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Progress in Combating Neglected Tropical Diseases (NTDs): U.S. and Global Efforts from FY2006 to FY2015

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Summary

The term "neglected tropical diseases" (NTDs) was coined by the World Health Organization (WHO) in 2003 to describe a set of diseases that are ancient, worsen poverty, and typically impair health and productivity while carrying low death rates. While the use of the term "NTDs" has helped to raise awareness about these long-standing health challenges, its use risks simplifying a complicated health challenge. Some of the diseases are treatable with drugs that can be administered by lay health workers irrespective of disease status, while others require diagnosis and can be treated only by trained health professionals who have access to appropriate equipment, electrical power, and refrigeration (to store the temperature-sensitive therapies).

Neglected tropical diseases primarily plague the poorest people in developing countries. Changes in the environment and population flows, however, make industrialized countries, including the United States, increasingly vulnerable to some NTDs, particularly dengue haemorrhagic fever, which can cause death and has no cure. Health interventions to address the array of NTDs vary, but a common factor to an enduring solution to these illnesses is economic development. Industrialized countries, including the United States, have controlled these diseases in their territories by combining drug treatment with the construction and use of improved sanitation, modernization of agricultural practices, and utilization of improved water systems.

The international community has made substantial progress in combating select NTDs, though some have been tackled more effectively than others. Guinea worm disease, for example, is on the cusp of eradication. More generally, expanding access to mass drug administration is contributing to decreases in prevalence of several NTDs, particularly across Latin America. Despite these advances, WHO cautions that these diseases cannot be banished without improving global access to clean water and sanitation, strengthening local health capacity (veterinary as well as human), and intensifying case detection and management. Making improvements in these areas will require long-term investments that are complex and may entail facing thorny issues such as addressing corruption, transferring ownership of health programs from donors to recipient countries, and evaluating the impact of political and economic policies on health programs (e.g., international lending requirements).

The United States has played an important role in combating NTDs. Congressional interest in NTDs has been growing. Appropriations for NTD programs have steadily increased from $15 million in FY2006 to $100 million in FY2014. In May 2014, President Barack Obama announced that the U.S. Agency for International Development (USAID) had supported the delivery of the one billionth NTD treatment and had reached nearly half a billion people. The Administration requested $86.5 million to support NTD programs in FY2015. Between FY2006 and FY2012, U.S. funding has supported the delivery of nearly 585 NTD treatments, reaching 258 million people. This report discusses the prevalence of NTDs, U.S. and global actions to address them, and options the 113th Congress might consider. For additional background on NTDs, including photographs and discussions about transmission of NTDs, descriptions of activities to combat NTDs by other agencies, and additional policy issues, see CRS Report R41607, *Neglected Tropical Diseases: Background, Responses, and Issues for Congress*.

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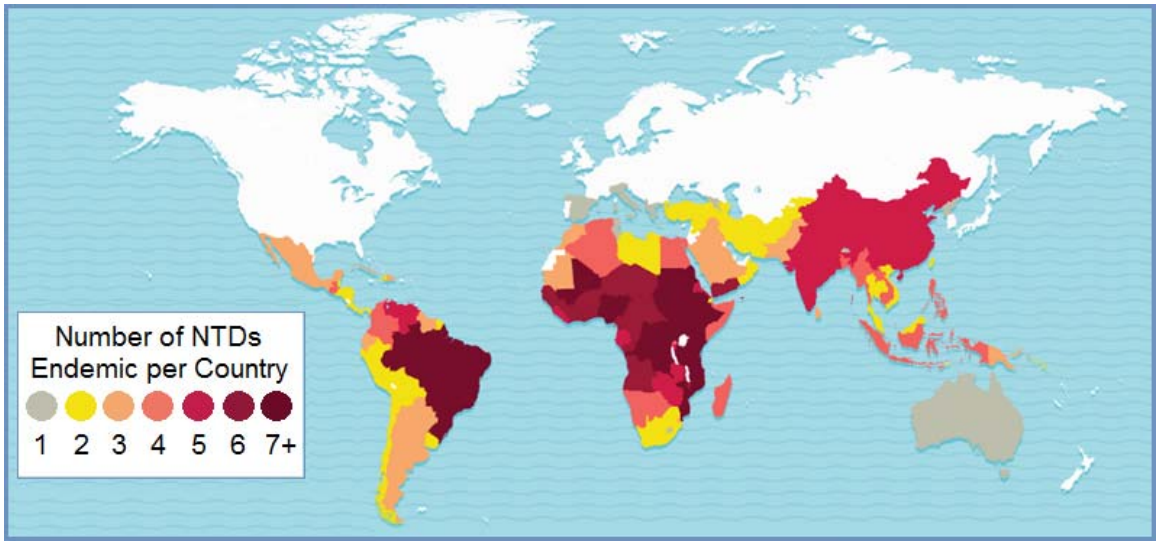
Introduction

Over the past decade, global health has become a priority in U.S. foreign policy, and U.S. appropriations for global health-related efforts have more than tripled. Neglected tropical diseases (NTDs) have become an important part of these efforts.[1] Congressional appropriations for NTDs have grown from $15 million in FY2006 to $100 million in FY2014. The Administration requested $86.5 million to support NTD programs in FY2015. Heightened congressional interest in combating NTDs has been reflected not only in higher appropriation levels but also in the development of caucuses on these issues. In October 2009, the House Malaria Caucus expanded its purview to include NTDs, and in September 2012, the Senate Malaria Caucus did the same.

Tropical diseases encompass all diseases that occur solely, or principally, in the tropics. Of these, the World Health Organization (WHO) describes 17 as "neglected," since resources for curing, controlling, and researching improved treatments for these were limited until recently. The 17 NTDs are found mostly among the poorest people in 149 countries and territories (**Figure 1**), primarily where access to clean water, sanitation, and health services is limited. Some NTDs are transmitted by people; others are spread by vectors like snails, flies, or mosquitoes; and several others proliferate in soil or water. Among the 17 NTDs, 7 account for roughly 90% of the global NTD burden (**Table 1**). These are the three soil-transmitted helminths (intestinal worms), schistosomiasis (snail fever), lymphatic filariasis (elephantiasis), trachoma, and onchocerciasis (river blindness). Intestinal worms, or STH, account for roughly 80% of the seven most common NTDs (**Figure 2**).

Figure 1. Global NTD Burden Map



Source: Adapted by CRS from Uniting to Combat NTDs, http://unitingtocombatntds.org/sites/default/files/resource_file/ntd_event_burden_map_updated.pdf, May 6, 2014.

[1] For additional background information on NTDs, see CRS Report R41607, *Neglected Tropical Diseases: Background, Responses, and Issues for Congress*, by Tiaji Salaam-Blyther.

Table 1. 17 Neglected Tropical Diseases

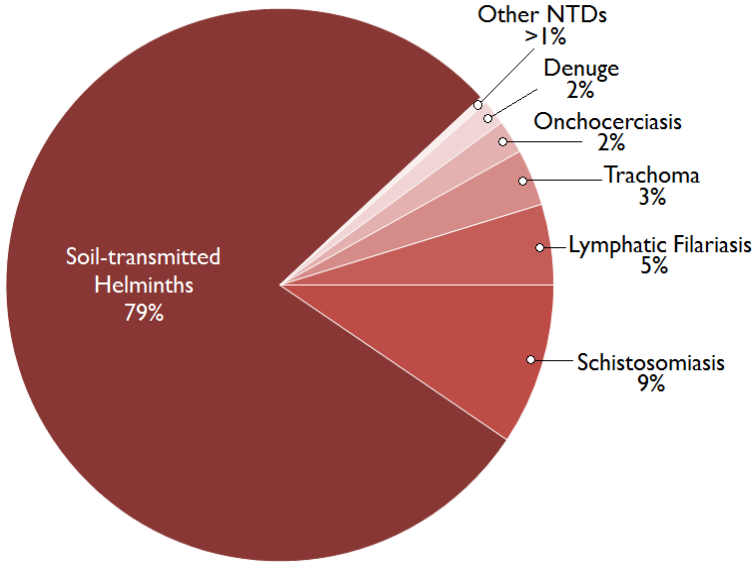
Seven Most Common NTDs (90% of all NTDs)	Other NTDs
Lymphatic Filariasis (Elephantiasis)	Buruli Ulcer
Onchocerciasis (River Blindness)	Chagas Disease
Schistosomiasis (Snail Fever)	Cysticercosis/Taeniasis
Soil-Transmitted Helminthiases (STH)	Dengue
• Hookworm	Dracunculiasis (Guinea worm disease)
• Whipworm	Echinococcosis
• Roundworm	Foodborne Trematode Infections
Trachoma	Human African Trypanosomiasis (Sleeping Sickness)
	Leishmaniasis
	Leprosy
	Rabies
	Yaws

Source: Created by CRS from WHO website on NTDs, http://www.who.int/neglected_diseases/diseases/en/, November 7, 2012.

