# Stakeholders' Meeting: Presidential Initiative for Neglected Tropical Disease (NTD) Control

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# Working Paper 3: *Operational Research to Support Implementation and Scale- up of Integrated NTD Programs*

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## Background

This paper is the product of a working group meeting held in Atlanta, Georgia on September 3, 2008, which included scientists and program managers with extensive experience in operational research on specific Neglected Tropical Diseases (NTDs) and/or the integration of NTDs. It summarizes many questions that can be considered for pursuing operational research on NTDs. While the majority of these issues extend beyond the scope of the President's Initiative for NTDs, it is anticipated that this list will be prioritized at the NTD Stakeholders' Meeting held in Washington D.C. on 20-21 October 2008, and will serve as a guide for other donors, technical agencies, implementing partners, and countries to prioritize their own operational research agendas.

## Introduction

The past five years have seen a dramatic expansion of interest in NTDs, a group of diseases which cause substantial morbidity for hundreds of millions of persons. For 5 of these NTDs – lymphatic filariasis (LF), onchocerciasis, schistosomiasis, soil transmitted helminths (Ascaris, Trichuris, hookworm), and trachoma – disease control or elimination is possible through strategies that include mass drug administration (MDA) with annual or semi-annual doses of safe and effective oral medicines. These programs have benefited from donations of drugs by large pharmaceutical companies and funding from USAID and the Bill & Melinda Gates Foundation. Traditionally, NTD programs have been driven by disease-specific interests; however, given the similarity of approaches to implementation, programs can increase their efficiencies by delivering drugs in a coordinated fashion. Initial experience from countries implementing integrated NTD programs has been positive and provided strong evidence that integration is feasible. President Bush's recent announcement of a Presidential Initiative to Combat Neglected Tropical Diseases presents exciting opportunities to build on this success and expand the scope and reach of NTD programs.

WHO guidelines for preventive chemotherapy provide a framework for countries that are implementing NTD programs based on our current understanding of best practices for program development and implementation; however, there are many unanswered questions about how to optimize these programs in terms of mapping, drug delivery, social mobilization and monitoring and evaluation. Global NTD efforts are more likely to be successful over the long term if supported by a vigorous operational research agenda that addresses these issues. The research issues summarized in the current document are based on extensive discussions with researchers and program managers working on NTDs. Priority areas for research include drug delivery, co-administration of drugs, and monitoring and evaluation. Though not an operational research issue *per se*, the development of effective diagnostic tools needed for the different stages of NTD programs was consistently identified by researchers and program managers as a top priority. Similarly, an integrated data management system would facilitate efforts at country level to use M&E data to effectively manage programs. Other important research priorities include mapping, social mobilization, and complementary program activities such as those focusing on surgery or water, sanitation and hygiene.

## Improving service delivery

The principle focus of the targeted NTD programs is MDA. Our ability to provide public health benefits to communities affected by NTDs is influenced by a number of factors, but especially by our ability to reach target populations and to achieve high coverage. Despite the remarkable success of community-directed treatment (CDT) programs for the control of morbidity due to onchocerciasis, a number of questions remain about optimal drug delivery strategies.

- What is the best delivery strategy for NTD programs, through CDT or schools or other channels?
- How can the role of health facilities be strengthened in the context of community-directed treatment?
- What is the best way to coordinate drug delivery through different channels (e.g., school, CDT and MDA campaigns)?
- How can drug delivery strategies be adapted to reach difficult to target populations?
- Can drug delivery strategies be optimized to achieve elimination?
- Where drug quantity is limiting, can morbidity control be achieved with drug rotations?

## Co-administration and co-implementation

WHO studies have established the safety and effectiveness of co-administration of drugs for combinations of drugs, including ivermectin, Albendazole/Mebendazole, and praziquantel; nonetheless, a number of obstacles continue to hamper integrated MDAs.

- Are there interactions between azithromycin and praziquantel or ivermectin that would prevent co-administration of these drugs?
- Is it feasible to co-administer combinations of four drugs (ivermectin, Albendazole/Mebendazole, praziquantel and azithromycin)?
- Will co-administration of drugs lead to an increase in adverse events or noncompliance?
- Can current systems for pharmacoviligilance be strengthened?
- Can treatment guidelines or delivery strategies be modified to increase NTD treatment options for pregnant women?
- Is it possible to develop standardized dosing thresholds, e.g. for ivermectin (>90 cm eligible for treatment) and praziquantel (>94 cm eligible for treatment)?

