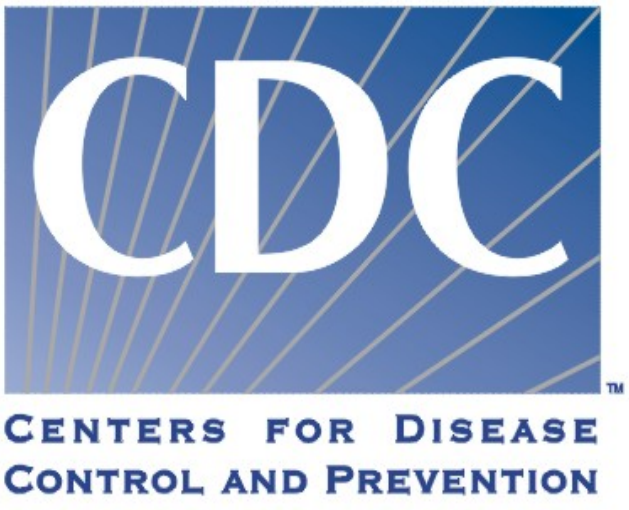
DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Division of Tuberculosis Elimination



Advisory Council for the Elimination of Tuberculosis
June 29-30, 2010
Atlanta, Georgia

Record of the Proceedings

TABLE OF CONTENTS

ATTACHMENT 1

List of Participants

ACET Members

Dr. Michael Fleenor, Chair
Dr. Iram Bakhtawar
Dr. Susan Dorman
Dr. Christine Hahn
Mr. Shannon Jones III
Mr. Joseph Kinney
Dr. Masahiro Narita
Dr. Barbara Seaworth
Ms. Sirlura Taylor

ACET Designated Federal Official

Dr. Hazel Dean, NCHHSTP Deputy Director

ACET *Ex-Officio* and Liaison Members

Dr. Robert Benjamin (National Association of County and City Health Officials)
Dr. Amy Bloom (U.S. Agency for International Development)
Ms. Anna Buchanan (Association of State and Territorial Health Officials)
Ms. Linda Danko (Department of Veterans Affairs)
Dr. Edward Desmond (Association of Public Health Laboratories)
Ms. Kimberly Field (National Tuberculosis Controllers Association)
Dr. John Halpin (National Institute for Occupational Safety and Health)
Mr. Warren Hewitt (Substance Abuse and Mental Health Administration)
Dr. Mamodikoe Makhene (National Institutes of Health)
Dr. Edward Nardell (International Union Against Tuberculosis and Lung Disease)
Ms. Susan Perez (Treatment Action Group)
Dr. Lee Reichman (American College of Chest Physicians)
Dr. Michael Tapper (Society for Healthcare Epidemiology of America)
Dr. Lornel Tompkins (National Medical Association)
Dr. Theresa Watkins-Bryant (Health Resources and Services Administration)

CDC Representatives

Dr. Kenneth Castro, DTBE Director
Ms. Marise Alexander
Mr. Gustavo Aquino
Ms. Eileen Bell
Dr. Stuart Berman
Ms. Smita Chatterjee
Dr. Terence Chorba
Ms. Ann Cronin
Dr. John Douglas
Ms. Molly Dowing
Ms. Heather Duncan
Dr. Michael Iademarco
Dr. Dolly Katz
Dr. Adam Langer
Ms. Ann Lanner
Dr. Philip LoBue
Ms. Suzanne Marks
Mr. Michael Melneck
Ms. Heather Mendes
Mr. John Moran
Dr. Thomas Navin
Ms. Christine Olson
Ms. Bonnie Plikaytis
Dr. Drew Posey
Mr. Andrew Rein
Ms. Cheri Rice
Mr. Joseph Scavotto
Ms. Margie Scott-Cseh
Mr. Arun Skaria
Ms. Melisa Thombley
Ms. Vicki Thurber
Dr. Andrew Vernon
Dr. Elsa Villarino
Dr. Wanda Walton
Ms. Kai Young

Guest Presenters and
Members of the Public

Dr. Eddy Bresnitz (Merck)
Dr. William Burman (Denver Public Health Tuberculosis Trials Consortium)
Dr. John Grabenstein (Merck)
Ms. Cornelia Jervis (Treatment Action Group)
Dr. Randall Reves (Stop TB USA)
Mr. John Seggerson (Stop TB USA)

