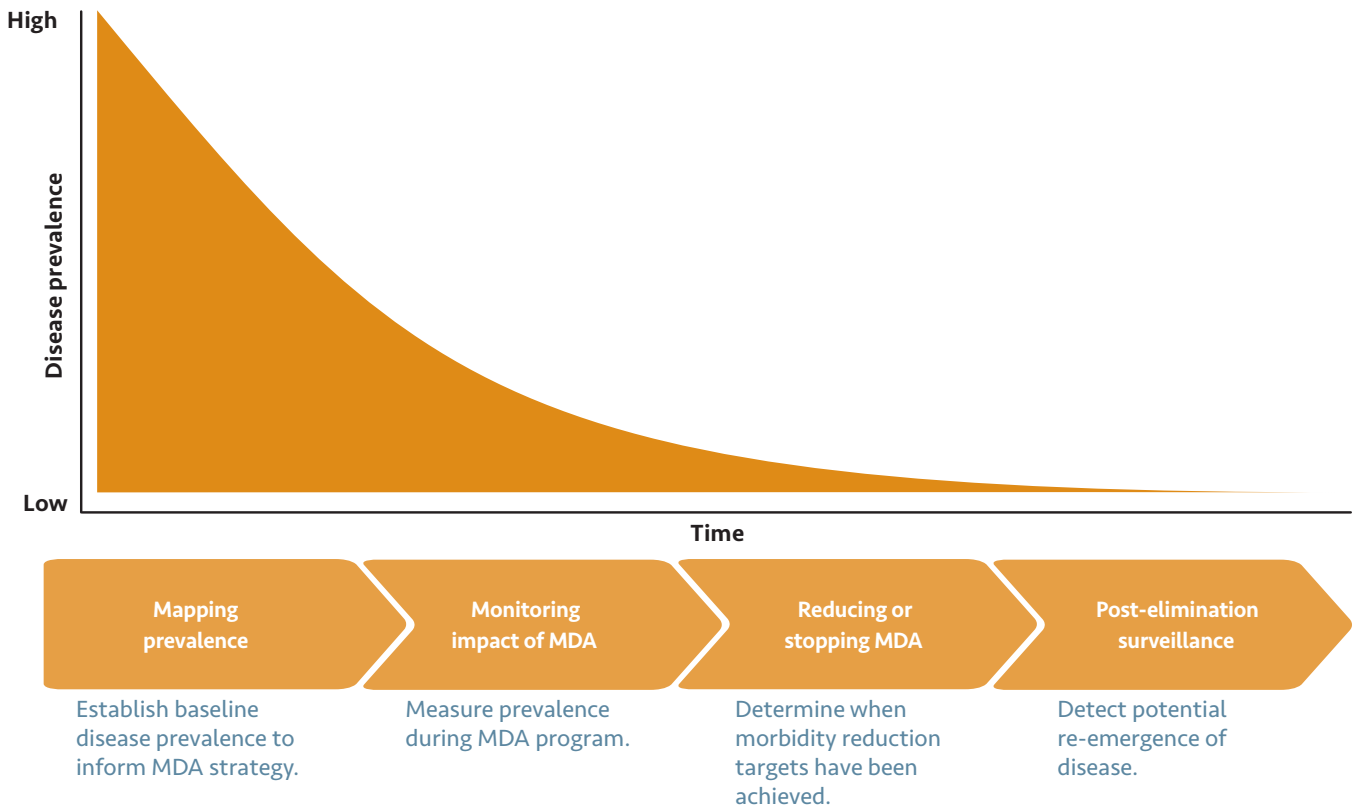
In order to make decisions on which biomarkers (Sidebar, Biomarkers) to use for tools, we began with general, technology- and biomarker-agnostic TPPs, and then customized them for particular choices as the technologies and biomarkers that could meet the requirements became clear. For example, if the goal for a tool for schistosomiasis is to be able to detect a very small number of worms in a patient, this must be translated

### USE CASE

A use case describes the interactions that occur between an “actor” and an object, or within the context of a “scene.” The scene of interest for developing TPPs for diagnostic tools for NTDs is a health system in a low-resource setting where clinicians or program managers make decisions about managing patients or treating NTDs at the community level. Some of the conditions taken into account are the expertise of the health care worker, target population, climate (temperature and humidity), and work flow at the health center.