NTD Control

NTD control efforts are grouped into two categories: those that require individual treatment and those that can be addressed by mass drug administration (MDA). Several NTDs can be addressed through MDA, when an entire community with known cases is treated irrespective of individual disease status.[2] Of the 17 NTDs, 8 can be treated with MDA. These include the seven most common NTDs as well as foodborne trematode infections.[3]

Figure 2. Share of NTD Burden by Disease



Source: Adapted by CRS from WHO fact sheets on NTDs. WHO, "Sustaining The Drive To Overcome The Global Impact Of Neglected Tropical Diseases," *Second WHO Report on Neglected Tropical Diseases*, 2013.

Although the seven most common NTDs can be treated with MDA, complex transmission cycles complicate efforts to eliminate or eradicate[4] them. STH, for example, is contracted through contact with or ingestion of

[2] WHO, "Sustaining The Drive To Overcome The Global Impact Of Neglected Tropical Diseases," *Second WHO Report on Neglected Tropical Diseases*, 2013, pp. 114.

[3] Ibid., pp. 18-106.

worm eggs that lie in soil. The eggs are deposited in the soil through fecal matter and can remain there for several years. Access to adequate sanitation facilities is a critical component of interrupting the STH transmission cycle, as the STH medicines kill the adult worms, but not the eggs. Due to the limitations of drugs, WHO recommends a five-pronged strategy:[5]

- mass drug administration
- innovative and intensified disease-management;
- vector control and pesticide management;
- safe-drinking water, basic sanitation and hygiene services, and education; and
- veterinary public-health services.

Global Progress in Combating NTDs

Since WHO coined the phrase "neglected tropical diseases" in 2003, global efforts to address these ailments have accelerated. In 2007, WHO released the *Global Plan to Combat Neglected Tropical Diseases*, which outlined several goals and targets to reach by 2015 for global control, elimination, and eradication of NTDs (**Figure 3**).[6] In 2012, WHO released a report, widely known as the *Roadmap*, which highlighted progress in reaching the 2015 goals and established new ones for 2020.[7] One year later, it released a report outlining progress in achieving the 2020 goals, as described in the *Roadmap*.

According to the reports, guinea worm disease has been nearly eliminated and was endemic in only four countries by 2012: Chad, Ethiopia, Mali, and South Sudan.

Figure 3. Timeline of Key Global Actions to Address NTDs

2003	WHO coins the phrase, "NTD"
2007	WHO releases *Global Plan to Combat Neglected Tropical Diseases*, which calls for global control, elimination, and eradication of several NTDs by 2015 by: • treating at least 65% of people affected by lymphatic filariasis; • treating at least 75% of school-aged children affected by STH and schistosomiasis; and • researching and developing new diagnostic, treatment, and control measures.
2012	WHO releases *Accelerating Work to Overcome the Global Impact of NTDS*, which highlighted progress on 2015 goals and set new ones for 2020 to: • eradicate Guinea Worm Disease; • eliminate lymphatic filariasis, leprosy, sleeping sickness, and trachoma; • control snail fever, STH, Chagas, visceral leishmaniasis, and river blindness; • research and develop new NTD tools.
	International leaders convene to affirm their commitment to fighting NTDS and release the *London Declaration on NTDs.*
2013	WHO releases *Second WHO Report on Neglected Tropical Diseases*.
	WHO adopts resolution on NTDs.
2014	A consortium of health groups release a report detailing progress on achieving the London Declaration goals: *Delivering on Promises and Driving Progress*.

Source: Created by CRS.

(...continued)

[4] *Eradicate* means to end all transmission of a disease worldwide by exterminating the agent. *Eliminate* means to reduce transmission of a disease (not necessarily zero) with the aim of interrupting the transmission cycle.

[5] WHO, "Sustaining The Drive To Overcome The Global Impact Of Neglected Tropical Diseases," *Second WHO Report on Neglected Tropical Diseases*, 2013, p. 113-129.

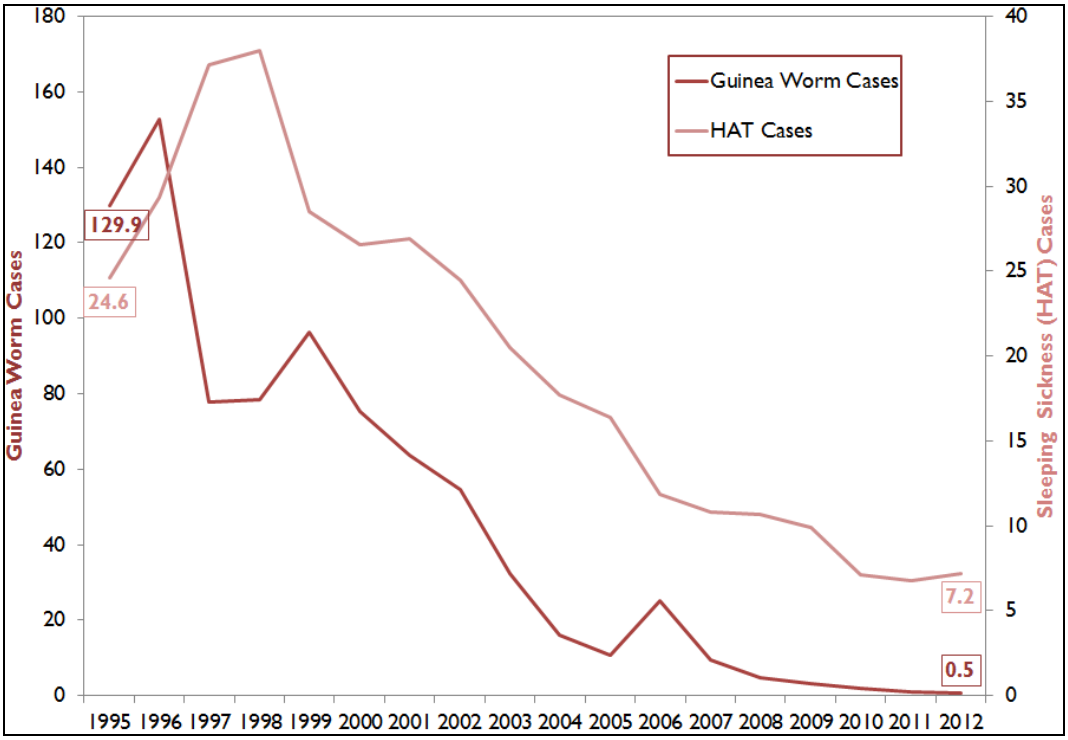
[6] WHO, *Global Plan to Combat Neglected Tropical Diseases 2008-2015*, 2007.

[7] Ibid., *Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases: A Roadmap for Implementation*, 2012.

Nearly 97% of the 542 cases identified in 2012 occurred in South Sudan, where instability remains a key threat to eradication. Since the 2012 report was released, WHO has noted further progress in addressing guinea worm disease, with 148 cases reported in 2013 and only 10 cases reported from January 1, through April 30, 2014.[8] WHO has also since noted progress in other areas. Annual sleeping sickness cases, for example, fell by more than 70% from 1995 through 2012 (**Figure 4**).[9]

Figure 4. Global Guinea Worm Disease and HAT Cases: 1995-2012

(millions)



Source: Created by CRS from WHO, *Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases: A Roadmap for Implementation*, 2012, p. 76 and WHO, *Control and Surveillance of Human African Trypanosomiasis*, WHO Technical Report Series, Number 984, 2013, pp. 16 and 18.

