

TB Trials Network

TBTN

Enhancing the U.S. Public Health System's Willingness
and Capacity to Engage in Clinical Research

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BRIEFING BOOK SUMMARY

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A. PROGRAM SUMMARY

1. INTRODUCTION

Through a novel collaboration model, the Duke Clinical Research Institute (DCRI) is partnering with the Centers for Disease Control and Prevention (CDC) funded Tuberculosis Trials Consortium (TBTC) to achieve the overall project goal to enhance the willingness and capacity for clinics within the U.S. public health system to engage in clinical research.

Within the context of the Roadmap project mission, we are developing a detailed approach for implementing a prioritized TB research agenda, identifying barriers to clinical research in the public health setting, creating data standards for tuberculosis, exploring interoperability with public health reporting systems and building advanced electronic capabilities to support data collection, transfer, analysis and reporting.

To carry out specific project aims, we have engaged over fifty public health research professionals from nearly 20 academic and research institutions (in addition to our project team at the DCRI) to work on multi-disciplinary teams to achieve our objectives. These TBTC members are clinicians/investigators that constitute the critical link to the public health arena and work closely with the DCRI project team. Although the following aims serve to achieve our project goals, the processes, collaboration models, and products developed will have broad application among clinical research networks.

B. BUILDING COLLABORATIONS FOR CLINICAL RESEARCH NETWORKS

Aim 1- Engage public health leadership, in TB clinical research in particular, by engaging them in priority-setting forums that will also help the TBTC to create a relevant, timely and dynamic scientific agenda to address the global burden of TB.

- In February 2007, we hosted our 2nd “Think Tank” where the project’s momentum was evident in that we successfully recruited global experts to contribute to this critical analysis of the TB research agenda. Thirteen expert panel members representing public health leadership, pharmaceutical interests, global and domestic TB programs, basic science, diagnostics, microbiology, private and public funding entities, academia and TB patient care examined critical end points, the complex nature of TB clinical trials in developing a regimen for the treatment of TB disease and the need to harmonize the systems and the science that support such trials.
- The expert panel, encompassing leadership from the NIH, FDA, the Global Alliance for TB Drug Development, the World Health Organization (WHO), the Gates Foundation and other key stakeholders, jointly wrote a position paper submitted to the leadership of the CDC regarding the proposed TB scientific agenda. The document outlined a strategy regarding how the CDC

sponsored TB Trials Consortium could align with global needs and contribute to advancing the development of new TB drug regimens by implementing a specific research agenda.

Key collaborations:

- *FDA*
- *WHO*
- *Gates Foundation*
- *Global Alliance for TB Drug Development*
- *NIH*
- *CDC; Division of TB Elimination*
- *Pharmaceutical leadership representing TB drugs in the pipeline*
- *Diagnostic and Vaccine trial experts*
- *Expert TB clinicians and investigators*

Aim 2- Identify and reduce barriers to clinical trials research in U.S. public health

clinics by working with representative TBTC-associated public health clinics to identify the most significant barriers to conducting clinical research in their setting and develop a responsive strategy to reduce the barriers.

- Formed a 20+ person team of R.N.s, M.D.s and Ph.D.s representing the TBTC, DCRI and CDC. Team members work in clinical settings (academic medical centers, public health clinics, V.A. hospitals) across the U.S.
- RTI International (sub-contractor) conducted focus groups and interviews at twelve US clinical research sites.
- RTI, DCRI and “Barriers to Research” team developed interventions based on data analysis
- DCRI implemented affordable, highest priority strategies at target sites
- Currently measuring effect of intervention (through Jan 2008)

Key collaborators:

- *Personnel at twelve (12) CDC sponsored, TBTC sites at academic medical centers and public health clinics- including Medical Directors, TB nurses, clinicians and investigators*
- *RTI International*
- *Project team members (listed above)*
- *CDC*

Aim 3- Develop, with public health leaders and networks engaged in multicenter trials, a model for improving the process of human subjects protection review in multicenter trials.

We have worked with members of the public health community, with multicenter trialists, and with ethicist who focus on “human subjects protection” to address 2 specific issues a.) Explore the impediments to expanded use of central IRBs in multicenter trials and b.) Address the complexities associated with informed consent among subjects who do not speak English

- Formed team that includes chairs/members of medical IRBs (Columbia, Emory, and Boston University), and public health clinicians and researchers. Also, Dr. Jeremy Sugarman, a Harvey M. Meyerhoff Professor of Bioethics and Medicine at The Johns Hopkins University has collaborated on the effort.
- Sub-contract with Dr. William Burman of the Denver Public Health Department
- Final protocols and instruments approved by Denver & Duke IRB
- Conducting data collection via various modes, including an online survey tool hosted on the project website
- Synthesized and presented findings at OHRP/Duke sponsored symposium and PRIM&R Conference.