ATTACHMENT 2

Glossary of Acronyms

AAs	African Americans
ACET	Advisory Council for the Elimination of Tuberculosis
ACIP	Advisory Committee on Immunization Practices
AHRQ	Agency for Healthcare Research and Quality
AIR	Airborne Infection Research
APHL	Association of Public Health Laboratories
ARV	Antiretroviral
ASTHO	Association of State and Territorial Health Officials
CDC	Centers for Disease Control and Prevention
CDRC	Clinical Diagnostic Research Center
Cmax	Maximum Concentration
CMS	Centers for Medicare and Medicaid Services
DOT	Directly Observed Therapy
DOTS	Directly Observed Therapy Short-Course
DSTDP	Division of STD Prevention
DTBE	Division of Tuberculosis Elimination
EDN	Electronic Disease Notification Center
EPC	Evidence-based Practice Center
FBP	Foreign-Born Persons/Populations
FDA	Food and Drug Administration
FOA	Funding Opportunity Announcement
GAP	Global AIDS Program
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HCV	Hepatitis C Virus
HHS	Department of Health and Human Services
HRSA	Health Resources and Services Administration
IDUs	Injection Drug Users
IGRAs	Interferon Gamma Release Assays
IMPAACT	International Maternal Pediatric Adolescent AIDS Clinical Trials
INH	Isoniazid
IOM	Institute of Medicine
IUATLD	International Union Against Tuberculosis and Lung Disease
LLR	Log-Likelihood Ratio
LTBI	Latent TB Infection
M.tb	*Mycobacterium Tuberculosis*
MDR-TB	Multidrug-Resistant TB
MIRU	*Mycobacterium* Interspersed Repetitive Units
MMWR	*Morbidity and Mortality Weekly Report*
MSM	Men Who Have Sex With Men
NACCHO	National Association of County and City Health Officials
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIH	National Institutes of Health

NTCA	National Tuberculosis Controllers Association
NTGS	National TB Genotyping Services
NTIP	National Tuberculosis Indicators Project
PCACA	Patent Care and Affordable Care Act
PCSI	Program Collaboration and Service Integration
PK	Pharmacokinetics
RIF	Rifampin
RTMCCs	Regional Training and Medical Consultation Center
RVCT	Report Verified Case of TB
SDH	Social Determinants of Health
SNTC	Southeastern National TB Center
TB GIMS	Tuberculosis Genotyping Information Management System
TBRU	TB Research Unit
TBTC	Tuberculosis Trials Consortium
TBTIs	TB Technical Instructions
TSTs	Tuberculin Skin Tests
USPSTF	U.S. Preventive Services Task Force
WHO	World Health Organization
XDR-TB	Extensively Drug-Resistant TB

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Division of Tuberculosis Elimination

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
June 29-30, 2010
Atlanta, Georgia

Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHHSTP) Division of Tuberculosis Elimination (DTBE) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on June 29-30, 2010 in Building 8 of CDC's Corporate Square Campus, Conference Room A/B/C in Atlanta, Georgia.

Opening Session

Dr. Hazel Dean, Deputy Director of NCHHSTP and Designated Federal Official of ACET, called the meeting to order at 8:39 a.m. on June 29, 2010. She welcomed the attendees to the proceedings and particularly recognized the new and alternate *ex-officios* and liaison members.

Ms. Anna Buchanan was serving as the alternate liaison to the Association of State and Territorial Health Officials (ASTHO) for Dr. José Montero. Ms. Linda Danko was serving as the alternate *ex-officio* to the Department of Veterans Affairs for Dr. Gary Roselle. Ms. Kimberly Field replaced Mr. Phillip Griffin as the liaison to the National Tuberculosis Association (NTCA). Ms. Coco Jervis would replace Ms. Susan Perez as the liaison to the Treatment Action Group at the next meeting.

Dr. Dean welcomed two guest speakers who would make presentations to ACET meeting on TB-related issues. Dr. William Burman is the Medical Director for the Denver Public Health Infectious Disease Clinic and a former ACET member. Dr. Randall Reves is an Infectious Disease Physician with the Denver Public Health Department.

Dr. Dean announced that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. She emphasized that ACET members should be mindful of potential conflicts of interest identified by the CDC Committee Management Office

and recuse themselves from participating in discussions or voting on issues in which they have a real or perceived conflict.