International Pledges to Combat NTDs

In January 2012, representatives from endemic countries, the private sector, and donor nations convened in London, England, to affirm their commitment to combatting NTDs. Participants signed the *London Declaration on Neglected Tropical Diseases*, which highlighted the role each signatory would play in reaching the 2020 goals outlined in the *Roadmap*. **Appendix A** lists donor commitments.[10] These pledges included the following:

[8] WHO, *Reaching WHO Roadmap Targets Is Top Priority In A Changing NTD Landscape*, press release, May 1, 2014.

[9] WHO, *Control and Surveillance of Human African Trypanosomiasis*, WHO Technical Report Series, Number 984, 2013, pp. 16 and 18.

[10] http://www.unitingtocombatntds.org/downloads/press/ntd_event_table_of_commitments.pdf.

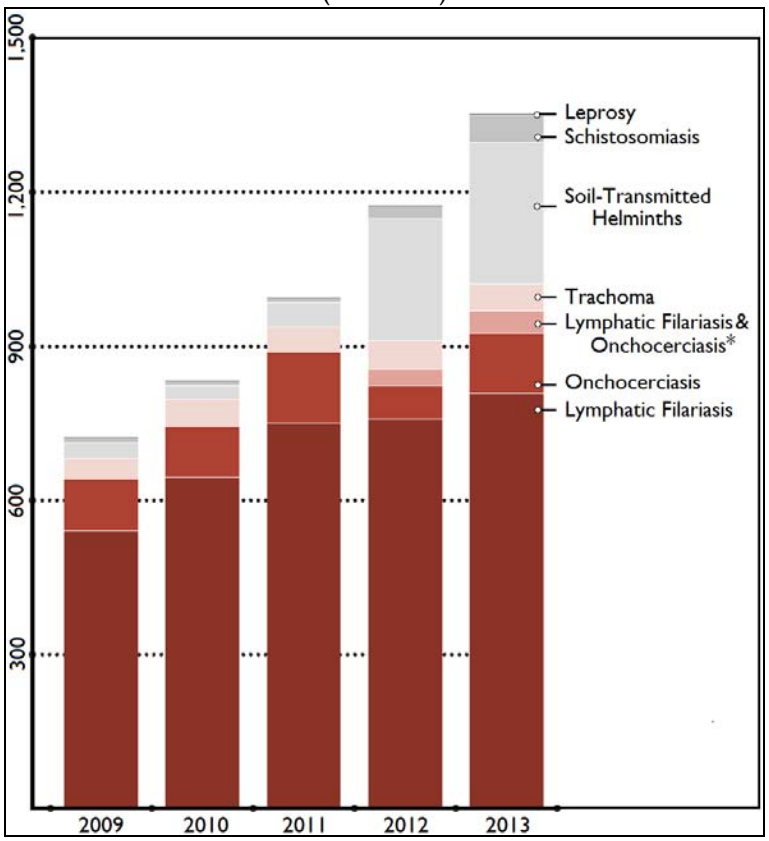
- $785 million (includes preexisting commitments) to strengthen drug distribution and program implementation;
- 1.4 billion drug treatments annually;
- access to drug compound libraries to identify new treatments;
- increased financial support for NTD programs (some of which amended previous commitments to ongoing efforts), such as:
- commitments by the governments of Bangladesh, Brazil, Mozambique, and Tanzania to devote political and financial resources to combat endemic NTDs.

Funding and Resource Gaps

Annual donations of NTD treatments have continued to grow (**Figure 5**). In 2013, donors provided nearly 1.35 billion NTD treatments, up from 995 million in 2011. Nonetheless, these treatments are expected to reach only 36% of those who need them, with some 1.4 billion people lacking access.[11] Treatment access rates vary per disease and region. For example, roughly 37% of children with STH in need of deworming received treatment in 2012 (**Figure 6**).[12] Regional treatment rates ranged from 7% in the Middle East to 47% in Southeast Asia.[13]

Pharmaceutical companies have donated sufficient supplies of medicines for most NTDs, yet a $1.4 billion funding gap persists.[14] Health analysts assert that an additional $200 million is needed annually between 2014

Figure 5. Donated NTD Treatments, 2009-2013
(thousands)



Source: Adapted by CRS from Uniting to Combat NTDs, *Delivering on Promises and Driving Progress*, 2014, p. 14.

[11] Uniting to Combat NTDs, *Delivering on Promises and Driving Progress*, 2014, p. 9.

[12] WHO, "Preventive Chemotherapy, Planning, Requesting Medicines, and Reporting," *Weekly Epidemiological Record*, (February 21, 2014), Number 8, Volume 89, pages 61-72.

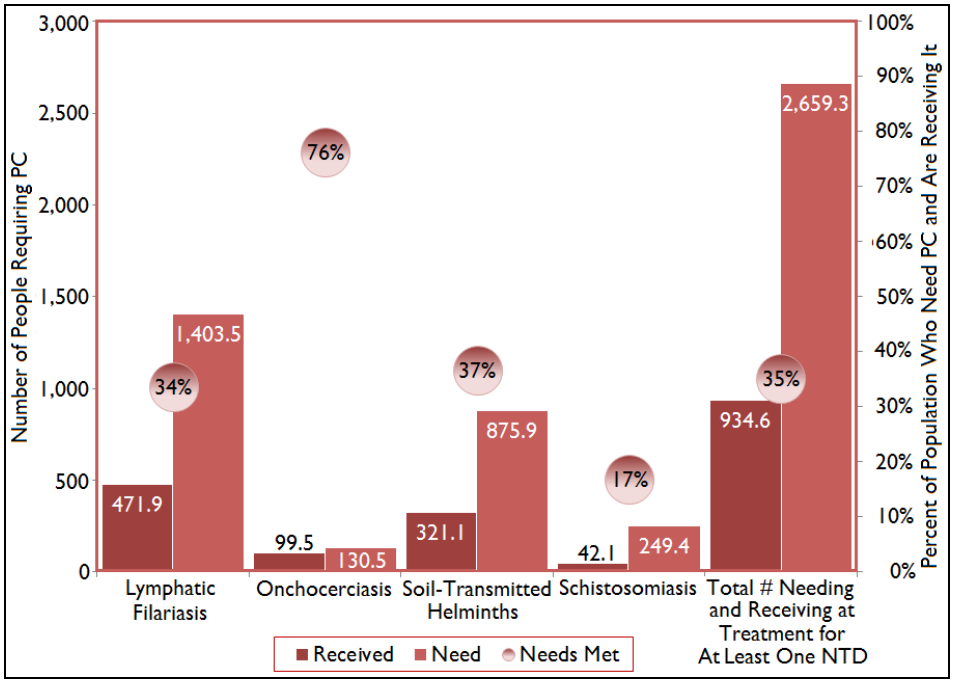
[13] WHO, "Soil-transmitted helminthiases: number of children treated in 2012," *Weekly Epidemiological Record*, 2014, volume 89, number 13, pp. 133-140.

[14] Uniting to Combat NTDs, *Delivering on Promises and Driving Progress*, 2014, p. 18.

and 2020 to deliver the donated drugs and meet other programming costs. The $1.4 billion does not include additional resources needed for research and development (R&D) of new treatments, vaccines, and testing supplies.

Figure 6. Numbers of People Needing and Receiving Treatment for Key NTDs

(thousands and percent)



Source: WHO, "Preventive Chemotherapy, Planning, Requesting Medicines, and Reporting," *Weekly Epidemiological Record*, (February 21, 2014), Number 8, Volume 89, pages 61-72.