The TPP first takes into account the use case, which informs the design of the tool. The design, in turn, informs the performance of the tool.

**Figure 2. Stages when disease control and elimination programs require diagnostic tools.**



Adapted from Solomon A, Engels D, et al. A Diagnostics Platform for the Integrated Mapping, Monitoring, and Surveillance of Neglected Tropical Diseases: Rationale and Target Product Profiles. *PLoS Neglected Tropical Diseases*. 2012;6(7). DOI: 10.1371/journal.pntd.0001746

into an amount of a worm-specific antigen that a tool can measure. For this disease, there is a known antigen that can be measured in very small amounts, so this became the designated biomarker in one of our TPPs for schistosomiasis.

#### BIOMARKERS

A biological marker—or biomarker—is a biological molecule found in body fluids or tissues that is a sign of a normal or abnormal process, or of a condition or disease.<sup>5</sup> Ideally, it is a substance that can be measured accurately and reproducibly.

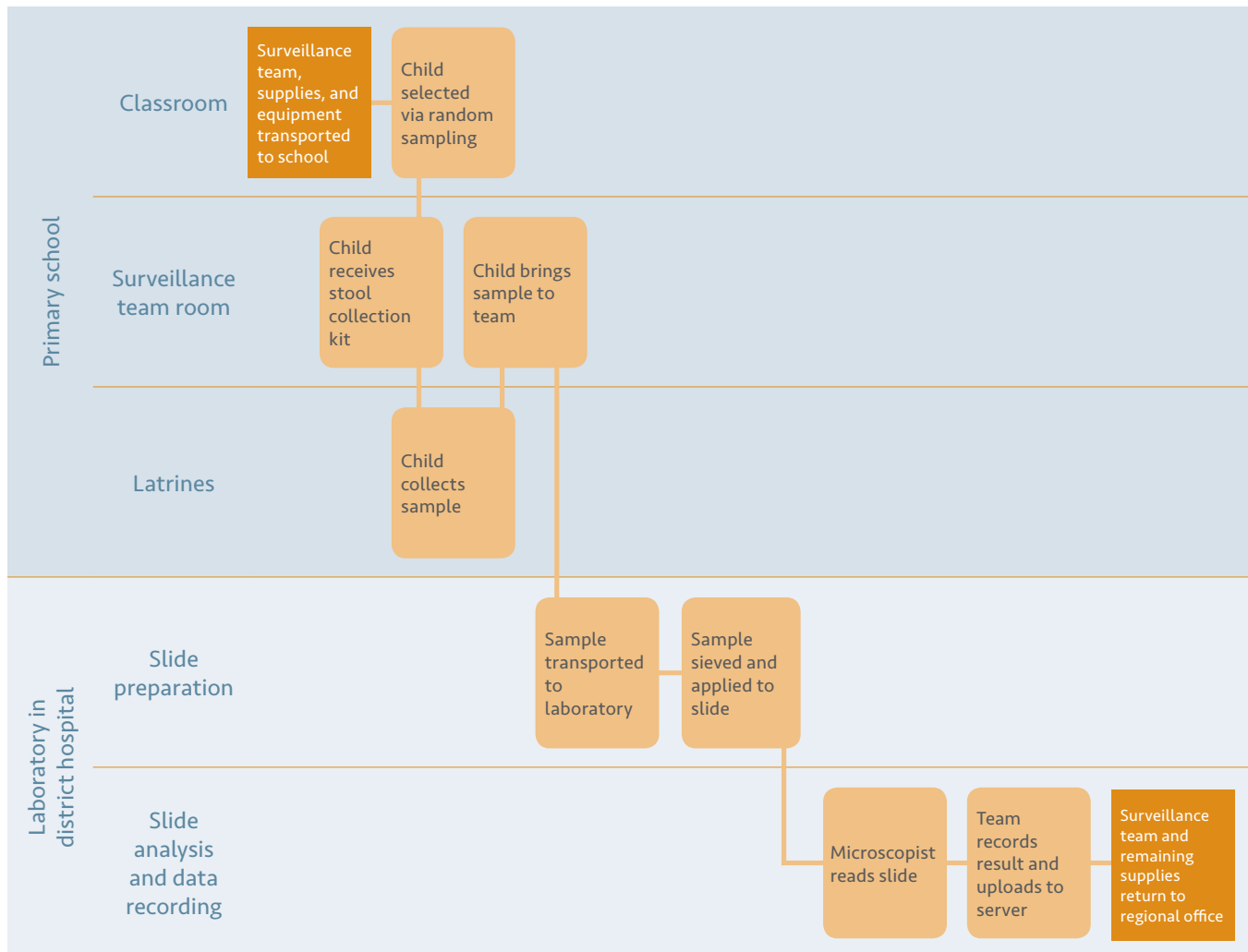
Different types of biological molecules can indicate the presence of an infection with NTDs. For example, material from pathogens includes antigens and nucleic acids: these biomarkers indicate an active infection.