Dr. Dean highlighted other changes to ACET's membership. The ACET charter was amended to add three external organizations: ASTHO, the Pacific Island Health Officers Association and RESULTS.

The terms of five ACET members would expire on June 30, 2010: Dr. Michael Fleenor (Chair), Mr. Joseph Kinney, Dr. Ana Lopez-de Fede, Dr. Masahiro Narita and Ms. Sirlura Taylor. However, the five outgoing ACET members would serve an additional 180 days until their replacements were officially appointed. The White House Liaison Office is currently reviewing nomination packages for the candidates who were proposed as new ACET members.

Dr. Dean presented certificates of appreciation, letters from Dr. Frieden and plaques to the five outgoing members whose terms would expire on June 30, 2010: Drs. Fleenor, Narita and Lopez-de Fede (*in abstentia*), Mr. Kinney and Ms. Taylor. The participants joined Dr. Dean in applauding the outstanding assistance, expert advice, personal sacrifices and commitments the five outgoing members have made to CDC and the broader the TB control community during their tenure on ACET. Dr. Fleenor was given an additional token of appreciation due to his dual role as the ACET Chair and a member.

Dr. Dean opened the floor for introductions. The list of participants is appended to the minutes as Attachment 1.

Dr. Fleenor, Chair of ACET, joined Dr. Dean in welcoming the participants to the meeting. He announced that the update on the Foreign-Born Guidelines as noted on the published agenda would not be presented, but the draft guidelines were distributed to ACET for review.

NCHHSTP Director's Report

Dr. Dean presented the update on behalf of Dr. Kevin Fenton, Director of NCHHSTP, who was unable to attend the meeting. At the agency level, Ms. Carmen Villar was appointed as the CDC Chief of Staff. Dr. Thomas Frieden, Director of CDC, recently announced his list of key domestic "winnable battles." CDC will focus on these areas to make a measurable public health impact in a short period of time.

To support this initiative, leaders across CDC will be encouraged to identify winnable battles and develop strategies to achieve measurable impact and make significant progress in key public health areas in a short time. All of the winnable battles are a leading cause of illness, injury, disability or death, are associated with existing evidence-based and scalable interventions, and can be broadly implemented.

Dr. Frieden utilized HHS priorities and broad input from CDC leadership to identify the six winnable battles: tobacco; nutrition, physical activity, obesity and food safety; healthcare-associated infections; motor vehicle injury prevention; teen pregnancy prevention; and HIV prevention.

NCHHSTP made several accomplishments in 2009 for the HIV prevention winnable battle. Collaborations were established with the White House to develop the National HIV/AIDS Strategy. The HIV Testing Initiative was expanded in which 1.5 million HIV tests were administered, 10,500 new HIV-positive persons were identified, and Hispanics/Latinos and men who have sex with men injection drug users (MSM/IDUs) of all racial/ethnic groups were included. Social media initiatives and campaigns were launched to increase HIV awareness and testing.

NCHHSTP plans to conduct additional activities in 2011 to further advance the HIV prevention winnable battle. The proportion of IDUs who share needles or syringes will be decreased. The proportion of HIV-infected persons who are linked to care will be increased, particularly with the prevention with positive initiatives. HIV counseling, testing and linkage to care will be expanded to non-healthcare settings.

Dr. Frieden testified before the House Committee on Energy and Commerce Subcommittee on antibiotic resistance in April 2010. TB was one of the high-priority infections Dr. Frieden covered in his Congressional testimony.

At the National Center level, a search for the Director of the Division of STD Prevention (DSTDP) was announced with an application deadline of July 16, 2010. Dr. John Douglas, former Director DSTDP, was recently named as the NCHHSTP Chief Medical Officer. In his new position, Dr. Douglas will serve as the principal medical advisor to the Director of NCHHSTP, represent NCHHSTP in CDC's high-level committees (e.g., the Advisory Committee on Immunization Practices), and chair cross-Center workgroups (e.g., the Blood, Organ and Other Tissue Safety Workgroup).

Dr. Douglas also will be responsible for three additional activities in his new role: (1) collaborate with the Senior Advisor on Prevention Through Healthcare to coordinate and accelerate NCHHSTP's involvement in health reform opportunities; (2) develop and implement NCHHSTP's cross-cutting and strategic priorities, including sexual and reproductive health; and (3) identify and develop new strategic partnerships with other federal agencies to accelerate implementation of NCHHSTP's prevention priorities.