Research and Development Needs[15]

NTD experts maintain R&D is vital. Some observers are troubled by emerging evidence that hookworm, one of the STHs (that comprise 80% of all NTDs), may be developing resistance to existing medication.[16] In addition, the international community cannot meet 2020 goals with existing tools (**Figure 7**). There is an urgent need for additional drug treatments and vaccines for those NTDs that are difficult to treat, are costly to manage, and can have severe clinical outcomes if left untreated.[17] These are Buruli ulcer, Chagas disease, human African trypanosomiasis, the leishmaniases, leprosy and yaws. Given the complexity of these diseases, patients must be seen at well-equipped health facilities by well-trained, specialized technicians; these types of facilities may not be available in many of the affected countries. Additionally, exposed populations need to

[15] Judith Glassgold, former Specialist in Health Policy, contributed to this section.

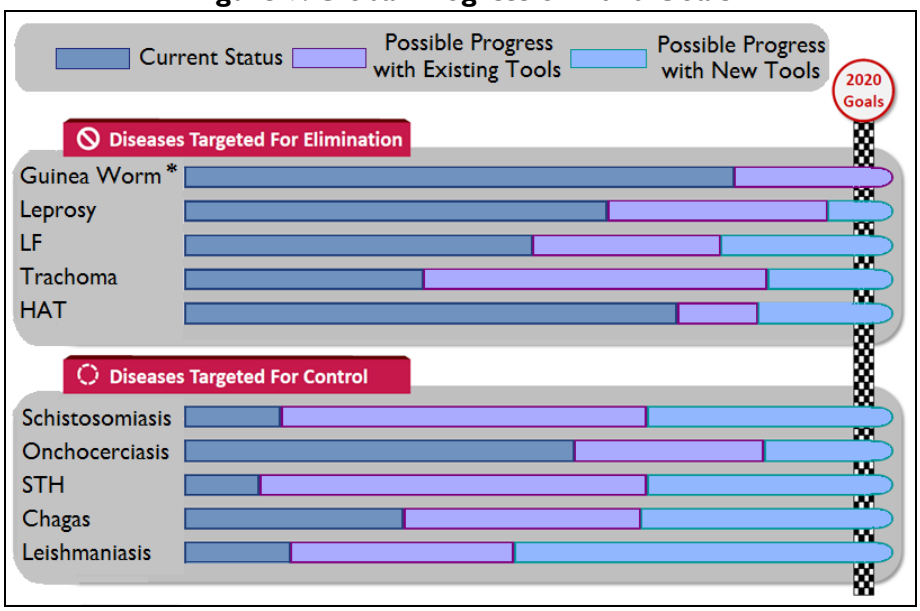
[16] Hotez, Peter "Mass Drug Administration and Integrated Control for the World's High-Prevalence Neglected Tropical Diseases," *Clinical Pharmacology & Therapeutics*, vol. 85, no. 6 (June 2009), pp. 659-664.

[17] WHO, "Sustaining The Drive To Overcome The Global Impact Of Neglected Tropical Diseases," *Second Report on Neglected Tropical Diseases*, 2013, p. 119.

be systematically screened because these diseases are generally asymptomatic during the periods when treatments would be most effective and carry the least dangerous side-effects.[18]

In addition to the above-mentioned diseases, dengue has become a growing global health problem.[19] Dengue is the leading cause of serious illness and death among children in some Asian and Latin American countries. More than 2.5 billion people are now at risk of infection, close to 40% of the world's population. Of these, between 50 million and 100 million contract the disease annually. Before 1970, only nine countries had experienced severe dengue epidemics. The disease is now endemic in more than 100 countries. Dengue has been detected in a number of U.S. states and territories, including Florida, Texas, and Puerto Rico.[20] There is no specific treatment or vaccine for dengue, which can lead to death if left untreated. Early detection and proper care can reduce fatality rates from about 20% to less than 1%.

Figure 7. Global Progress on 2020 Goals



Source: Adapted by CRS from Uniting to Combat NTDs, October 25, 2012.

Notes: "Possible progress with existing tools" predicts advancement of elimination and control efforts without development of new tools. "Possible progress with new tools" predicts advancements that could be made if new tools were developed, such as more effective treatments and vaccines.

* Guinea worm disease is targeted for eradication.

Acronyms: Lymphatic Filariasis (LF), Human African Trypanosomiasis (HAT), Soil-Transmitted Helminths (STH).

Congress has taken steps to encourage drug development for certain diseases; some NTDs are among them. Two pieces of legislation established a framework for incentivizing drugs for rare diseases or disorders: The Orphan Drug Act of 1983, P.L. 97-414, followed by the Rare Diseases

[18] Ibid., p. 116.

[19] Information in this paragraph was summarized from WHO, *Dengue and Severe Dengue*, fact sheet, number 117, November 2012.

[20] G. Vaidyanathan, "Dengue Re-emerges in the U.S., Spurring Race for Vaccine," *New York Times,* June 28, 2012; M. McKenna, "Dengue, aka 'Breakbone Fever,' is back," *Slate,* December 12, 2012. See also, Centers for Disease Control and Prevention http://diseasemaps.usgs.gov/del_us_human.html.

Act of 2002, P.L. 107-280. These acts defined rare diseases or disorders as those that affect fewer than 200,000 individuals in the United States. This definition includes NTDs and other rare or orphan conditions.[21] Through these programs, 26 drugs received a new drug approval (NDA) or a biologic license application in 2012.[22]

The FDA Amendments Act of 2007 (P.L. 110-85) created a priority review voucher (PRV) to incentivize the development of drugs and biologic products for tropical diseases. The applicant would receive a voucher at the time of approval of certain tropical disease products that "offer major advances in treatment where no adequate therapy exists."[23] This voucher would allow the applicant a priority review of another drug product. This voucher could be transferred (sold) to one other sponsor. The draft guidance issued by the FDA describes the diseases and conditions covered by the PRV.

The act also permits the Secretary to designate other diseases by regulation, which could include "any infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations.... "[24] The list includes tropical diseases beyond the 17 NTDs, namely cholera, malaria, and tuberculosis (TB). At the same time, the act excludes some NTDs listed by WHO, including rabies, cysticercosis/taeniasis, and Chagas disease.

U.S. Efforts to Tackle NTDs

A variety of U.S.-based institutions support global efforts to control NTDs. These institutions include the federal government, pharmaceutical companies, philanthropic organizations, and NGOs. Key U.S. government players include the U.S. Agency for International Development (USAID), U.S. Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), and Department of Defense (DOD).[25] NGOs include groups like the Carter Center and RTI International; philanthropic organizations include the Gates Foundation and the Sabin Vaccine Institute; and private companies include Merck, Johnson & Johnson and Pfizer. While each of these plays an important role in combating NTDs, this section focuses exclusively on the USAID-managed NTD Program.[26]

The USAID NTD Program

In 2006, the Bush Administration launched the Neglected Tropical Disease Control Program, the first U.S. effort to address a group of NTDs. The program was created in response to language in the FY2006 Foreign Operations Appropriations Act, which made available up to $15 million "to

[21] Information from the FDA on orphan and rare conditions is available at http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/ucm216147.htm, including a database or rare conditions.

[22] Email from FDA Office of Legislation on March 8, 2013.

[23] See FDA "Guidance for Industry: Tropical Disease Priority Review Vouchers, October 2008, p.3.