An infection also can be detected by the host’s immune response to the pathogen in the form of antibodies. This biomarker indicates exposure to the pathogen, which may be an active or a past infection, but does not distinguish between the two.

For each of the three diseases considered here, TPPs have been created for two use cases: first, for reducing or stopping MDA; and second, for post-elimination surveillance. In the first case, the biomarker to be measured by the diagnostic tool is either an antigen or a nucleic acid. These biomarkers identify active infection: they are molecules from the parasite that are found in human body fluids, and their presence in the people surveyed can inform decisions about adjusting or stopping MDA.

For post-elimination surveillance, the diagnostic tool biomarker is an antibody against a component of the parasite in human blood; thus, it is an indirect assay for the parasite. The goal of this type of testing is to identify geographic areas of re-emergence of disease. If antibodies are found in people in age cohorts that should be negative because they were born after elimination was certified, antibody-positive results could mean there has been re-emergence of disease. Follow-on interventions can be focused in that area.

**Figure 3. A process map for soil-transmitted helminthiasis surveillance.**



## TPPs for schistosomiasis, STH, and blinding trachoma

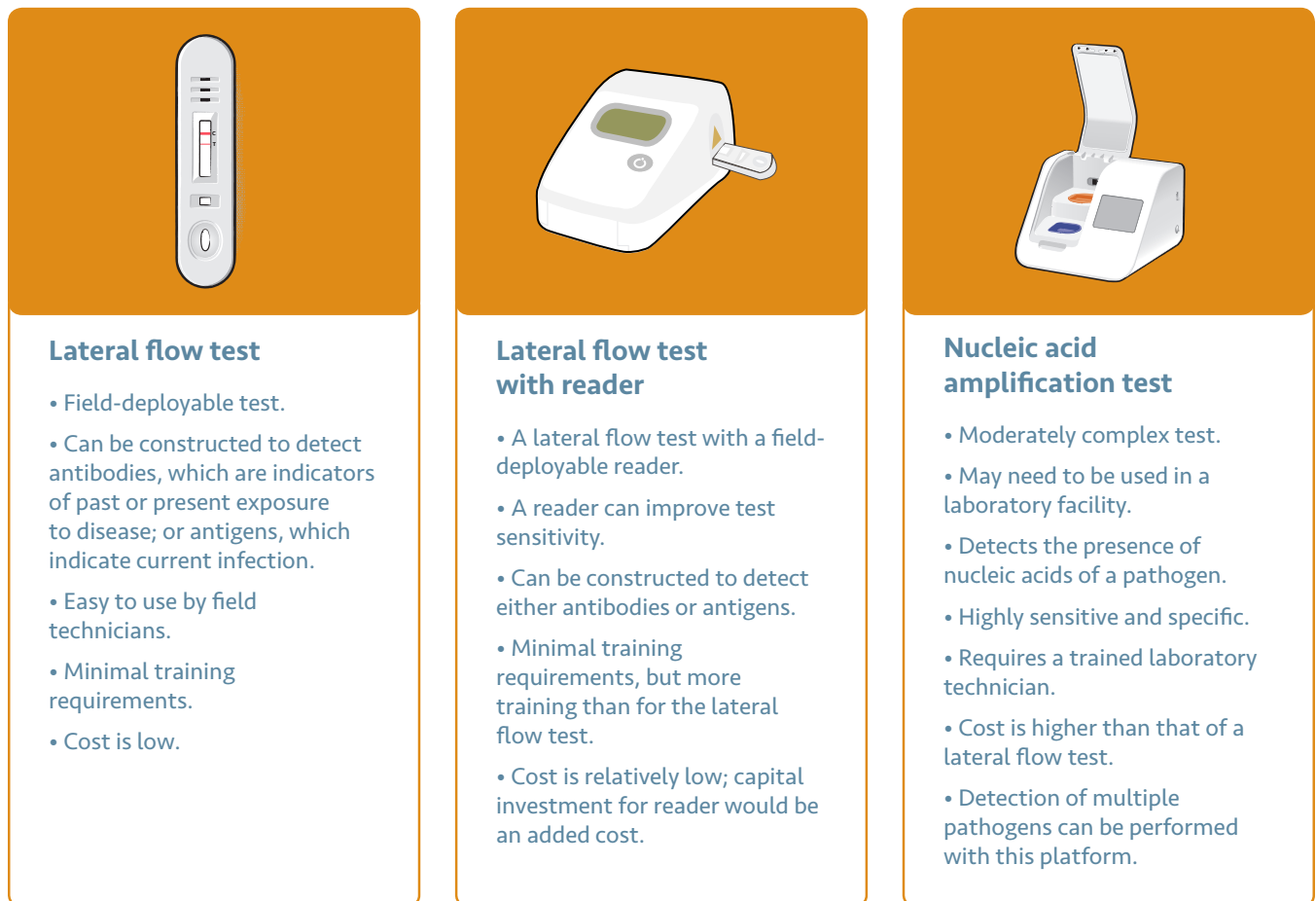
The TPPs developed for the two use cases for three selected NTDs are the result of input from key thought leaders, opinions of the larger NTD community, and the research activities described earlier. For the first use case—reducing or stopping MDA—there are two types of tools described: one for detecting antigens and one for detecting nucleic acids. For the second use case—post-elimination surveillance—the tool is for detecting antibodies (Figure 4).