Though clearly more than an operational research issue, it is important to recognize that the presence of *Loa loa* continues to represent an important obstacle to the implementation of integrated NTD programs in West and Central Africa. New approaches to treat persons in Loa-endemic areas or to reduce the risk of severe adverse events are urgently needed.

## Monitoring and evaluation (M&E)

To document program impact and success, it is essential that NTD programs be well monitored. Although disease-specific programs have established a strong foundation for M&E, there is a clear need to develop and validate integrated approaches to M&E of integrated NTD programs.

Developing M&E guidelines is a key priority for WHO and a major focus of ongoing efforts. In addition, the critical role of diagnostic tools, both to detect infection in humans as well as vectors, is well recognized; new, field friendly, robust diagnostic techniques are urgently needed, both for initial mapping but especially for the determination of endpoints and to conduct surveillance.

- How accurate are coverage surveys for assessing participation rates in MDA?
- Can we develop alternative methods for coverage assessment that are simple, cost effective and meet program needs?
- How can we best evaluate the impact of programs targeting the NTDs? Are sentinel sites the most cost effective option?
- What are the ancillary benefits of integrated MDA on other health indicators, including anemia, acute respiratory infections, skin infections and malaria?
- What is the broader impact of integrated MDA, e.g., on DALY's and school attendance and performance?
- What is the impact of malaria control on certain NTDs, such as the effect of insecticide impregnated bed nets on LF?
- How do we assess stopping points or drug rotation schedules for individual diseases in the context of integrated MDA?
- What is the most cost-effect strategy for post-MDA surveillance?
- Can mathematical models facilitate programmatic decision-making?

**Program development and support**

**Mapping:** The first step in developing integrated programs is to define the distribution and degree of overlap of the different infections in order to treatment decisions at the operational level. Mapping the distribution of NTDs has been challenging because of the cost of the activity, the nature of the surveys and tests needed to diagnose the infection (blood, stool, urine or clinical exam) and the different approaches used by the programs to select implementation units. In addition, the distribution of NTDs is often defined by ecological zones rather than political boundaries.

- Is it possible to develop an integrated mapping protocol for NTDs which can be implemented rapidly and effectively by Ministries of Health?
- What is the predictive value of integrated mapping methods, including those based on spatial modeling?
- Can rapid, field applicable diagnostic tests be developed? Is it possible to have one rapid test for different NTDs? Can lab capacity be strengthened at the country level?
- What is the best strategy for selecting implementation units (IU) for integrated NTD programs?
- How do choices of implementation units influence program cost, both in terms of missed treatment opportunities (e.g. cases not prevented/treated) or over-treatment (e.g., cost of drugs, unnecessary side effects)?

**Social mobilization:** Social mobilization and health education is important for the success of NTD programs. It not only helps to achieve optimal drug coverage, but it is also necessary to

inform the population of the other aspects of the program, such as hygiene, use of clean water and latrines and management of disease-related morbidity. Despite a significant investment by WHO in the development of social mobilization efforts based on communication for behavioral impact (COMBI), many programs neglect this important program component, presumably because of the cost of the activity.

- What motivates people to participate in MDA?
- How do social mobilization and advocacy efforts contribute to compliance?
- How do health education campaigns lead to behavioral change and reduced transmission of NTDs?
- What are the best conduits for delivery of integrated NTD messages when resources are limited?
- How important is directly observed treatment for attaining high levels of population compliance?
- What is the best integrated message in different settings/ with different combinations of NTDs? What is the optimum amount of information needed to achieve high coverage?

**Complementary programmatic activities:** The long term success of NTD programs will be influenced by other health development efforts. For several NTDs, water, sanitation and hygiene programs will protect the health gains achieved by MDA. Morbidity control programs (e.g., trichiasis surgery, lymphedema management), while important in their own right, may also increase community support for MDA. Though beyond the scope of the USAID NTD program, it will be important to quantify the contribution of these other efforts to NTD programs.

- How do water, sanitation and hygiene efforts contribute to the success of NTD programs?
- How do morbidity control programs contribute to the success of NTD programs?

**Development of an Operational Research Agenda**

Operational research on NTDs is needed to guarantee that integrated programs provide optimal benefit to affected populations. Research activities at present are actively supported by WHO/TDR and Gates Foundation-funded multi-institutional collaborations as well as a number of academic and research institutions. Coordination with these ongoing research activities will be important to maximize the gain to be achieved from a new USAID investment in operational research. Moving forward, this can be achieved through a series of partners' meetings organized existing meeting venues (e.g., annual Tropical Medicine or Gates grant meetings)