Report on Emerging and Neglected Tropical Disease Sentinel Surveillance

As Required by

2018-19 General Appropriations Act, Senate Bill 1, 85th Legislature, Regular Session, 2017 (Article II, Department of State Health Services, Rider 35)

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Table of Contents

Executive Summary

The 2018-19 General Appropriations Act, Senate Bill 1, 85th Legislature, Regular Session, 2017 (Article II, Department of State Health Services, Rider 35) directs the Department of State Health Services (DSHS) to allocate $300,000 in General Revenue in each fiscal year of the 2018-19 biennium to implement a sentinel surveillance program to monitor emerging and neglected tropical diseases (ENTDs), as outlined in Health and Safety Code, Chapter 100. Previously, House Bill 2055, 84th Legislature, Regular Session, 2015 amended the code by adding Chapter 100.

To fulfill these legislative directives, DSHS performed the following activities:

- Consulted with the Centers for Disease Control and Prevention (CDC) about neglected tropical diseases with the potential to naturally occur or become established in Texas;
- Amended Texas Administrative Code §97.3 to add six new neglected tropical diseases to the list of notifiable conditions as follows: ancylostomiasis, ascariasis, echinococcosis, fasciola hepatica, paragonimus kellicotti, and trichuriasis[1];
- Conducted educational events for providers, infectious disease specialists, and healthcare facilities;
- Funded two ENTD sentinel surveillance projects in fiscal year 2017 (FY17), totaling $277,806, as shown in Table 1; and
- Funded three ENTD sentinel surveillance projects for both fiscal years of the 2018-19 biennium, totaling $600,000, as shown in Table 1;

[1] Neglected tropical diseases already on the list of notifiable conditions included: Chagas, chikungunya, dengue, leishmaniasis, Hansen's disease (leprosy), neurocysticercosis, rabies, and taeniasis.

Table 1. ENTD Projects Funded by DSHS in Fiscal Years 2017-2019

Fiscal Year	Project	Institution	Significant Findings
2017	Antibody Prevalence to Selected ENTDs and Associated Risk Factors in Brownsville, Cameron County, Texas	The University of Texas Health School of Public Health, Brownsville Campus ($209,470)	Detected antibody prevalence: Ascaris: 24.3% Echinococcus: 13.1% Strongyloides: 10.2% Chagas: 2.8% Leishmania: 0% Dengue: 47.9%-52.6% Chikungunya: 2.0% Zika: 6.6%
2017	Prevalence of Soil Transmitted Helminths (STHs) in Northeast Texas Children	The University of Texas at Tyler ($68,336)	No findings of STHs or non-target ENTDs in 198 children tested
2018-2019	Expanded Study of a Random Cohort Population in South Texas for Evidence of Infection by ENTDs and Expansion to Surveillance for Active Infection	The University of Texas Health School of Public Health, Brownsville Campus ($297,520)	Study in process – preliminary results not yet available
2018-2019	Chagas Disease and Dengue, Chikungunya, and Zika Virus Screening at the Texas-Mexico Border (Starr County, Texas)	The University of Texas Health Science Center at Houston ($94,650)	Study in process – preliminary results not yet available
2018-2019	Enhanced Surveillance of Chagas Disease, Northeast Texas	The University of Texas at Tyler ($207,830)	Study in process – preliminary results not yet available

The FY17 projects indicated that several ENTDs are circulating or have previously been present in parts of Texas. These findings corroborate cases of these same and other ENTDs identified through Texas' existing passive disease surveillance system. The three projects for the 2018-19 biennium are expected to further characterize the prevalence of several ENTDs in Texas, as well as demographic, behavioral, and geographic risk factors associated with infection. All three university contractors are currently implementing their 2018-19 biennium project activities.

Across all projects, the university contractors have tried different approaches to overcome challenges within their projects. Given the low prevalence of ENTDs, along with potential participants' hesitation to submit stool specimens, the contractors have taken steps to increase participation in these public health surveillance activities. DSHS follows each project closely via quarterly reports and, starting in the fall of 2018, with monthly conference calls to ensure the contractors are on target and receive assistance as needed.