The summary tables of TPPs presented in the Annex were compiled from the full versions, which are available at [sites.path.org/dx/ntd/resources](https://sites.path.org/dx/ntd/resources). The full versions address each disease individually and include

not only the acceptable product features, but also ideal attributes, which can improve ease of use for health workers and patients or provide higher performance. In the summaries, each table includes all three NTDs—schistosomiasis, STH, and blinding trachoma—to show where there are characteristics in common for the technologies. Given the level of shared attributes across tools for these diseases, it may be possible to integrate testing in the future, to make the process of diagnosing NTDs more efficient in low-resource settings.

- Table 1 is a summary of TPPs for lateral flow tests for antigen biomarkers. The use case for these tests is to inform decisions to adjust or stop MDA.
- Table 2 is a summary of TPPs for nucleic acid amplification tests. The use case for these tests is to inform decisions to adjust or stop MDA.

**Figure 4. Diagnostic tools for two use cases—reducing/stopping MDA and post-elimination surveillance. For the first, a lateral flow test can detect an antigen, or a nucleic acid amplification test can detect a nucleic acid, both from the parasite. For surveillance after elimination, a lateral flow test can detect human antibodies to the parasite. The middle panel shows the addition of a reader to a lateral flow test.**



- Table 3 is a summary of TPPs for lateral flow tests for antibody biomarkers. The use case for these tests is for post-elimination surveillance. It is important to note that there are few guidelines for post-elimination surveillance of NTDs, because few geographic areas have reached this goal. Attributes were informed by current knowledge and will benefit from further refinement as new guidelines are created.