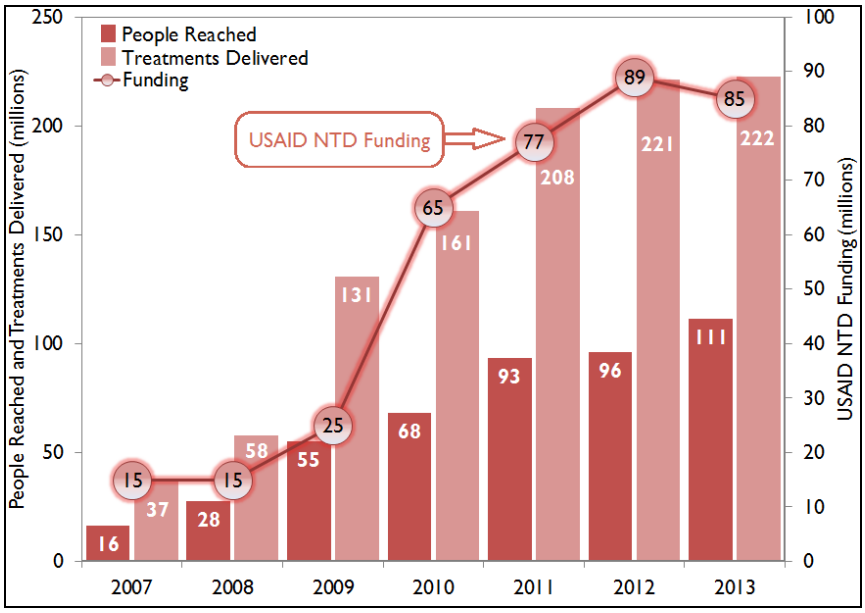
[24] Ibid.

[25] For more information on related efforts by these agencies, see CRS Report R41607, *Neglected Tropical Diseases: Background, Responses, and Issues for Congress*, by Tiaji Salaam-Blyther.

[26] See respective websites of each organization for additional information on their NTD Programs.

support an integrated response to the control of neglected diseases including intestinal parasites [STH], schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma and leprosy."[27] The language signaled congressional support for calls to integrate and expand access to drugs for the seven most common NTDs. Until that time, most countries and their implementing partners focused on tackling a single NTD. The NTD Program sought to document the feasibility of integrating treatment for several NTDs and expanding this strategy. At the outset, the NTD program aimed to support the provision of 160 million NTD treatments to 40 million people in 15 countries. In 2008, President George W. Bush reaffirmed his commitment to the program and proposed spending $350 million over six years (from FY2008 through FY2013) on expanding the program to 30 countries.[28]

Figure 8. USAID NTD Program: FY2007-FY2013



Source: Created by CRS from NTD Program website at http://www.neglecteddiseases.gov/approaches/index.html, May 9, 2014.

During his first term, President Barack Obama named the NTD Program a priority. The Obama Administration announced several goals for addressing NTDs, including

- administer 1 billion NTD treatments,
- halve the prevalence of the seven most common NTDs by 2013,
- eliminate leprosy in all endemic countries and onchocerciasis in Latin America by 2016, and
- eliminate lymphatic filariasis globally by 2017.

On May 8, 2014, the Obama Administration announced that it had administered its one billionth NTD treatment, reaching 465 million people and surpassing one of its goals.[29] From FY2007 through FY2013, USAID spent more than $370 million on global NTD programs (**Figure 8**). In FY2014, Congress appropriated $100 million for NTD programs and the Administration requests $86.5 million for NTD programs in FY2015. A map of the countries receiving USAID support for combating NTDs is in **Appendix B**.

[27] Section 593, P.L. 109-102, FY2006 Foreign Operations Appropriations.

[28] See White House, "President Bush Announces New Global Initiative To Combat Neglected Tropical Diseases," press release, February 20, 2008.

[29] USAID NTD website, http://www.neglecteddiseases.gov/, May 9, 2014.

Issues for Congress

The international community has made substantial progress in combating select neglected tropical diseases. Some NTDs have been tackled more effectively than others. Guinea worm disease, for example, is on the cusp of eradication and with expanding mass drug administration campaigns, the prevalence of several NTDs is declining, particularly in Latin America. Despite these advancements, WHO cautions in the 2020 Roadmap that these diseases cannot be banished without expanding global access to clean water and sanitation, improving hygiene practices, strengthening local health capacity (veterinary as well as human), and intensifying case detection and management.

The United States has played an important role in combating NTDs and will likely be a central player in global efforts to advance the 2020 NTD goals. The section below discusses a range of issues U.S. and international organizations may face as they attempt to reach the WHO 2020 goals, as well as those set by the Administration (see "U.S. Efforts to Tackle NTDs"). Some of the discussion includes an analysis of steps the 113th Congress might consider.

Accessing Clean Water and Sanitation

Transmission of most NTDs is facilitated by insufficient access to clean water, sanitation, and hygiene (WASH).[30] An estimated 880 million children are carrying soil-transmitted helminths, for example, which are spread primarily through openly defecating on the ground. Eggs of these intestinal worms, which account for roughly 80% of NTDs, can persist in the environment for many years.

Experts at the CDC assert that WASH should be a central component of any effective and sustainable approach to controlling NTDs.[31] One estimate indicates that improved sanitation and water safety can reduce the prevalence rates of other NTDs as well, including schistosomiasis and blinding trachoma.[32] Water and sanitation improvement are particularly important when addressing pathogens that cannot be eliminated by drugs alone, such as STH and schistosomiasis.

Several experts urge greater investments in water and sanitation and see attainment of global water and sanitation goals as an important step towards eliminating NTDs.[33] Through the Millennium Development Goals (MDGs), the international community sought to halve the share of people without access to clean water and basic sanitation by 2015.[34] WHO estimated that

[30] For more information on U.S. and international efforts to improve access to clean water and sanitation, see CRS Report R42717, *Global Access to Clean Drinking Water and Sanitation: U.S. and International Programs*, by Tiaji Salaam-Blyther.

[31] See CDC, *WASH Away Neglected Tropical Diseases*, Activity Summary, June 2010, http://www.cdc.gov/healthywater/pdf/global/programs/wash-away-ntd-summary.pdf and CDC, *WASH Away Neglected Tropical Diseases*, Program in Brief, June 2010.

[32] Philip Musgrove and Peter Hotez, "Turning Neglected Tropical Diseases Into Forgotten Maladies," *Health Affairs*, vol. 28, no. 6 (November/December 2009), p. 1698.

[33] Burton Singer, "Viewpoint by Burton Singer: Bring Back Primary Prevention for Relieving the Burden of NTDs," *PLoS Medicine*, vol. 7, no. 5 (May 2010), p. e1000255; and TR Burkot et al., "The Argument for Integrating Vector Control with Multiple Drug Administration Campaigns to Ensure Elimination of Lymphatic Filariasis," *Filaria Journal*, vol. 5, no. 10 (August 2006).

[34] The United Nations (U.N.) General Assembly adopted a declaration in 2000, which among other things, committed (continued...)

between 2005 and 2015, it would cost $72 billion annually to implement and maintain enough water and sanitation schemes to meet global water and sanitation targets, of which $54 billion would need to be spent on maintaining the systems.[35] In 2010, members of the Organization for Economic Cooperation and Development (OECD) committed $7.8 billion towards improving global access to clean drinking water and sanitation.[36] U.S. and global investments in sanitation would need to increase significantly to meet this funding gap.

Integrating the U.S. NTD Program

Investments in WASH are considered important, as mass drug administration campaigns cannot be used in isolation to eliminate NTDs. The process of combating diseases by combining responses by practitioners across sectors, particularly those related to health, agriculture, water, construction, and waste disposal, is known as integrated vector management. Indeed, the United States was unable to control hookworm (an STH) within its own borders until the early 1900s, when an integrated vector management (IVM) approach was applied.[37]

Documents by the Administration maintain the NTD Program is part of a complete package of services the United States provides to improve the health of women and children across sectors.[38] The Administration intends, for example, to expand the provision of drugs that treat STH in children within USAID-supported education programs.[39] Similarly, the Obama Administration underscores the intersection between water and sanitation and categorizes it as a "cross-cutting area" under global health. Nonetheless, in reports to Congress on progress towards advancing global health (through congressional budget justifications, for example) the Administration provides little information about how water and sanitation programs advance global health efforts or how they are integrated within global health projects.

The structure of the FY2013 Foreign Operations budgetary request suggests some separation between these activities. Requests for water programs are made across a variety of accounts,

(...continued)

member states to advance health development around the world. See, *United Nations Millennium Declaration*, September 18, 2000, http://www.un.org/millennium/declaration/ares552e.pdf. Shortly thereafter, delegates developed the *Millennium Development Goals* (MDGs) to guide attainment of the priorities outlined in the Millennium Declaration. The eight MDGs are: (MDG1) eradicate poverty and hunger, (MDG2) achieve universal primary education, (MDG3) promote gender equality and empower women, (MDG4) reduce child mortality by two-thirds, (MDG5) reduce maternal mortality by two-thirds, (MDG6) combat HIV/AIDS, malaria, and other diseases, (MDG7) ensure environmental sustainability, and (MDG8) develop a global partnership for development. MDG7 includes the water and sanitation targets.