1. Introduction

The 2018-19 General Appropriations Act, Senate Bill 1, 85th Legislature, Regular Session, 2017 (Article II, Department of State Health Services, Rider 35) directs the Department of State Health Services (DSHS) to allocate $300,000 in General Revenue in each fiscal year of the 2018-19 biennium to implement a sentinel surveillance program to monitor emerging and neglected tropical diseases (ENTDs), as outlined in Health and Safety Code, Chapter 100, and requires DSHS to submit a report to the Legislative Budget Board outlining program implementation and performance by December 1, 2018.

This report outlines ENTD program implementation during fiscal year 2018 (September 1, 2017 to August 31, 2018), summarizing three ENTD sentinel surveillance projects funded for the 2018-19 biennium and the progress achieved to date. Additionally, it highlights projects carried out in fiscal year 2017 as mandated by House Bill 2055, 84th Legislature, Regular Session, 2015, which created Health and Safety Code, Chapter 100.

2. Background

Emerging infectious diseases are those that have never been seen before, new strains of known pathogens that manifest different disease characteristics, occur in new geographic locations, or affect new populations. Neglected tropical diseases are a diverse group of known infectious diseases that primarily occur in the tropical and subtropical areas of the world. As a group, emerging and neglected tropical diseases (ENTDs) occur overwhelmingly in lesser-developed tropical and subtropical countries or regions, and their occurrence is strongly associated with poverty, inadequate public health and sanitation infrastructure, and close contact with domestic and wild animal and arthropod vectors (e.g. biting insects, ticks, etc.). The World Health Organization (WHO) has identified 17 neglected tropical diseases estimated to affect over one billion people in 149 countries each year, causing significant morbidity and mortality in addition to billions of dollars of negative economic impacts.[2]

Several environmental and socioeconomic attributes of Texas are conducive to the establishment or continued spread of several ENTDs within the state, including:

- Subtropical areas and climates in Texas that support year-round activity of disease vectors, particularly mosquitoes;
- Large numbers of travelers, animals, and goods from around the world entering Texas through ports, airports, and international border crossings;
- Inadequate access to healthcare in areas of Texas with high poverty rates, particularly along the Texas-Mexico border, resulting in a higher likelihood that ENTD infections may go undiagnosed, untreated, and unreported to public health authorities, and raising the risk of establishment of non-endemic ENTDs in these areas, sustained transmission, and outbreaks;
- Inadequate public sanitation infrastructure in some areas, particularly in colonias along the Texas-Mexico border;

[2] "Investing to Overcome the Global Impact of Neglected Tropical Diseases: Third WHO Report on Neglected Tropical Diseases," World Health Organization, February 2015, http://www.who.int/neglected_diseases/9789241564861/en/.

- Lengthy international border, with many adjacent areas of Mexico characterized by low socioeconomic status, inadequate public sanitation, and public health infrastructure; and

- Transit of significant numbers of migrants and/or refugees from Mexico and lesser-developed nations farther south.

DSHS maintains a significant infectious disease surveillance program, and coordinates with 63 local public health departments and eight Public Health Regions across the state to investigate cases of infectious diseases on the list of notifiable conditions. This coordination helps to build a comprehensive knowledge base of these diseases, define risk parameters, mitigate or prevent individual cases and outbreaks, and efficiently direct public health resources.

Health & Safety Code, Chapters 81, 84, and 87 require specific information regarding notifiable health conditions to be reported to DSHS, and Chapter 97, Title 25, Texas Administrative Code requires healthcare providers, hospitals, laboratories, schools, veterinarians, and others to report patients suspected of having a notifiable condition.

Table 2 provides a 10-year history of human case counts for ENTDs known or suspected to occur in Texas, or which pose a risk of introduction into Texas, and are included in the list of notifiable conditions.[3] This data includes travel-associated cases acquired outside of Texas or the U.S. by Texas residents.

[3] The full list of notifiable conditions can be found at https://www.dshs.texas.gov/idcu/investigation/conditions/.

