STATE OF TEXAS §
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COUNT OF HIDALGO §

MEMORANDUM OF AGREEMENT BETWEEN HIDALGO COUNTY AND THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO

This Memorandum of Agreement is made on this 6th day of May 2014 by and between **HIDALGO COUNTY** by and through its Department of Health and Human Services hereinafter referred to as "COUNTY", with administrative offices located at 1304 S 25th, Edinburg, TX 78539, and THE **UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO, a component institution of The University of Texas System,** by and through the Department of Medicine/Division of Infectious Diseases herein referred to as "UTHSCSA", located at 7703 Floyd Curl Drive, Mail Code 7828, San Antonio, Texas 78229-3900.

The aim of this Agreement is to establish an agreement for the exchange of information and for cooperative research between both institutions in the field of reportable communicable diseases.

I. PROVISIONS OF SERVICES

The COUNTY coordinates directly for health services to patients with reportable communicable diseases from Hidalgo County, and therefore has information of the characteristics of the patient and access to data on the strain(s) of infectious agents that has infected them. The faculty at UTHSCSA has developed a comprehensive research program in tuberculosis, latent tuberculosis infection and other infectious diseases.

Through this Agreement the parties shall develop by a cooperative agreement the following:

1. **Evaluation of standard and new tests to detect early infection.** The aim of this collaboration is to evaluate treatment regimens for tuberculosis (TB) and latent tuberculosis infection (LTBI) and laboratory assays that can help predict if an individual is in the early stages of active disease or how effective the treatment has been. The results will benefit the Mexican-American community that is vulnerable to contracting infectious diseases by:
   A. Developing and implementing new treatments for TB and LTBI that are effective, safe and tolerable;

   B. Providing diagnostic tools that can detect early infection, before the infection is spread to other individuals in the community; and

   C. Providing an additional tool to complement the current standard methods of detection for infectious diseases.

Studies on the nature of the association between reportable communicable diseases environmental, behavioral and health factors. These studies will benefit all patients with reportable diseases on the U.S.-Mexico border by providing information to the COUNTY, the public, and health providers. For each study, the UTHSCSA Principal Investigator will forward a written narrative describing the study to the COUNTY Health Administrator. An **APPENDIX OF**

CURRENT TBTC STUDIES is attached to this Memorandum of Agreement. The COUNTY, through the Health Administrator, may refuse to participate in a particular new study upon written notice to UTHSCSA.

The participation of COUNTY in this initiative shall consist of the following:

1. Provide UTHSCSA researchers with information on the patients thought to be infected with a reportable communicable disease, as well as individuals at high risk of contracting the infection.

2. Thereafter the Texas Department of State Health Services physician, Richard Wing, MD, will inform the patient about the study, and request his/her authorization to have the UTHSCSA researchers provide further details.

3. Facilitate the administration of new treatments for TB and LTBI provided by UTHSCSA researchers to enrolled patients.

4. Provide UTHSCSA researchers with retrospective and prospective data for analysis and publication on infectious disease trends in COUNTY.

The participation of UTHSCSA in this initiative shall consist of the following:

1. UTHSCSA researchers will explain the study to the patient and invite him/her to participate. If the patient voluntarily decides to do so, he/she will sign the informed consent document and HIPPA authorization form approved by the Department of State Health Services (DSHS) Committee for the Protection of Human Subjects.

2. Specimen collection will be taken from the Consenting Patient based upon the nature of the disease at a scheduled time and place agreed to between the Consenting Patient and the UTHSCSA researcher.

None of the studies will put the Consenting Patient at any unnecessary risk. Potential risks to the patient associated with the research study are described in detail in the study Informed Consent Document and will be explained to the patient prior to asking him/her to agree to participation in the study.

II. TERM OR AGREEMENT

The term of this Agreement will begin on the June 1, 2014 and end on May 31, 2015.

III. COMPENSATION

COUNTY will receive no reimbursement from UTHSCSA for any services provided. UTHSCSA will receive no reimbursement from COUNTY for any services provided.

IV. CONFIDENTIALITY

This collaborative work requires the mutual sharing of certain information made confidential by the statute at Texas Health and Safety Code §81.046, specifically, reports, records, and information relating to cases or suspected cases of diseases. This information is disclosed by

COUNTY only to assist UTHSCSA researchers; in compliance with statutory duties under Chapter 81 of the Health and Safety Code. These are the control of communicable disease (§81.081), investigation of the causes of communicable disease and methods of prevention (§81.061), and to prevent the introduction of communicable disease into this state (§81.021).