## Summary and next steps

The London Declaration on Neglected Tropical Diseases states, “there is a tremendous opportunity to control or eliminate at least 10 devastating NTDs by the end of the decade... with the right commitment, coordination and collaboration, the public and private sectors

will work together to enable the more than a billion people suffering from NTDs to lead healthier and more productive lives—helping the world’s poorest build self-sufficiency.”<sup>73</sup> The lack of sensitive, effective, and field-friendly diagnostic tools for NTDs that also have appropriate cost and operational characteristics for low-resource settings remains a critical gap in the global health community’s ability to direct control and elimination efforts and to track progress in the fight against NTDs. PATH has joined the effort to provide these tools, and is identifying and focusing on technologies that will have the most potential to accelerate achievement of targets for control or elimination of NTDs. As an important first step, PATH has constructed TPPs for improved diagnostic tools for monitoring schistosomiasis, STH, and blinding trachoma during disease control and elimination phases.

In addition to supporting the development and evaluation of new diagnostic tools, PATH will work with partners to identify opportunities for commercialization that will bring these products to market. Additional resources will be needed to ensure that tools are produced and made available to national NTD control and elimination programs. Once these tools are implemented in the field, the evidence generated will help to guide policy development and encourage political and financial support for NTD programs.



PATH/Dunia Faulx

## References

1. World Health Organization (WHO). *Accelerating work to overcome the global impact of neglected tropical diseases – A roadmap to implementation*. Geneva: WHO/HTM/NTD; 2012. Available at: [whqlibdoc.who.int/hq/2012/WHO\\_HTM\\_NTD\\_2012.1\\_eng.pdf](http://whqlibdoc.who.int/hq/2012/WHO_HTM_NTD_2012.1_eng.pdf).
2. Neglected tropical diseases page. World Health Organization (WHO) website. Available at: [www.who.int/neglected\\_diseases/en/](http://www.who.int/neglected_diseases/en/). Accessed June 24, 2015.
3. Uniting to Combat Neglected Tropical Diseases. *The London Declaration on Neglected Tropical Diseases*. 2012. Available at: [unitingtocombatntds.org/resource/london-declaration](http://unitingtocombatntds.org/resource/london-declaration).
4. Uniting to Combat Neglected Tropical Diseases. Country leadership and collaboration on neglected tropical diseases: Third progress report of the London Declaration. 2015. Available at: [unitingtocombatntds.org/sites/default/files/document/UTCNTD%20FULL%20REPORT.pdf](http://unitingtocombatntds.org/sites/default/files/document/UTCNTD%20FULL%20REPORT.pdf).
5. Uniting to Combat Neglected Tropical Diseases. Delivering on promises and driving Progress. 2014. Available at: [unitingtocombatntds.org/resource/delivering-promises-and-driving-progress-second-progress-report](http://unitingtocombatntds.org/resource/delivering-promises-and-driving-progress-second-progress-report).
6. National Cancer Institute (NCI) dictionary of cancer terms page. National Cancer Institute website. Available at: [www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45618](http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45618). Accessed June 16, 2015.

## Annex

**Table 1.** Lateral flow tools for antigens: summary of acceptable\* requirements. Use case: reducing or stopping mass drug administration.

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
<b>Context</b>			
Intended use	To support the goals of disease control and regional elimination, the tool will monitor disease prevalence following mass drug administration and inform the decision to adjust the treatment strategy.	To support the goal of disease control, the tool will monitor disease prevalence following mass drug administration to inform the decision to adjust the treatment frequency.	To support the goal of elimination, the tool will monitor disease prevalence following mass drug administration and inform the decision to adjust the treatment strategy.
Patient population	Children 6 to 14 years old and other high-risk populations	Children 6 to 14 years old	Children 1 to 5 years old
Tooling location	The tools will be used in tier-2 facilities, households, or school settings. Minimal or no infrastructure is required.		
Tool user	Surveillance teams made up of technicians from the regional level, such as community health workers	Surveillance teams made up of technicians from the regional level, such as community health workers	Health care professional trained in eye examination
Stability and storage requirements	Withstand daily temperature fluctuations from 25°C to 40°C 40% to 88% relative humidity		
Cold chain	Not required		
<b>Tool design</b>			
Diagnostic biomarker	Circulating anodic antigen (genus-specific antigen)	Species-specific antigens; not yet identified	Species-specific <i>Chlamydia trachomatis</i> antigens; not yet identified
Specimen type and volume	Clean-catch urine: 4 mL, or finger-stick blood: 100 µL	Stool	Dry swab of conjunctiva of eye; only one swab required
Specimen preparation	Minimal collection or processing steps		
Time to result	No more than 24 hours		
Nature of result	Qualitative		
Throughput	At least 50 specimens per user per day		
Tool format and complexity	Field-based, rapid diagnostic tool; few timed steps; no technically difficult procedures		
Training requirements	Minimal: one day or less		

