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 2nd day of June 2015 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 2, , 2015 and end on May 31 , 2016.

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, complete the Texas Department of State Health Services on line security training accessed at: : https://tx.train.org and sign the Texas Department of State Health Services TB/HIV/STD/Hepatitis Unit 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

APPROVED BY
COMMISSIONERS' COURT
ON: 6/2/15

Ramon Garcia, Hidalgo County Judge

ATTEST:

Arturo Guajardo, JR. Hidalgo County Clerk

APPROVED AS TO FORM:
Office of Criminal District Attorney
Ricardo Rodriguez

By: Josephine Ramirez Solis
Assistant District Attorney

APPENDIX OF CURRENT TBTC STUDIES:

1. **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: 12/2014
Enrollment: Pending

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.

2. **Study 31** – *"Rifapentine-containing treatment shortening regimens for pulmonary tuberculosis: A randomized, open-label, controlled phase 3 clinical trial"*

Sponsored by: CDC/Tuberculosis Trials Consortium (TBTC) and The National Institute of Allergy
Initiated: estimated 05/2015
Enrollment will be initiated upon approval of Department of State Health Services IRB and COUNTY acceptance of IRB documentation.

The study is an international, multicenter, randomized, controlled, open-label, phase III clinical trial conducted in pulmonary tuberculosis (TB) suspects, both HIV-infected and HIV-uninfected, 12 years of age and older. The primary objective is to evaluate the efficacy of two rifapentine-containing regimens to determine whether it is possible to reduce the duration of treatment to seventeen weeks for drug-susceptible pulmonary tuberculosis:

- One regimen will substitute rifapentine 1200 mg/dose for rifampin 600 mg/dose.
- One regimen will substitute rifapentine 1200 mg/dose for rifampin 600 mg/dose, moxifloxacin 400 mg/dose for ethambutol (weight based dosing) and will continue moxifloxacin 400 mg/dose during the continuation phase of treatment.
- A third control regimen will be the standard treatment with rifampin for 26 weeks duration.

Secondary objectives are to evaluate the safety and tolerability of the investigational regimens; to determine the correlation of mycobacterial and clinical markers with time to culture conversion, culture status at completion of eight weeks of treatment, treatment failure, and

relapse; to evaluate the pharmacokinetics/pharmacodynamics (PK/PD) of the test drugs to characterize study drug PK parameters and to determine relationships between treatment outcomes and PK parameters; to evaluate the pharmacokinetics of efavirenz-based antiretroviral treatment among patients with TB/HIV co-infection taking efavirenz-based combination antiretroviral therapy and TB treatment with rifapentine; and to collect and store biospecimens for the purpose of future research on discovery and validation of TB biomarkers.

- All participants will be randomized to one of three treatment regimens and will receive treatment 7 days per week given by directly observed therapy (DOT) at least 5 days per week throughout the duration of the study regimen.
- All TB medications will be provided by Sanofi-Aventis and distributed by the CDC Drug Service.
- Participants will have scheduled study visits every 2 weeks for the first 8 weeks, every 4 - 5 weeks until 6 months after enrollment and then every 3 months until 18 months after enrollment.

TB is one of the most important global health problems. According to recent estimates from the World Health Organization (WHO), 8.6 million new cases and 1.3 million deaths from TB occurred in 2012 (World Health Organization 2013). The vast majority of TB cases and TB deaths are in developing countries. The spread of HIV has fueled the TB epidemic. TB is the second most common infectious cause of death in the world and the leading cause of death among patients infected with HIV. TB predominantly affects young adults in their most productive years of life and has substantial impact on economic development.

Although effective therapy for drug susceptible *Mycobacterium tuberculosis* is available, TB continues to cause significant morbidity and mortality worldwide, and rates of multi-drug resistant (MDR) and extensively-drug resistant (XDR) TB cases are on the rise. A major obstacle to the control of TB is poor adherence with lengthy (at minimum 6 months) and complicated treatment regimens. Incomplete TB treatment can lead to increased morbidity and mortality, prolonged infectiousness and transmission, and the development of drug resistance. The development of new treatment strategies with more potent antimycobacterial activity could lead to shorter and better tolerated regimens. A TB treatment regimen that allowed a decrease in treatment duration would potentially have important public health implications by facilitating DOT, increasing cure rates, potentially reducing transmission and preventing emergence of MDR TB. It is estimated that improved regimens that shorten treatment duration for drug-susceptible strains and are efficacious against resistant strains could reduce the incidence of TB by up to 27% by 2050 and reduce deaths by 25% from current global numbers of incident cases and deaths per year.