Table 2. Human Cases of Notifiable ENTDs, 2008-2017

Disease	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Ancylostomiasis	NR[4]	NR	NR	NR	NR	NR	NR	NR	0	0	**0**
Ascariasis	NR	NR	NR	NR	NR	NR	NR	NR	6	12	**18**
Chagas Disease	NR	NR	NR	NR	NR	19	20	25	27	33	**124**
Chikungunya	NR	NR	NR	NR	NR	NR	114	55	20	15	**204**
Cysticercosis	5	9	6	9	10	7	16	14	16	10	**102**
Dengue	22	14	19	7	16	95	34	32	45	43	**327**
Echinococcosis	NR	NR	NR	NR	NR	NR	NR	NR	2	0	**2**
Fascioliasis	NR	NR	NR	NR	NR	NR	NR	NR	0	0	**0**
Hansen's Disease (leprosy)	23	24	26	16	10	16	19	20	18	23	**195**
Leishmaniasis	0	2	0	4	6	11	12	6	13	8	**62**
Paragonimiasis	NR	NR	NR	NR	NR	NR	NR	NR	0	0	**0**
Rabies (human)	0	1	0	0	0	0	0	0	0	0	**1**
Taeniasis	0	2	1	1	1	0	1	6	2	1	**15**
Trichuriasis	NR	NR	NR	NR	NR	NR	NR	NR	0	1	**1**
Zika	NR	NR	NR	NR	NR	NR	1	8	315	55	**379**

[4] NR: Not Reportable

3. Emerging and Neglected Tropical Disease Sentinel Surveillance Projects, Fiscal Year 2017 – Fiscal Year 2019

Steps Toward Establishing Emerging and Neglected Tropical Disease Sentinel Surveillance in Texas

In order to fulfill legislative requirements to establish a sentinel surveillance program for emerging and neglected tropical diseases (ENTDs), the Department of State Health Services (DSHS) consulted with the Centers for Disease Control and Prevention (CDC) in 2015 to determine which neglected tropical diseases had the potential to occur naturally or become established in Texas, identifying 14 diseases that would meet these criteria. Eight of these diseases - Chagas disease, chikungunya, dengue, leishmaniasis, Hansen's disease (leprosy), cysticercosis, rabies, and taeniasis - were already required to be reported to DSHS per Texas Administrative Code §97.3. In April 2016, DSHS amended Texas Administrative Code §97.3 to add six additional neglected tropical diseases meeting criteria for inclusion on the list of notifiable conditions: ancylostomiasis, ascariasis, echinococcosis, fascioliasis, paragonimiasis, and trichuriasis. In addition, DSHS conducted ENTD-related educational events for providers, infectious disease specialists, and healthcare facilities. Lastly, DSHS entered into contracts with two state universities in fiscal year 2017 and three state universities for the 2018-19 biennium to conduct ENTD sentinel surveillance, as outlined below.

Fiscal Year 2017 Sentinel Surveillance Projects

In fiscal year 2017, DSHS entered into contracts with two state universities to conduct ENTD sentinel surveillance, totaling $277,806:

1. The University of Texas Health School of Public Health, Brownsville Campus (UTSPH-Brownsville) – March 15, 2017 – August 31, 2017: $209,470

2. The University of Texas at Tyler (UT-Tyler) – May 1, 2017 – August 31, 2017: $68,336

The contracting process was non-competitive, given the short time frame between passage of the legislation and the feasible timelines of the contracting process. A description of each contractor's target population, diseases studied, and results is outlined below.

1. UTSPH-Brownsville – "Antibody Prevalence to Selected Neglected Tropical Diseases and Associated Risk Factors in Brownsville, Cameron County, Texas"

This project sought to identify a variety of ENTDs, including three intestinal parasitic worms (*Ascaris lumbricoides*, *Echinococcus* species (*spp.*), and *Strongyloides stercoralis*); two single-celled protozoan parasites (*Trypanosoma cruzi*, the agent of Chagas disease, and *Leishmania spp.*); and three arboviruses (chikungunya, dengue, and Zika virus) in a population of 305 randomly recruited subjects from a group of previously collected contacts and specimens known as the Cameron County Hispanic Cohort. Population-based studies for this group of diseases in the U.S. are largely lacking. Most information in the U.S. comes from clinic-based studies and is not reflective of what may be occurring in the general population. Because the subjects in this study were randomly selected, the results should better reflect the true prevalence of these diseases in the wider South Texas population.