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
Instrumentation size and weight	Small; easily deployable in the field		
Shelf life	12 months		
<b>Tool performance</b>			
Clinical sensitivity	At least 70%		
Clinical specificity	At least 95%		
Reproducibility	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive specimens classify the same $\geq 95\%$ of the time
Comparative reference method	Standard microscopic assessment of number of parasite eggs	Standard microscopic assessment of number of parasite eggs	Current laboratory-based, regulatory-approved nucleic acid amplification tool

\*The detailed target product profiles, available at [sites.path.org/dx/ntd/resources/](https://sites.path.org/dx/ntd/resources/), also define “ideal” requirements, which are more stringent but provide greater ease of use or higher performance. For example, ideal tools would provide results in 15 minutes rather than 24 hours, and would provide clinical sensitivity of at least 95% rather than 70%.

The detailed target product profiles also include the following attributes that are not presented in this summary table:

#### Context

- Clinical and/or surveillance need (value proposition)
- Target countries
- Fit with clinical work flow/linkage to action (process map)

#### Tool design

- Specimen transport stability
- Waste management
- Infrastructure requirements
- Ancillary supplies
- Quality control
- Calibration

#### Performance

- Analytical limit of detection
- Analytical specificity



**Table 2.** Nucleic acid amplification tools: summary of acceptable\* requirements. Use case: reducing or stopping mass drug administration.

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
<b>Context</b>			
Intended use	To support the goals of disease control and regional elimination, the tool will monitor disease prevalence following mass drug administration and inform the decision to adjust the treatment strategy.	To support the goal of disease control, the tool will monitor disease prevalence following mass drug administration to inform the decision to adjust the treatment frequency.	To support the goal of elimination, the tool will monitor disease prevalence following mass drug administration and inform the decision to adjust the treatment strategy.
Patient population	Children 6 to 14 years old and other high-risk populations	Children 6 to 14 years old	Children 1 to 5 years old
Tooling location	Tier- 2 facilities or school settings. Minimal or no infrastructure requirements	Tier- 2 facilities or school settings. Minimal or no infrastructure requirements	Tier- 3 facilities such as clinics or health posts (outpatient). Moderate infrastructure requirements
Tool user	Surveillance teams made up of technicians from the regional level, such as community health workers	Surveillance teams made up of technicians from the regional level, such as community health workers	Health care professional trained in eye examination
Stability and storage requirements	Withstand daily temperature fluctuations from 25°C to 40°C 40% to 88% relative humidity		
Cold chain	Not required		
<b>Tool design</b>			
Diagnostic biomarker	<i>Schistosoma</i> genus-specific nucleic acid	Species-specific nucleic acid	<i>Chlamydia trachomatis</i> nucleic acid
Specimen type and volume	Clean-catch urine: 4 mL; or finger-stick blood: 100 µL	Stool	Dry swab of conjunctiva of eye; only one swab required
Specimen preparation	Minimal collection or processing steps		
Time to result	No more than 24 hours		
Nature of result	Qualitative		
Throughput	At least 50 specimens per user per day		

