

Neglected Tropical Diseases: Diagnostics for Elimination and Programmatic Decision-Making

Many neglected tropical diseases (NTDs) lack simple, affordable diagnostics suitable for community-level case finding, programmatic decision-making, and surveillance. These diagnostic gaps slow case detection, limit targeted mass drug administration (MDA) and other programmatic interventions, and weaken progress toward case-finding, transmission-interruption, and elimination goals.¹ Diseases of particular programmatic concern include visceral leishmaniasis (VL)², lymphatic filariasis (LF)³, soil-transmitted helminthiasis (STH)⁴, human African trypanosomiasis (HAT)⁵, guinea worm disease⁶, onchocerciasis⁷, trachoma⁸, and schistosomiasis⁹; each presents distinct diagnostic challenges across case detection, mapping, monitoring, and validation of elimination.¹

Existing tools are often laboratory-based, insufficiently sensitive at low prevalence, or ill-suited to repeated community-level surveillance. Many rely on specimen transport to centralized laboratories and skilled personnel to perform and interpret results. For example, microscopy and conventional assays can miss low-intensity infections that matter for elimination decision-making and often require laboratory infrastructure, overnight slide preparation, functional microscopes, and trained technicians to identify and quantify organisms.¹⁰ Antibody assays may detect past exposure without distinguishing active infection, and many molecular tests, while sensitive, require infrastructure and have costs that preclude routine program use in peripheral settings.¹¹ These constraints create operational tradeoffs between sensitivity, programmatic feasibility, and cost that reduce the effectiveness of MDA targeting and surveillance for recrudescence.¹²

The World Health Organization (WHO) NTD Roadmap emphasizes diagnostics as a cross-cutting accelerator for ending NTDs as a public-health problem.¹ The Roadmap calls for innovation to close diagnostic gaps that impede mapping, programmatic decision-making, case-finding, and post-MDA surveillance, and it highlights the need for tools that are sensitive at low prevalence, suitable for community deployment, and integrated into routine program workflows.¹ WHO's Diagnostic Technical Advisory Group (DTAG) further operationalizes these needs through disease-specific and cross-cutting target product profiles (TPPs) and diagnostic guidance to align development with program endpoints.¹³

Accordingly, high-value diagnostic opportunities for NTDs are those that directly inform programmatic decisions at advanced stages of control and elimination, where prevalence is low, transmission is focal, and the cost of false positives or false negatives is high.

As programs approach elimination targets, diagnostic needs shift from identifying heavy infections to determining whether ongoing transmission persists. A persistent challenge is that antibody responses can remain detectable after transmission has been interrupted, while some antigen or nucleic-acid signals may lag or persist depending on parasite biology and test target. DTAG-aligned TPPs and guidance emphasize the need for assays that better reflect current infection or recent exposure in low-prevalence settings to support stop-MDA and post-validation decisions, where even small false-positive rates can drive unnecessary continuation of MDA.¹⁴⁻¹⁵

For filarial NTDs, tests that detect circulating parasite antigens or other biomarkers of viable worms can improve specificity for ongoing infection relative to exposure-only serology. In lymphatic filariasis, circulating filarial antigen (CFA) testing has been central to mapping and monitoring; the Filariasis Test Strip illustrates how antigen-based POC tools can be developed and introduced for program use.¹⁶ WHO's LF surveillance TPP specifies stringent performance targets (especially specificity) for post-MDA

surveillance and recrudescence detection at low prevalence.^{14,17} Similarly, WHO has published onchocerciasis diagnostic TPPs to support preventive chemotherapy and elimination-phase decisions, emphasizing rapid, field-deployable formats and very high specificity in low-prevalence settings.¹⁸⁻¹⁹

Operational barriers can be biology-driven: for example, microfilariae periodicity historically required night blood collection for microscopy-based LF diagnosis, complicating community surveys. Alternatives that reduce or eliminate time-restricted sampling and reliance on blood or venous sampling through different specimen types, simplified collection, or non-invasive sampling can materially improve feasibility in elimination settings. WHO's LF surveillance TPP explicitly prioritizes finger-stick blood and discourages venipuncture, reflecting the need to simplify sampling at scale.¹⁴ In parallel, systematic reviews in low-prevalence settings highlight the need for more sensitive surveillance approaches than standard survey designs and for diagnostics that are fit-for-purpose as programs move beyond MDA.¹⁵

Guinea worm eradication has been complicated by animal reservoirs, particularly domestic dogs, which can sustain environmental contamination even as human cases approach zero. A diagnostic capable of detecting prepatent infection in dogs before worm emergence would enable targeted containment actions (e.g., water-source protection) at the most programmatically valuable time point. Modeling work suggests that a prepatent canine diagnostic could materially accelerate elimination when combined with existing interventions.²⁰ Recent laboratory research has evaluated candidate antigens for detecting prepatent infection in dogs, illustrating a plausible technical pathway for such tools.²¹

As prevalence falls, programs must test larger populations to detect rare infections, making single-disease surveillance increasingly inefficient. Integrated approaches that leverage multiplex serology and high-throughput platforms can support coordinated post-MDA mapping across multiple NTDs (e.g., onchocerciasis, LF, schistosomiasis, and STH), while lowering per-disease costs and simplifying logistics. Reviews highlight the growing use of multiplex bead assays for integrated serosurveillance, including in LMIC settings.²² A post-elimination surveillance perspective further underscores the need to institutionalize integrated surveillance platforms and strengthen interpretation of low-prevalence signals.²³ Field studies demonstrate feasibility of integrated serosurveillance across multiple NTDs using shared sampling and platform approaches.²⁴ For schistosomiasis specifically, WHO guidance now explicitly addresses diagnostic testing in low-transmission areas and evaluating interruption of transmission, and systematic reviews continue to assess comparative performance of diagnostic tools.²⁵⁻²⁶

Innovations across these use cases should address program realities including simplified specimen collection, heat/dust/intermittent power tolerance, simple training models, data interoperability for program reporting, and must include credible pathways to affordable manufacturing and/or supply chains in endemic regions.

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