COUNTY requires that any individual who will view or handle the confidential information to comply with this confidentiality agreement. Therefore, COUNTY and UTHSCSA; agree that:

1. The confidential information shall be disclosed only for the purpose for which it was received.

2. The information shall be labeled as confidential.

3. The confidential information shall be kept securely.

4. The number of copies made of the confidential information or the notes taken from the confidential information that implicate the confidential nature of the information shall be controlled and all copies or notes that are not destroyed shall remain confidential and subject to the confidentiality agreement.

5. The confidential information shall not be re-disclosed to any other party or individual (other than the parties and individuals who have signed this agreement) for any purposes whatsoever.

None of these studies will result in extra cost for the COUNTY. None of the studies will put the Consenting Patient at any unnecessary risk. Potential risks to the patient associated with the research study are described in detail in the study Informed Consent Document and will be explained to the patient prior to asking him/her to agree to participation in the study.

V. NOTICES

All notices or other writing required under this Agreement shall be deemed to have been made when sent by certified or registered mail, return receipt request, to the following address:

TO UTHSCSA:
Department of Medicine/Division of Infectious Diseases
Attn: Marc Weiner, MD
7703 Floyd Curl Drive, Mail Code 7881
San Antonio, Texas 78229-3900

TO COUNTY:
Hidalgo County Health Department
Attn: Mr. Eduardo Olivarez
1304 S 25th
Edinburg, TX 78539

With a copy to:
Chris G. Green, CPA
UTHSCSA
Office of Sponsored Programs
7703 Floyd Curl Drive, MSC 7828
San Antonio, Texas 78229-3900

V. TERMINATION

This Agreement may be terminated by either party by giving thirty (30) days written notice via certified mail, return receipt requested to the other party hereto of the intention to terminate.

VI. LAW GOVERNING VENUE

This Agreement shall be governed by and construed in accordance with the laws of the State of Texas, and, obligations and undertakings of each of the parties to this Agreement shall be performable in Hidalgo County, Texas.

WITNESS THE HANDS OF THE PARTIES effective as of the day and year first written above.

THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO

Chris G. Green, CPA
Director, Sponsored Programs

Marc Weiner, MD
TB Study Principal Investigator

HIDALGO COUNTY TEXAS

Ramon Garcia, Hidalgo County Judge

ATTEST:

Arturo Guajardo, JR. Hidalgo County Clerk

APPROVED AS TO FORM:
Office of Criminal District Attorney
Rene Guerra

By: Josephine Ramirez Solis
Assistant District Attorney

APPROVED BY COMMISSIONERS' COURT ON: 5/6/14

APPENDIX OF CURRENT TBTC STUDIES:

1. Study 33 – *"An evaluation of adherence to LTBI treatment with 12 doses of once weekly rifapentine and isoniazid given as self-administered versus directly-observed therapy: iAdhere"*

Sponsored by: CDC/Tuberculosis Trials Consortium (TBTC)
Initiated: 4/2012
Enrollment was initiated on 12/18/2012.

The study is an open label, multicenter, phase IV randomized controlled clinical trial conducted in adult patients diagnosed with latent tuberculosis infection (LTBI) who are recommended for treatment. The primary objective is to evaluate adherence to a three-month (12-dose) regimen of weekly rifapentine and isoniazid given by directly observed therapy (DOT) compared to self-administered therapy. Treatment completion, defined as taking at least 90% of the doses (11/12 doses of each drug) within 16 weeks of treatment initiation, will be used as the primary measure of adherence. A secondary objective is to evaluate the use of weekly short messaging service (SMS) reminders as an intervention to maximize the adherence to SAT. Participants will be randomized to DOT, SAT without reminders, or enhanced SAT with weekly SMS reminders.

All participants will:

- Receive rifapentine 900 mg, INH 900mg and pyridoxine 50 mg once-weekly x 12 doses (3RPT/INH).
- Be randomized to one of three arms to receive LTBI treatment either given by DOT or self-administered therapy without reminders or self-administered therapy with weekly SMS reminders.
- Be assessed for their interest and ability to receive weekly SMS reminders. Because access to SMS may be a marker for other important differences affecting adherence, randomization will be independent of the participants' access to SMS.

The World Health Organization (WHO) estimates that approximately 2.3 billion people are infected with *Mycobacterium tuberculosis*, 9.4 million new cases of active tuberculosis (TB) occurred (137 per 100,000 population) in 2009, and that approximately 1.7 million people die of TB each year, making it the second most common infectious cause of death in the world. Of the 9.4 million new cases annually, an estimated 44% (4,136,000) are smear-positive and at high risk for transmitting TB to their close contacts. The contacts infected with *M. tuberculosis* every year become the source for new TB cases in the future. In order to improve TB control worldwide, an affordable, effective, short course treatment for latent TB infection (LTBI) is a global priority.