[35] Guy Hutton and Jamie Bartram, *Regional and Global Costs of Attaining the Water Supply and Sanitation Target of the Millennium Development Goals*, WHO, 2008, p. iv, http://www.who.int/water_sanitation_health/economic_mdg_global_costing.pdf.

[36] OECD, *Aid Activity Database*, http://stats.oecd.org/Index.aspx, July 31, 2012. For more information on U.S. spending on improving global access to water and sanitation, see CRS Report R42717, *Global Access to Clean Drinking Water and Sanitation: U.S. and International Programs*, by Tiaji Salaam-Blyther.

[37] In the early 1900s, the Rockefeller Foundation and its implementing partners combined wide-scale sanitation projects with drug administration and public education to eliminate hookworm infections, which plagued much of the southeastern United States at the time. For more on this approach, see E.A. Alderman et al., *The Rockefeller Sanitary Commission for the Eradication of Hookworm Disease* (Washington, DC: Offices of the Commission, 1915). This book is available on-line at http://www.archive.org/details/cu31924005710839.

[38] Department of State, *Implementation of the Global Health Initiative: Consultation Document*, February 2010, p. 20.

[39] Ibid., p. 15.

primarily Development Assistance (DA) and Economic Support Fund (ESF). In FY2013, for example, the Administration requested only 12% of water and sanitation funds through the Global Health Programs account and 76% through the DA and ESF accounts. These two accounts support a wide range of governance and economic development activities, which do not typically focus on health objectives.

Despite the limitations of mass drug administration, the U.S. NTD Program focuses almost exclusively on MDA. Administration officials recognize the importance of a comprehensive NTD Program, but maintain that "the directive from Congress was to focus on mass drug administration. [G]iven the limited resources, [MDA] is the most efficient and cost-effective way to control [and] eliminate these diseases."[40] The 113th Congress might debate the merits of applying an intersectoral approach to the NTD Program. Broadening the U.S. approach may not necessarily entail raising spending, but could involve improving the integration of U.S. health and development programs. The 113th Congress could, for example, request information on how key leaders at USAID (e.g., the Deputy of the Global Health Initiative and the Water Coordinator) coordinate their programs.

Strengthening Health Systems

Although pharmaceutical companies have donated sufficient supplies of NTD medicines, more than 60% of those in need of NTD treatment lack access to the drugs. Broader issues associated with weak health systems within endemic countries can affect the delivery of drugs and the effectiveness of NTD programs.[41] Since many endemic countries are largely responsible for disseminating the donated medicines, human resource constraints and supply chain deficiencies inhibit supply of the drugs and leave many without access to treatment. Streamlining and simplifying treatments are becoming increasingly important.[42] The international community is increasingly integrating treatments and services, particularly for multiple diseases that can be treated with one pill. Lymphatic filariasis and the three most common intestinal worms, for example, can be treated with the same medication. Health providers are partnering with schools to couple LF and STH treatment with school feeding programs. Some are concerned, however, that deworming treatment rates are declining among children who are not yet old enough to attend school (**Figure B-2**).

Weak veterinary and public health systems limit the ability of several affected countries to enhance NTD programs or maintain them after international support wanes. Many critics of "vertical" or "disease-specific" programs see the poor conditions of health systems in several developing countries as an outcome of the burgeoning investments in vertical disease programs. One argument is that disease-specific efforts divert investments from the very public health systems that are needed to support vertical programs. Supporters of disease-specific initiatives argue, on the other hand, that such activities facilitate dramatic, measurable progress. Advocates of this approach point to dramatic reductions in recent years of deaths associated with HIV/AIDS and malaria. The merits of vertical disease programs have been long debated in the global health community and evidence supports both sides of the debate.

[40] Emily Wainwright, USAID, Senior Operations Advisor, Neglected Tropical Diseases Program, December 27, 2012.

[41] See WHO Report on Infectious Diseases, "Removing Obstacles to Healthy Development," http://www.who.int/infectious-disease-report/pages/textonly.html. For more information on these issues see CRS Report R41607, *Neglected Tropical Diseases: Background, Responses, and Issues for Congress*, by Tiaji Salaam-Blyther.

[42] Ibid.

Addressing Research and Development Needs[43]

Despite support by health analysts and scientists for increasing drug and vaccines for NTDs,[44] funding for pharmaceutical R&D is considered by many to be insufficient.[45] To date, efforts to encourage private development of NTD vaccines and drugs have met tepid responses, due in part to the belief that there is no viable commercial market for these products.[46] It is widely understood that NTDs affect primarily the poorest in developing countries, most of whom lack resources to afford drugs. Without guarantees of cost recovery, drug manufacturers appear reluctant to initiate the lengthy, and potentially costly, discovery process.[47] Estimates indicate that the average time for a drug to reach approval in the United States ranges from 6 to 10 years.[48]

Some analysts question whether the PRV provides sufficient financial incentives for NTD products.[49] To date, only two companies have received the voucher, Novartis (for the drug Coartem, which treats malaria) and Johnson and Johnson (for the drug Sirturo, which treats drug-resistant TB). Novartis failed to see any market return on its voucher as it used the voucher for a product whose new drug application failed to win FDA approval.[50] Johnson & Johnson has not yet used its voucher, which it earned in 2012. Some market analysts believe that the utility of the voucher will remain uncertain until a PRV is sold and has a clear market value.[51] It remains to be seen whether the PRV, on its own, will provide a strong enough incentive to encourage drug development.[52] For example, in the development of Sirturo, Johnson and Johnson applied for a PRV as well as two other FDA development incentives.[53]

Congressional interest in this issue may focus on the strategic investments that could spur added drug treatments, vaccines, and diagnostic tools. For example, some might prioritize NTDs with serious clinical outcomes that are difficult to treat and manage (e.g., Buruli ulcer, Chagas disease,

[43] Judith Glassgold, former Specialist in Health Policy, contributed to this section.

[44] P. Hotez et al., "Control of Neglected Tropical Disease," *New England Journal of Medicine*, vol. 357, no 10, (2007), pp. 1018-1027.

[45] Global Challenges in Global Health, "New Approaches in Model Systems, Diagnostics, and Drugs for Specific Neglected Tropical Diseases," September 2012.

[46] A.S. Robertson et al., "The Impact of the US Priority Voucher on Private Sector Investment in Global Health Research and Development," *PLOS Neglected Tropical Diseases*, vol. 6, no. 8 (August, 2012), pp. 1750-1755; P. Trouiller et al., "Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Failure," *Lancet*, vol. 359, no. 9324 (2002), pp. 2188-2194.

[47] Ibid.

[48] R. Stefanakis et al., "Analysis of Neglected Tropical Disease Drug and Vaccine Development Pipelines to Predict Issuance of FDA Priority Review Vouchers over the Next Decade," *PLOS Neglected Tropical Diseases*, October 25, 2012.

[49] W. Noor, Placing Value on FDA's Priority Review Vouchers," In Vivo, vo. 27, no. 9, (September 2009), http://www.imshealth.com/imshealth/Global/Content/Document/Placing_Value_on_FDA_Priorities.pdf; A.S. Robertson et al., "The Impact of the US Priority Voucher on Private Sector Investment in Global Health Research and Development," *PLOS Neglected Tropical Diseases*, vol. 6, no. 8 (August, 2012), pp. 1750-1755.

[50] A.S. Robertson et al., "The Impact of the US Priority Voucher on Private Sector Investment in Global Health Research and Development," *PLOS Neglected Tropical Diseases*, vol. 6, no. 8 (August, 2012), pp. 1750-1755.

[51] Ibid.

