Request for Proposals: Optimizing NTD diagnostics and sampling strategies for low-prevalence settings

The Neglected Tropical Diseases (NTD) Support Center, a program of The Task Force for Global Health, with support from the United States Agency for International Development (USAID) through the COR-NTD grant, is soliciting proposals for:

1. Research targeting the near-term development of highly specific diagnostic markers, tools and technologies to monitor and evaluate programs aimed at lymphatic filariasis (LF) and onchocerciasis (oncho) in low-prevalence settings.
2. Research on application of epidemiological and statistical methods that maximize the programmatic effectiveness of survey sampling strategies to detect specific LF and oncho signals in low-prevalence settings.

Background

NTDs are a diverse group of 20 diseases that affect more than 2 billion people in 149 countries. People affected by these diseases suffer from significant long-term disabilities such as visual, physical or cognitive impairments, social stigma, and sometimes even death. NTDs often prevent people from working or attending school, thus costing developing economies billions of dollars annually.

Some NTDs (including LF and oncho) can be controlled through the administration of preventive chemotherapy to the entire eligible at-risk population via mass drug administration (MDA). For these diseases, control/elimination programs are based on a four-stage process:

- Mapping disease prevalence to determine if treatment is warranted and where it is needed
- Monitoring prevalence levels during treatment
- Stopping treatment once prevalence has declined below a defined threshold
- Surveillance to ensure that disease prevalence does not increase again after treatment has stopped.

At each stage of this process, programs rely on the availability of high-quality diagnostic tools to make important decisions. Diagnostics for these diseases must inform population-level decisions on stopping mass treatment, enable disease surveillance and allow for confidence in validating or verifying elimination.

Traditionally, NTD programs have relied on clinical and parasitological techniques for mapping disease distribution and for monitoring the progress of NTD interventions. However, as programs progress, prevalence declines and case finding becomes more difficult, the need for improved diagnostics comes into much sharper focus. The NTD community has traditionally underinvested in the development and improvement of diagnostic tools with the result that the currently available diagnostic tools are not capable of fully supporting the needs of late-stage control/elimination programs.

To address this critical gap, the World Health Organization (WHO) launched a Diagnostics Technical Advisory Group (DTAG) which was tasked with reviewing and prioritizing diagnostic needs for NTD programs, defining use cases and target product profiles (TPPs) for needed tools, working with national NTD programs and implementing partners to support test development and validation, and providing WHO with guidance and recommendation on adoption of new tools. Disease-specific DTAG subgroups have now developed TPPs and use-case analyses that can be used by product developers to understand the specific needs and contexts of NTD programs.

Defining the general problem: Diagnostic specificity in low-prevalence settings

In order to decide when mass treatment is warranted or can be safely stopped, NTD control/elimination programs use population-based surveys to show that disease prevalence in a given area is likely above or below a certain threshold. During the surveillance stage, programs continue to monitor prevalence to ensure that it does not exceed that threshold, thus necessitating re-treatment.

This reliance on population-based surveys for decision making, rather than individual diagnosis, requires that test performance be considered in the context of such surveys. Stop/start-treatment decisions, along with surveillance, are typically made by comparing the observed survey prevalence against a target threshold. This observed prevalence is dependent on the number of individuals testing positive, which will include true positives and those testing positive falsely.

As programs approach elimination and the prevalence of disease decreases, the probability that a positive test is indicative of a true positive (i.e., the positive predictive value) also decreases; consequently, as diseases become rare, specificity becomes the main driver of positive tests. In this situation, the number of false positives may lead to over-treatment, thus wasting valuable resources and time. It is therefore essential to maximize specificity in diagnostics used to support programmatic decisions based on cluster surveys. Furthermore, the target prevalence thresholds in these situations are, by necessity, extremely low.

The following tables summarizes the priority use cases, target thresholds, and TPPs as defined by the LF and oncho DTAG sub-groups.

	Use case description	Target threshold	TPP
LF	IDA stopping	<1%*	IDA stopping
	Surveillance	<5%**	LF surveillance
Oncho***	Oncho Elimination Mapping & MDA Stopping	>2%	Mapping
		<1%	Oncho MDA Stopping

* LF stopping threshold in areas where *Culex* or *Anopheles spp*. are the primary vector. In areas where *Aedes spp*. are the primary vector the stopping threshold is 0.5%
** Potentially as low as 1% depending on the analyte
*** The draft Oncho TPPs are currently under a 28-day period of public review and may change slightly as the result of feedback received. Finalized TPPs are expected in January 2021.

Scope of this RFP
This RFP covers two topic areas:

1. New or improved diagnostic markers/tools/technologies -
Innovative approaches to improve existing diagnostic tools or develop new tools with very high specificity to support programmatic decision making based on population-based surveys. It may be possible to achieve high specificity through modification of the biomarker, of the test platform or by basing a positive test on the presence of a combination of biomarkers for a single infection.

2. Application of new epidemiological or statistical methods to maximize the effectiveness of survey sampling strategies to detect specific LF and oncho signal in low-prevalence settings
It may be possible to get away from the need for extremely high specificity requirements by employing innovative sampling strategies that are better able to detect very low true prevalence signal. Such methods have been suggested, but have not been systematically evaluated in programmatic setting. Proposals on implementation of new epidemiological strategies can be based on existing diagnostic tools.

Proposals can address technologies or epidemiological methods used previously in the global health context or new products or methods which have never been tested before. Proposals must align with the needs and contexts outlined by the DTAG TPPs and landscape summaries.

Review process overview

Proposals in line with the scope of this RFP will be reviewed by a panel of objective reviewers from the NTD Support Center, Centers for Disease Control and Prevention, USAID, World Health Organization and other partner organizations based on how well they address these criteria:

Technical merit	Proposals must be technically sound, well written, with clear objectives and contextual evidence justifying the proposed research.
Alignment with programmatic needs	Proposals must align with the needs identified in the TPPs and use case documents
Scalability and Potential for impact	Proposed research must have the potential to improve community-based surveys to support

	decision making as described by the use case documents. Proposals should make consideration for how the research/innovations have potential for impact at scale. Proposals should outline plans for knowledge dissemination and next steps Proposals must demonstrate that the proposed tools or methods have use beyond the scope of the RFP
Sustainability	Proposed research should lead to new tools or methods that can realistically be made available to national NTD programs with or without external funding
Projected costs	Proposals must be in line with maximum funding available per project ($500,000). Proposals focused on development or improvement of diagnostic tools must take into account the cost requirements outlined by the TPPs Proposals focused on epidemiological methods/survey strategies must demonstrate that new methods are in line with existing methods All proposals must demonstrate value for money and follow the budget guidance provided

Award information

Maximum duration: 12 months

Maximum total funding available for all projects:
Biomarkers/tools/products: $2,500,000
Epidemiological methods: $500,000
Maximum funding available per project: $500,000

Submission instructions:
All proposals must be submitted using the following web form:
https://app.smartsheet.com/b/form/39d06350cb4f465e8c93a7611e98ccdd

Submissions should include the following documents:

- Study protocol
- Study budget (Budgets using any template will be accepted as long as they follow these budget requirements. The NTDSC budget template can also be used)
- Budget narrative for proposals over $300,000
- Project timeline
- Relevant supporting documents (additional background information, references, theory of change/conceptual framework, documentation of national per diem rates, etc)

Submissions must be received by January 31, 2021 at11:59 PM EST in order to be considered.

For questions concerning this RFP, please contact Ashley Souza (asouza@taskforce.org).