Key Collaborators

- *Denver Public Health (sub contractor with Bill Burman, MD)*
- *Core project team involving Duke, Columbia, Hopkins, Emory and Boston PIs and/or IRB Chairs*
- *OHRP*
- *PRIM&R*
- *TBTC/CDC*
- *NIH*

Aim 4- Improve interoperability by creating a secure web-based electronic data capture system to capture Adverse Events/ Serious Adverse Events (AE/SAE) and a Query- Tracking System for the TBTC, building an interface with the public health surveillance systems and creating data standards for tuberculosis.**AE/SAE Electronic Data Capture, Query Tracking Systems and TBTC website for TBTC:**

- Fully functional Query Tracking System in production and being utilized by the TBTC for a 8000 patient, international trial.
- Fully functional AE/SAE electronic data capture system launched in March 2006
- TBTC website developed and fully utilized to provide access to protocols, CRFs, SOPs, training manuals, etc.
- *Key Collaborators: DCRI, CDC, TBTC teams*

TB Data Standards: Formed team to work on methodology to standardized data elements for tuberculosis. Team includes Dr. William Hammond (Professor Emeritus, Duke), Dr. Carol Hamilton and Dr. Robert Harrington's Roadmap project teams at DCRI, and CDISC sub-contractors.

- TB data standards effort approved as official project of HL-7 within the Public Health Special Interest Group (PH-SIG). Sept 05
- Story boards depicting data flow, and directory instrument to capture data elements based on CDISC and ISO standards models.
- Convened 1st TB Data Standards Stakeholders meeting in Washington DC- October 2005; the F.D.A., NIH, CDC, I.D. professional societies, National TB

- Controllers Association, TB researchers, the TB Global Alliance and data standards community members attended.
- 2nd TB Data Standards Stakeholders meeting held in Washington DC- February 2006: In addition to previous attendees, several pharmaceutical companies, International research experts, and other TB Community members participated.
 - Convene bi-weekly calls with physicians, microbiologists, vaccine and diagnostic foundation representatives, pharmaceutical company representatives and other clinicians working in TB patient care, research or surveillance to work on TB data elements
 - Hosted “international” data standards meeting in conjunction with IUATLD Conference in Paris, France Oct 2006. Attendees included the WHO, international program leaders representing numerous countries affected by high TB rates, pharmaceutical representatives, leadership from ex-US based vaccine and diagnostic foundations, and TB clinicians and investigators.
 - TB Package #1 (a sub-set of over 70 data elements with corresponding valid value sets) being reviewed by CDISC technical committee.
 - TB Package #1 to be posted for public comment on CDISC website within the month
 - To begin work on TB Package #2 in June 2007

Key collaborators:

- **HL7**- Specifically through contract with Ed Hammond and working through the Public Health Special Interest Group within HL7.
- **CDISC** - Facilitate development of terminology & data elements (Bron Kisler and Jane Diefenbach). Leverage CDISC experience, relationships, stakeholders, and standards development process. Facilitate the public comment process.
- **NCI Enterprise Vocabulary Service (EVS) and cancer Data Standards Repository (caDSR)** - Host the vocabulary and data elements in the online repository
- **Clinical community** including experts in basic science, laboratory, patient care, research, surveillance, international TB programs, WHO, NIH CDC, vaccine and diagnostic groups, and representatives from pharmaceutical companies with TB compounds.

*** The Roadmap Human Subjects Protection and Regulatory Strategies**

Working Group (Chaired by Carol Hamilton) is pleased to be collaborating with the many Roadmap Working Group members evaluating regulatory guidelines for human subjects protection, how it translates to evidence-based human subjects protection and the burden on investigators and study coordinators conducting clinical research. Dr. Bill Burman from Denver Public Health is collaborating on this effort as well.

C. ROADMAP PRESENTATIONS AND PUBLICATIONS

ABSTRACTS:

- Accepted for presentation at CDISC European Interchange Meeting April 2007 in Switzerland; “Development of Disease Specific Data Standards: A Global Project & Case Study in Tuberculosis”
- Accepted for presentation at DIA Conference, June 2007; “NIH Roadmap Program and Development of Therapeutic Area Data Standards: Case Studies in TB and Cardiology”
- Pending acceptance for International Union Against TB and Lung Disease Conference, November 2007 in Cape Town; “Improving Information Sharing Between Tuberculosis (TB) Clinicians and Researchers”

PUBLICATIONS;

- No new publications submitted this quarter

PRESENTATIONS:

- “Development of Disease Specific Data Standards: A Global Project & Case Study in Tuberculosis” CDISC European Interchange Conference, Montreux, Switzerland, April 26, 2007