[52] A.S. Robertson et al., "The Impact of the US Priority Voucher on Private Sector Investment in Global Health Research and Development," *PLOS Neglected Tropical Diseases*, vol. 6, no. 8 (August, 2012), pp. 1750-1755.

[53] Sirturo used the fast track program, PRV, and orphan-product designation. See http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm333695.htm.

human African trypanosomiasis, the leishmaniases, leprosy and yaws). Others might focus on diseases that lack any drug treatment, such as dengue, or diseases that affect the greatest number of individuals, such as STH. Vaccines do not exist for NTDs except for rabies, and diagnostic measures are limited, so that vaccines could be prioritized. There is a case for developing diagnostic tools for diseases that are difficult to detect, such as Buruli ulcer.[54] Finally, another potential investment could advance promising treatments that are already in development, such as a vaccine for certain filarial infections (onchocerciasis and lymphatic filariasis).[55]

[54] WHO, see http://www.who.int/mediacentre/factsheets/fs199/en/.

[55] G. Dakshinamoorthy et al., "Multivalent Fusion Protein Vaccine for Lymphatic Filariasis," *Vaccine*, vol. 31, no. 12, (March 15, 2012), pp. 1616-1622; S. A. Babayan, J.E. Allen, and D.W. Taylor, "Future Prospects and Challenges of Vaccines Against Filariasis," *Parasitic Immunology*, vol. 34, no. 5 (May 2012), pp. 243-253.

Appendix A. London Declaration: Table of Donor Commitments

Table A-1. London Declaration: Table of Donor Commitments

NTD Disease	Activity	Financial Commitment	Contributor
Multiple NTDs	Outline disease-specific goals and strategies for control and elimination		World Health Organization (WHO)
	Research and develop new programs and country-specific approaches for combating Guinea worm disease, lymphatic filariasis, river blindness, schistosomiasis, blinding trachoma, visceral leishmaniasis	£195 million 2011-2015	U.K. Department for International Development (DFID)
	Maintain support in over 20 countries; expand support to include Mozambique, Senegal, Cambodia	Build on U.S. $301 million investment since 2006	U.S. Agency for International Development (USAID)
	Overcome barriers to success to achieve the control and elimination of targeted NTDs by 2020	$363 million over five years	Bill and Melinda Gates Foundation
	Expand work in NTD control and program enhancement	$5 million to selected sites in the Americas and Africa	Mundo Sano
	Country level: build stronger community health systems and integrate NTD elimination and control. Regional level: oversee finances for trust fund to fight river blindness in Africa and partner with other entities to expand trust fund to eliminate or control preventable NTDs in Africa	$120 million	World Bank
	Apply WHO recommendations for implementing coordinated NTD plan		Brazil
	Implement fully integrated, multi-sectoral NTD plan; reach full geographic coverage of all endemic areas for lymphatic filariasis, STH, and schistosomiasis; map and reach full geographic coverage of trachoma by 2018; build capacity for surveillance and action to sustain gains from PC		Mozambique
	Implement integrated plan to control and eliminate NTDs		Tanzania
	Implement integrated plan to control and eliminate NTDs		Bangladesh
	Consider use of Ivermectin for other NTDs		Merck
	Provide third parties, including Drugs for Neglected Diseases *initiative (*DND*i)*, access to selected substances out of compound libraries to find new NTD treatments		Bayer
	Provide third parties, including DNDi, access to selected proprietary compound libraries to develop new medicines for certain NTDs		Bristol-Myers Squibb
	Donate Azithromycin to a study on the potential for the drug to reduce mortality in young children		Pfizer
	Mobilize resources from individual, foundation, and corporate donors to fund NTD treatments, fund mapping initiatives, and fill programming gaps	$30 million	END Fund

NTD Disease	Activity	Financial Commitment	Contributor
Blinding Trachoma	Elimination of trachoma in China	$6.9 million	Pfizer
	Continued donation of Azithromycin for blinding trachoma until at least 2020	$4 million	Lions Clubs International Foundation
	Elimination of trachoma in Commonwealth countries	$60 million	Queen Elizabeth Diamond Jubilee Trust
	Elimination of trachoma	$12 million	Conrad N. Hilton Foundation
Chagas Disease	Double existing annual donation of Nifurtimox to 1 million tablets through 2020		Bayer
	Provide DNDi targeted access to proprietary compound libraries to develop new medicines		Abbot, AstraZeneca, Eisai, GlaxoSmithKline, MSD, Novartis, Pfizer, and Sanofi
Guinea worm disease	Fill global funding gap	Gates Foundation ($23.3 million); DFID (£20million); United Arab Emirates ($10 million); Children's Investment Fund Foundation ($6.7 million)	DFID, Gates Foundation, United Arab Emirates, Children's Investment Fund Foundation
Leprosy	Extend existing donation of rifampicin, clofazimine, and dapsone through 2020 in quantities requested by WHO		Novartis
	Organize multi-stakeholder initiative to intensify leprosy control efforts		Novartis
Lymphatic Filariasis	Provide 120 million DEC tablets to WHO for its Global Lymphatic Filariasis Elimination program; ensure a sufficient supply of DEC from 2012 through 2020		Gates Foundation, Eisai, and Sanofi
	Donate 2.2 billion tablets of DEC from 2014-2020		Eisai
	Maintain annual donation of 600 million tablets of Albendazole indefinitely		GlaxoSmithKline
Lymphatic Filariasis and Onchocerciasis	Repurpose Flubendazole to kill adult worms associated with lymphatic filariasis and river blindness; conduct drug reformulation studies; provide expertise for pre-clinical development and provide technical and supply assistance. If pre-clinical development is successful, Johnson & Johnson will co-fund clinical development; obtain regulatory approval; provide technical support		Abbot, DNDi, Johnson & Johnson, Pfizer
	Provide DNDi with access to proprietary compound libraries to develop new medicines that kill adult worms associated with lymphatic filariasis and river blindness		AstraZeneca, Johnson & Johnson, Novartis, Sanofi