Dr. Stuart Berman was recently named as the Senior Advisor to the Director of NCHHSTP. In his new position, he will serve as the lead for "Prevention Through Health Care: Increasing Compliance with NCHHSTP's Care-Based Recommendations." Dr. Berman also will serve as the lead in two other areas: strengthening assessment of morbidity and service delivery by utilizing investments in health information technology and overseeing program improvement activities in support of NCHHSTP's mission.

Dr. Berman's other major role as the Senior Advisor to the Director of NCHHSTP will be to collaborate in facilitating the transition of program roles from service provision to assurance of service and quality, particularly among highly impacted populations.

Governance of the Global AIDS Program (GAP) has been fully transitioned from NCHHSTP to the CDC Office of Global Health. However, NCHHSTP has made a commitment to ensure that existing programmatic relationships remain unchanged. The transition will provide NCHHSTP with opportunities for new and exciting collaborations as the new Center for Global Health is established.

NCHHSTP recently released the "Addressing Syndemics through Program Collaboration and Service Integration" (PCSI) funding opportunity announcement (FOA) with a deadline to submit applications through June 15, 2010. Grantees will be required to conduct demonstration projects that support activities described in the December 2009 PCSI white paper. NCHHSTP held a webcast on May 10, 2010 to promote the content of the PCSI White Paper and convened the "Surveillance Confidentiality Consultation" on June 28, 2010.

NCHHSTP is conducting a number of activities to address health equity. The *Public Health Reports Social Determinants of Health Supplement* was recently published. Surveillance systems across NCHHSTP are being critically reviewed to identify areas where social determinants of health (SDH) variables are collected and recommendations will be made to the four divisions on effectively collecting and utilizing these data in programmatic activities.

The *NCHHSTP Social Determinants of Health White Paper* will be published in the fall of 2010. ACET submitted comments to NCHHSTP on the outline of the draft SDH white paper. Efforts are underway to include language on SDH and health equity in future NCHHSTP FOAs.

At the Division level, DTBE is conducting several activities to address health equity in the research, guidance and programs domains. More information will be provided on these efforts in the DTBE Director's report.

ACET was extremely disappointed that Dr. Frieden did not identify TB as a winnable battle, particularly with his strong background in TB and DTBE's mission to "eliminate" TB. ACET also noted that data have shown strong linkages between TB and many of the domestic winnable battles (*i.e.*, tobacco, obesity/diabetes and HIV).

ACET raised the possibility of leveraging opportunities to integrate TB into winnable battle activities that would be conducted by CDC operating units outside of DTBE. This strategy might lead to a positive benefit of further eliminating silos across programs. Some ACET members requested placing this issue on a future agenda for a more in-depth discussion and inviting Dr. Frieden to this meeting for ACET to present its compelling argument.

Other ACET members strongly opposed using a public forum to address the exclusion of TB from CDC's winnable battles with Dr. Frieden. These members believed that a more effective approach would be for ACET to express its concerns to Dr. Frieden in private.

ACET pointed out that Dr. Ronald Valdiserri, the former Deputy Director of NCHHSTP and the former Executive Secretary of ACET, was recently appointed as the Deputy Assistant Secretary for Health, Infectious Diseases, in the HHS Office of the Assistant Secretary for Health. The members requested inviting Dr. Valdiserri to a future ACET meeting to make a presentation on TB/HIV issues at the HHS level.

DTBE Director's Report

Dr. Castro, Director of DTBE, covered the following areas in his update. The National TB Conference was held on June 22-24, 2010 with a theme to "Innovate to Accelerate: On the Move to Eliminate TB." The key topics covered during the conference included laboratory diagnosis and medical management of TB cases, training and education, and programmatic aspects of TB.

The participants included two NTCA subgroups (the National Society of TB Clinicians and the National TB Nurse Coalition) and the Association of Public Health Laboratories (APHL). APHL's co-sponsorship of the conference provides an opportunity to focus on the laboratory aspects of TB programmatic activities as a core component.

The "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection" were published in the June 25, 2010 edition of the *Morbidity and Mortality Weekly Report* (*MMWR*). The guidelines are intended to provide guidance to U.S. public health officials, healthcare providers and laboratory workers for the use of interferon gamma release assays (IGRAs) approved by the Food and Drug Administration (FDA) in the diagnosis of *Mycobacterium tuberculosis* (*M.tb*) infection in adults and children.