Blood specimens from the 305 study subjects were tested for the presence of immunoglobulin G (IgG) antibodies to the diseases specified above using enzyme-linked immunosorbent assays (ELISAs). Detection of IgG antibodies does not necessarily indicate current infection, as these antibodies may persist in blood specimens long after an infection has resolved. It does, however, indicate likely exposure to the infectious agent at some point in the past. Results of the study are presented in Tables 3-5.

Table 3. Results of UTSPH-Brownsville Testing for Intestinal Parasitic Worms

Intestinal Parasitic Worms	Total Tested	Total Positive	% Positive
Ascaris lumbricoides	305	74	24.3%
Echinococcus spp.	305	40	13.1%
Strongyloides stercoralis	305	31	10.2%

Table 4. Results of UTSPH-Brownsville Testing for Protozoans

Protozoan	Total Tested	Total Positive	% Positive
***T. cruzi* (Chagas)**	176	6	3.4%
Leishmania spp.	88	0	0.0%

Table 5. Results of UTSPH-Brownsville Testing for Arboviruses

Arbovirus	Total Tested	Total Positive	% Positive
Dengue - Abcam brand test	305	146	47.9%
Dengue - Euroimmun brand test	192	101	52.6%
Zika	305	20	6.6%
Chikungunya	305	6	2.0%

Several issues complicate the interpretation of the study's results, most of which are common to antibody serological surveys.

First, the presence of antibodies to an infectious agent does not necessarily indicate current infection, as antibodies (particularly the IgG antibodies measured in this study) can persist for months or years after an infection resolves.

Second, a positive result on a particular test may result from antibodies to a related agent, rather than the agent to which the test is targeted, an issue known as cross-reactivity. In the case of this study, antibodies to dengue and Zika virus, both of which are members of the genus *Flavivirus*, cross-react on serological tests for either agent. As a result, a positive test result for dengue may actually be due to current or previous Zika virus infection (or infection with other members of the *Flavivirus* genus, like West Nile virus) and vice versa.

Third, approximately two thirds of the Cameron County Hispanic Cohort were born in Mexico and a large majority of residents in Cameron County have frequent travel to Mexico. As a result, many, or even most, of the positive lab reports in this study may be due to exposures in Mexico rather than in Texas.

Lastly, IgG antibodies are often not detectable during the early stages of infection, so some current infections may not have been detected in this study.

The study results were not unexpected for Texas, particularly for the population in the Lower Rio Grande Valley, where many of these diseases are endemic. The exception is the reported prevalence of antibodies to the intestinal parasitic worms *Ascaris lumbricoides*. The 24.3 percent prevalence reported by this study is higher than the Centers for Disease Control and Prevention's (CDC's) estimates of approximately seven percent prevalence in Mexico and 17 percent prevalence worldwide. The authors of the study offered no hypotheses for the higher reported prevalence, but cross reactivity to another organism is likely.

2. UT-Tyler – "Prevalence of Soil Transmitted Helminths in Northeast Texas Children"

This project sought to identify the presence of three different intestinal parasites in stool samples of Northeast Texas children. The three parasites, collectively referred to as soil-transmitted helminths (STHs), which are parasitic worms, are *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whip worm), and *Necator americanus* (hookworm). These three species of worms are strictly human parasites and do not thrive in other animal hosts. They can be found in soil that has been contaminated with infected human feces.