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
Tool format and complexity	Field-based; rapid diagnostic tool; few timed steps; no technically difficult procedures		
Training requirements	Minimal	Minimal	Moderate (less than three days)
Instrumentation size and weight	Small; easily deployable in the field		
Shelf life	12 months		
<b>Tool performance</b>			
Clinical sensitivity	At least 90%		
Clinical specificity	At least 95%		
Reproducibility	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive specimens classify the same $\geq 95\%$ of the time
Comparative reference method	Standard microscopic assessment of number of parasite eggs	Standard microscopic assessment of number of parasite eggs	Current laboratory-based, regulatory-approved nucleic acid amplification tool

\*The detailed target product profiles, available at [sites.path.org/dx/ntd/resources/](https://sites.path.org/dx/ntd/resources/), also define “ideal” requirements, which are more stringent but provide higher performance or greater ease of use. For example, ideal tools would provide results in 15 minutes rather than 24 hours; ideal tools provide clinical sensitivity of at least 95% and specificity of at least 99%.

The detailed target product profiles include the following attributes that are not presented in this summary table:

#### Context

- Clinical and/or surveillance need (value proposition)
- Target countries
- Fit with clinical work flow/linkage to action (process map)

#### Tool design

- Specimen transport stability
- Waste management
- Infrastructure requirements
- Ancillary supplies
- Quality control
- Calibration

#### Performance

- Analytical limit of detection
- Analytical specificity

**Table 3.** Lateral flow tools for antibodies: summary of acceptable\* requirements. Use case: post-elimination surveillance.

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
<b>Context</b>			
Intended use	To support the goals of disease control and regional elimination, the tool will monitor disease re-emergence after stopping mass drug administration	To support the goal of disease control, the tool will monitor disease re-emergence after stopping mass drug administration	To support the goal of elimination, the tool will monitor disease re-emergence after stopping mass drug administration
Patient population	Children 6 to 14 years old and other high-risk populations	Children 6 to 14 years old	Children 1 to 5 years old
Tooling location	The tools will be used in tier-2 facilities, households, or school settings. Minimal or no infrastructure is required.		
Tool user	Surveillance teams made up of technicians from the regional level, such as community health workers	Surveillance teams made up of technicians from the regional level, such as community health workers	Health care professional trained in eye examination
Stability and storage requirements	Withstand daily temperature fluctuations from 25°C to 40°C 40% to 88% relative humidity		
Cold chain	Not required		
<b>Tool design</b>			
Diagnostic biomarker	<i>Schistosoma</i> genus-specific antibody	STH species-specific antibody	<i>Chlamydia trachomatis</i> species-specific antibody
Specimen type and volume	Finger-stick blood: 100 µL		
Specimen preparation	Minimal collection or processing steps		
Time to result	No more than 24 hours		
Nature of result	Qualitative		
Throughput	At least 50 specimens per user per day		
Tool format and complexity	Field-based, rapid diagnostic tool; few timed steps; no technically difficult procedures		
Training requirements	Minimal: one day or less		
Instrumentation size and weight	Small; easily deployable in the field		
Shelf life	12 months		

Attribute	Schistosomiasis	Soil-transmitted helminthiasis	Blinding trachoma
<b>Tool performance</b>			
Clinical sensitivity		At least 75%	
Clinical specificity		At least 95%	
Reproducibility	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive and weak negative specimens classify the same $\geq 95\%$ of the time	Replicate determinations of weak positive specimens classify the same $\geq 95\%$ of the time
Comparative reference method	Standard microscopic assessment of number of parasite eggs	Standard microscopic assessment of number of parasite eggs	Standardized immunoassay

\*The detailed target product profiles, available at [sites.path.org/dx/ntd/resources/](https://sites.path.org/dx/ntd/resources/), also define “ideal” requirements, which are more stringent but provide greater ease of use or higher performance. For example, ideal tools would provide results in 15 minutes rather than 24 hours, and would provide clinical sensitivity of at least 90% rather than 75%.

The detailed target product profiles also include the following attributes that are not presented in this summary table:

#### Context

- Clinical and/or surveillance need (value proposition)
- Target countries
- Fit with clinical work flow/linkage to action (process map)

#### Tool design

- Specimen transport stability
- Waste management
- Infrastructure requirements
- Ancillary supplies
- Quality control
- Calibration

#### Performance

- Analytical limit of detection
- Analytical specificity