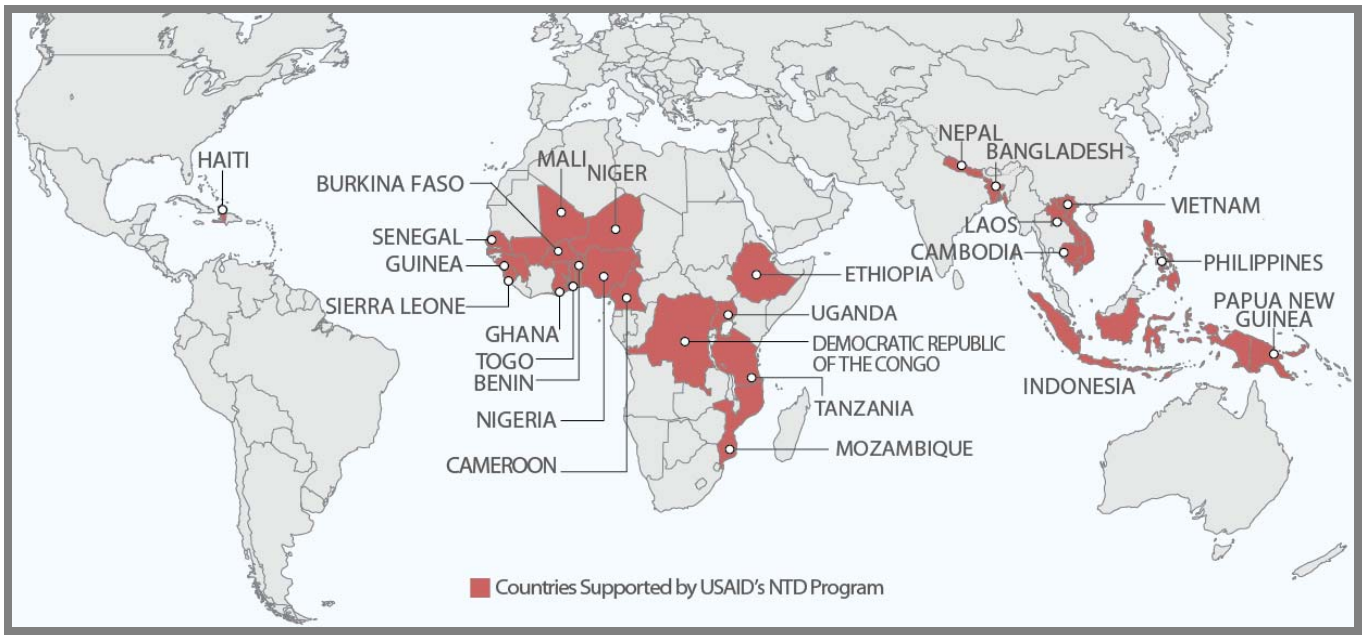
NTD Disease	Activity	Financial Commitment	Contributor
	Increase annual donation of Praziquantel from 25 million to 250 million tablets/year indefinitely		Merck KGaA
	Develop child-friendly formulation of Praziquantel		
Onchocerciasis	End onchocerciasis transmission in Cameroon	$1 million	Lions Club International Foundation
River Blindness	Maintain unlimited donation of Ivermectin indefinitely		MSD
Schistosomiasis	Provide financial support for a WHO school-based schistomiasis program		Merck KGaA
Human African Trypanosomiasis	Extend existing donations of related treatments through 2020		Sanofi
	Extend existing donations of related treatments through 2020		Bayer
	Provide DNDi with access to proprietary compound libraries to develop new medicines		Abbot, AstraZeneca, Eisai, GlaxoSmithKline, MSD, Novartis, Pfizer and Sanofi
	Partner with DNDi to develop a new oral drug candidate for sleeping sickness		Sanofi
	Logistical support to ensure drugs reach patients at point of care free of charge		
Soil-Transmitted Helminthiases	Extend donation of 400 million Albendazole tablets/year through 2020		GlaxoSmithKline
	Extend donation of 200 million Mebendazole tablets/year to 2020		Johnson & Johnson
	Support programs, partnerships, and research to address intestinal worms	$120 million and technical assistance	Global Partnership for Education
	Technical assistance to national deworming programs, including improved monitoring and evaluation and operational research aimed at exploring the possibility of elimination beyond 2020	$50 million	Children's Investment Fund Foundation
	Explore the feasibility of blocking transmission and mitigating the risks of drug resistance, as well as helping build the evidence base for effective cross-sector approaches	$50 million	Gates Foundation
	Test strategies in partnership with local governments for deworming and combination treatments, particularly in the Americas	$8 million	Mundo Sano
	Scale up deworming with vitamin A distributions and provide implementation support through local partners to eligible pre-school children	$4.5 million	Vitamin Angels
Visceral Leishmaniasis	Provide DNDi with access to proprietary compound libraries to develop new medicines		Abbot, AstraZeneca, Eisai, Novartis, Pfizer, Sanofi, GlaxoSmithKline, and MSD

NTD Disease	Activity	Financial Commitment	Contributor
	Partner with DNDi to transform drug currently in trials for Chagas Disease as a new treatment for leishmaniasis		Eisai
	Donate AmBisome for 50,000 patients in South Asia and East Africa from 2012-2017; continue program to offer VL at cost; investigate and invest in technologies and process to reduce cost of Ambisone in resource-limited countries		Gilead
	Develop new training tools for leishmaniasis care for health care providers and patients		Sanofi

Source: Adapted by CRS from Uniting to Combat Neglected Tropical Diseases, *Table of Commitments*, January 30, 2012, http://www.unitingtocombatntds.org/downloads/press/ntd_event_table_of_commitments.pdf.

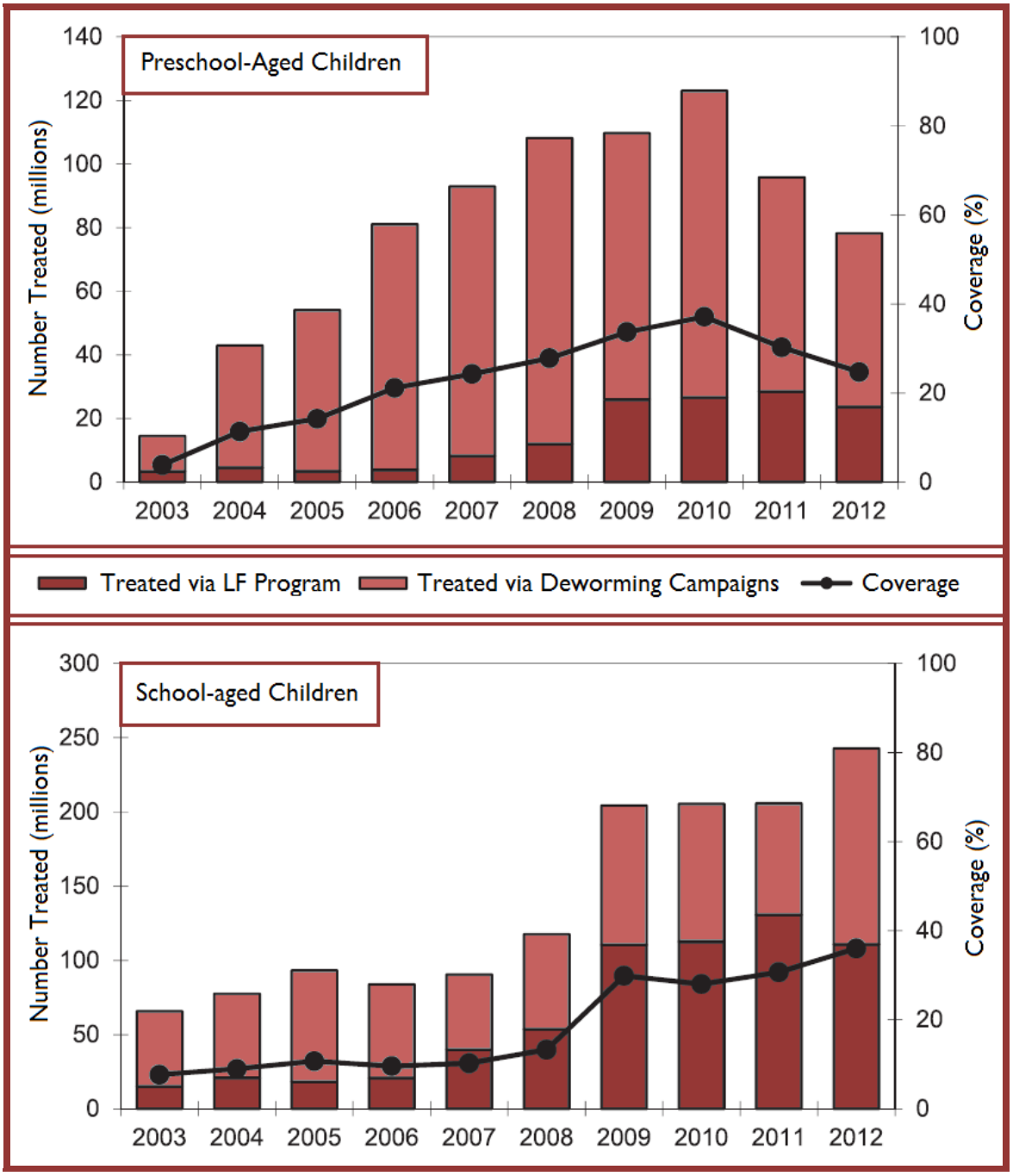
Appendix B. Map of USAID NTD Program

Figure B-1. NTD Program Countries



Source: Adapted by CRS from USAID website on NTDs, http://www.neglecteddiseases.gov/countries/index.html, May 29, 2014.

Figure B-2. Deworming Treatment Access Trends: 2003-2012



Source: Created by CRS from WHO, "Soil-Transmitted Helminthiases: Number of Children Treated in 2012," *Weekly Epidemiological Record*, (March 28, 2014), Volume 13, Number 89, pp. 133-140.

Notes: Coverage refers to the percent of people who are in need of treatment who receive it.

Acronyms: lymphatic filariasis (LF).

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