The Prevent TB study (TBTC Study 26) was an open-label, randomized, phase III controlled clinical trial with over 8,000 high risk TST reactors enrolled comparing rifapentine and INH given once-weekly by DOT for three months/12 doses (3RPT/INH) with 9 months of daily, self-administered INH. The results demonstrated the safety and efficacy of the shorter regimen (NEJM. 2011;365(23):2155-2166). Moreover, the once weekly therapy had significantly higher

treatment completion rates than the standard 9 INH regimen (81% vs. 69%, p< 0.001). Due in part to cost and logistical constraints, self-administered therapy remains the standard of care for the majority of LTBI patients. Therefore, to apply the Prevent TB study results more broadly, a new study evaluating treatment completion of 3RPT/INH given as self-administered therapy is required.

2. **Study 36** – *"TBTC Study 36: Platform for Assessment of Tuberculosis (TB) Treatment Outcomes An Observational Study of Individuals Treated for Pulmonary TB"*

Sponsored by: CDC/Tuberculosis Trials Consortium (TBTC)
Initiated: Pending regulatory approval
Enrollment: Pending regulatory approval

This is a prospective observational study that will enroll individuals with suspected pulmonary TB and follow those with culture-confirmed, rifamycin-sensitive TB for 18 months, from the initiation of TB treatment and for 12 months after completion of TB treatment. The primary objectives of this study are to collect and analyze sputum to define optimal methods to detect and quantify MTB during treatment; to assess the outcomes of treatment failure, cure, relapse, and death in a standardized manner; and to assess sputum parameters as surrogate markers for these outcomes. No treatment is provided through this study. The study does not specify any particular regimen of anti-TB medications for treatment of pulmonary TB, or the length of time, dosage or frequency of anti-TB medications prescribed. Study participants may receive TB medications from any locally approved source, provided that they consist either of a combination recommended by the World Health Organization (WHO), or are a combination regimen obtained through co-enrollment in any arm of a locally approved investigational TB treatment protocol.

Eligible study participants will include individuals 15 years of age and older, both HIV-infected and HIV-uninfected, and allows the enrollment of pregnant and breastfeeding women. The CDC IRB determined that the study poses minimal risk to subjects.

- Childhood TB represents an important minority among TB cases. Recorded cases of childhood TB account for an estimated 6% of reported TB cases worldwide. In highly TB-endemic areas, however, this percentage is at least double that seen worldwide. This study will enroll adolescents whose TB can be detected in sputum to allow the assessment of treatment response and outcomes. As with other participants in this study, adolescents will receive blood and radiographic testing that is the current standard of care for persons with TB disease. The inclusion of children was found to be permissible under 45 CFR 46.404.
- Approximately 13% of all new TB cases worldwide occur in HIV-infected persons. All participants will have HIV infection status documented. The study does not specify the clinical management of HIV co-infection, including choice of antiretroviral therapy (ART) or timing of initiation of ART. As with other participants in this study, participants with HIV co-infection will receive blood and radiographic testing that is the current standard of care for persons with TB disease. Blood will also be obtained for monitoring CD4 cell count and HIV viral load four times during the 18 month study period.

- TB is among the three leading causes of death among women aged 15–45 years. Pregnancy is common among this age group. Because of restrictions/barriers to including pregnant women in studies of TB, there is little detailed information available regarding the response to TB therapy or treatment outcomes among pregnant women. The blood tests obtained over the course of this study are part of the standard of care for persons receiving treatment for TB. The inclusion of pregnant women was reviewed under Subpart B and was found to be permissible under 45 CFR 46.204.

Tuberculosis (TB) is a major global public health problem. Given the tremendous burden of disease as well as the increasing incidence of MDR TB, new strategies are needed to prevent and treat TB. One significant barrier to efficient treatment is a lengthy and complicated standard therapy regimen. New drugs to both shorten treatment duration as well as treat MDR TB are urgently needed. Fortunately, TB drug development has been active in recent years, several drugs have entered the clinical phase of testing and several potential TB treatment-shortening regimens will soon be entering into Phase 3 trials. However these clinical trials use a standard, but relatively insensitive, microbiological marker (culture conversion at week 8 of TB therapy) as a surrogate for long-term treatment outcomes. Clearly, optimization of existing surrogate endpoints and discovery of better surrogate markers for TB treatment outcomes are important goals to move TB drug development forward faster. To assess surrogate markers of TB relapse, it is critical that multicenter trials are conducted in a rigorous, safe, and systematic manner to characterize the relationship between putative surrogate markers and the outcomes of treatment. This observational study platform is designed to allow the Tuberculosis Trials Consortium to address essential scientific questions pertaining to current microbiological methods and new diagnostic/prognostic tests.