The researchers recruited parents of children at several clinic sites in Northeast Texas. Parents were asked to enroll their children and if they agreed, were provided a stool test kit to take home so that a sample of their child's stool could be collected for testing. Although 492 stool collection kits were distributed, only 198 were returned. No STHs were detected; however, 14 samples were positive for several non-STH and non-ENTD protozoal parasites of variable health significance, including eight *Blastocystis hominis* (a common single-celled parasite), five *Dientamoeba fragilis* (a common protozoan parasite), and one *Giardia lamblia* (a very common protozoal parasite).

Fiscal Years 2018 and 2019 Sentinel Surveillance Projects

For fiscal years 2018 and 2019, DSHS entered into contracts with three state universities to conduct ENTD sentinel surveillance, totaling $600,000 over the biennium:

1. UTSPH-Brownsville – September 1, 2018 – August 31, 2019: $297,520

2. The University of Texas Health Science Center at Houston (UTHealth) – January 1, 2018 – August 31, 2019: $94,650

3. UT-Tyler – September 1, 2018 – August 31, 2019: $207,830

As with the fiscal year 2017 awards, the contracting process was non-competitive, given the short time frame between passage of Rider 35 and the feasible timelines of the contracting process. A description of each contractor's target population, diseases studied, and progress achieved in fiscal year 2018 is outlined below.

1. UTSPH-Brownsville – "Expanded Study of a Random Cohort Population in South Texas for Evidence of Infection by ENTDs and Expansion to Surveillance for Active Infection"

This project seeks to identify the prevalence of the parasitic infections ancylostomiasis, cysticercosis, echinococcus, leishmania, paragonimiasis, and taenia, as well as the arboviruses chikungunya, dengue, West Nile virus, and Zika in at-risk populations of the Rio Grande Valley region of south Texas. The researchers are collaborating with clinical partners in federally qualified health centers and other clinical practices to identify individuals from at-risk populations for testing. The project will utilize polymerase chain reaction (PCR) testing of stool samples to detect the presence of active parasitic infections and serological testing to determine active or past infection with the various arboviruses.

According to UTSPH-Brownsville's interim report, which covered its progress made in fiscal year 2018, researchers have enrolled patients and begun testing, but no preliminary results are available.

2. UTHealth – "Chagas Disease and Dengue, Chikungunya, and Zika Virus Screening at the Texas-Mexico Border (Starr County, Texas)"

This project is utilizing serological testing to identify the prevalence of current and past infections of *Trypanosoma cruzi* (the causative parasitic agent of Chagas disease), chikungunya, dengue, West Nile, and Zika virus in up to 1,200 individuals from Starr County, Texas. Test samples will include newly recruited participants in addition to those for whom the researchers have banked blood specimens collected during previous research projects conducted over the past 10 years.

According to UTHealth's interim report, which covered its progress made in fiscal year 2018, the project has enrolled 314 participants thus far, including 140 newly recruited participants and 174 participants for whom banked blood specimen samples were available. Initial screening tests have been run on 314 participants for chikungunya, West Nile, and Zika virus; 210 participants for dengue; and 240 participants for Chagas disease. Those samples testing positive on the screening tests must undergo confirmatory testing before they can be confirmed positive.

3. UT-Tyler – "Enhanced Surveillance of Chagas Disease, Northeast Texas"

This project originally sought to identify the presence of the protozoan parasite, leishmaniasis, in blood or skin samples of Northeast Texas adults 18 years or older who came to a clinic or hospital with complaints of skin rash, sores, or ulcers during the last three years. However, due to technical issues with commercially available tests for leishmania, the contract was amended in January 2018 to change the scope of the project. It now seeks to determine the extent to which, if any, undiagnosed Chagas disease may be a cause of cardiomyopathy (disease of the heart muscle) in Texas residents and, by extension, the degree to which Chagas disease may be undiagnosed and underreported in Texas.

Between 2013 and 2017, 124 cases of Chagas disease in Texas residents were reported to DSHS. However, as with almost all disease reporting systems, the true number of cases is likely much higher, particularly given that this disease has an asymptomatic, chronic infection stage and that many physicians are not familiar with Chagas disease and so do not consider it among their differential diagnoses when evaluating potentially infected patients.

Acute Chagas disease, if untreated, typically leads to chronic lifetime infection with the causative organism, *Trypanosoma cruzi*. A majority of those chronically infected remain asymptomatic for life; however, they may present an infection risk to others through blood or tissue transplantation, via maternal transmission, or by serving as a host for infection for the blood-feeding insects that typically transmit the disease. Among asymptomatic chronic infections, 20–30 percent will advance to chronic symptomatic forms, which typically manifest as cardiomyopathy or gastrointestinal disease.

A recent California study of patients with cardiac conduction abnormalities, a potential early indicator of Chagas cardiomyopathy, who had lived in Latin America

for at least 12 months, found that 5.2 percent had evidence of Chagas infection.[5] A 2010 survey of physicians indicated a general deficit of knowledge about Chagas disease, even among cardiologists. Among cardiologists completing the survey, 23 percent had never heard of Chagas disease and did not know the disease symptoms, 34 percent never considered risk for Chagas disease in their patients, and 44 percent were not confident that their knowledge of Chagas disease was up-to-date.[6]

This project is a serological study of up to 300 participants suffering from non-ischemic forms of cardiomyopathy (cardiomyopathy not caused by coronary artery blockage) to determine if any are infected with *T. cruzi*, which may be the underlying cause of their cardiomyopathy. Patients will be recruited through multiple cardiology practices in Northeast Texas.

According to UT-Tyler's interim report, which covered its progress made in fiscal year 2018, investigators have identified a potential study population of over 3,000 patients, but so far, only six have been enrolled and tested. No positive cases of Chagas disease were identified in these patients. The investigators are currently working to expand the study inclusion criteria in order to increase the size of the potential study population from which they will recruit and enroll participants.

[5] Traina MI, Hernandez S, Sanchez DR, Dufani J, Salih M, Abuhamidah AM, et al. (2017) Prevalence of Chagas Disease in a U.S. Population of Latin American Immigrants with Conduction Abnormalities on Electrocardiogram. *PLoS Negl Trop Dis* 11(1): e0005244. https://doi.org/10.1371/journal.pntd.0005244.

[6] Stimpert, Kelly K. and Montgomery, Susan P. Physician Awareness of Chagas Disease, USA. *Emerging Infectious Diseases*, Vol. 16, No. 5, May 2010.

4. Conclusion

The two emerging and neglected tropical disease (ENTD) sentinel surveillance projects during fiscal year 2017 indicated that several ENTDs are circulating or have previously been present in parts of Texas, particularly the arboviruses chikungunya, dengue, and Zika; the parasitic protozoal diseases Chagas and leishmania; and the parasitic worm diseases ascariasis, echinococcosis, and strongyloidiasis. These findings corroborate cases of the same and other ENTDs identified through Texas' existing passive disease surveillance system. The three 2018-19 biennium projects currently in progress are expected to further characterize the prevalence of ENTDs in Texas, as well as demographic, behavioral, and geographic risk factors associated with infection.

Across all of the ENTD sentinel surveillance projects, the university contractors have tried different approaches to overcome challenges within their projects. Given the low prevalence of ENTDs, along with potential participants' hesitation to submit stool specimens, the contractors have taken steps to increase participation in these public health surveillance activities. The Department of State Health Services is monitoring all of the university contracts closely via quarterly reports. Beginning in the fall of 2018, monthly conference calls began taking place to ensure contractors are on target and assistance is being provided as needed.

List of Acronyms

Acronym	Full Name
CDC	United States Centers for Disease Control and Prevention
DSHS	Texas Department of State Health Services
ELISA	Enzyme-Linked Immunosorbent Assay
ENTD	Emerging and Neglected Tropical Disease
FY	Fiscal Year
IgG	Immunoglobulin G
PCR	Polymerase Chain Reaction
STH	Soil-Transmitted Helminths
UTHealth	University of Texas Health Science Center at Houston
UTSPH - Brownsville	University of Texas Health School of Public Health, Brownsville Campus
UT-Tyler	University of Texas at Tyler
WHO	World Health Organization