The guidelines note that IGRAs and tuberculin skin tests (TSTs) may be used as aids in diagnosing *M.tb* infection, for surveillance purposes, and for the identification of persons likely to benefit from treatment. The guidelines provide additional recommendations to address quality control, the selection of TB testing, and medical management after testing.

DTBE is conducting a number of activities to address health equity as one of the six priority areas in the 2010-2015 NCHHSTP Strategic Plan. DTBE began this effort by agreeing to use two definitions to guide its activities. The *Healthy People 2020 Initiative* defines "health equity" as a goal or standard to improve the health of those experiencing social or economic disadvantage. The World Health Organization (WHO) defined SDH in 2009 as circumstances in which persons are born, grow up, live, work and age, and the systems put in place to deal with illness. These circumstances are shaped by economics, social policies and politics.

DTBE's health equity activities target three major domains. In the "research" domain, DTBE is addressing TB among African Americans (AAs) in the Southeast and conducting research on the determinants of early diagnosis, prevention and treatment of TB in AAs. In the "guidance" domain, DTBE developed ethnographic guides for TB in Mexican, Vietnamese, Lao Hmong,

Somalian and Chinese communities. DTBE also has created and distributed TB educational materials to Hispanic-serving organizations.

In the "program" domain, DTBE has collaborated with the Health Resources and Services Administration (HRSA) to increase testing, detection and treatment of TB and viral hepatitis C virus (HCV), primarily among AAs, in HRSA-funded Community Health Centers. DTBE also is establishing a Binational Multidrug-Resistant-TB (MDR-TB) Consultation Network between the United States and Mexico to enhance cross-border identification and management of persons with MDR-TB.

DTBE's rationale for taking an SDH approach to address TB is clearly defined. TB is more concentrated in socioeconomically disadvantaged populations. An SDH approach will allow DTBE to address the root causes of TB transmission, prevent a "revolving door" phenomenon, facilitate comprehensive approaches beyond categorical programs, foster novel partners for prevention, achieve and sustain results over time, and improve multiple health outcomes beyond TB.

CDC sponsored the Southeastern National TB Center (SNTC) to develop the "Toolkit for Partnerships to Eliminate TB in African American Communities" in collaboration with the Research Triangle Institute. The goals of the toolkit are to provide public health staff with tools to help raise awareness of TB in AA communities and also to help TB programs conduct TB forums to foster collaboration among community groups, minority health programs and public health programs.

DTBE is considering the possibility of extending support to help programs pilot the toolkit in ten sites. SNTC plans to offer training sessions to the pilot sites on using the toolkit to facilitate and implement a TB forum in their communities. The pilot sites will be expected to conduct a community TB forum and provide feedback and suggestions to improve the toolkit.

CDC, FDA and the National Institutes of Health sponsored the "New TB Diagnostics Workshop" on June 7-8, 2010. Key topics covered during the workshop included strategies for expedited discovery, evaluation and implementation of new rapid methods for laboratory confirmation of TB, and identification of drug resistance.

The strategies proposed during the workgroup focused on regulatory perspectives, partnerships and needs for a bio-bank repository, and point-of-care tests and evaluation of biomarkers. Following the workshop, a suggestion was made to use the ACET meeting in the fall of 2010 as a forum to review Class I, II and III regulatory criteria for new TB diagnostics. The suggestion was well received by FDA.

ACET emphasized the critical need to shift its focus and agenda on advancing toward TB elimination and fostering a strong TB elimination policy in CDC, HHS and the broader public health community. The members noted that TB elimination does not appear to be a priority at the HHS level.

The members pointed out that one of ACET's most significant challenges in addressing TB elimination is its charter to provide advice and guidance on domestic TB, but the disease is a global issue. Most notably, the goal of TB elimination cannot be achieved in the United States with a sole focus on domestic TB because foreign-born persons/populations (FBP) account for the largest proportion of cases.

To address these concerns, ACET suggested devoting a major portion of its future agendas, including DTBE updates and presentations, to TB elimination tactics and strategies in the United States and global TB issues. The members also raised the possibility of expanding ACET's charge to include providing advice and guidance on global TB issues (e.g., the cost of treating MDR-TB cases, directly observed therapy short-course (DOTS), and more aggressive strains of TB overseas).

Dr. Castro made several remarks in follow-up to the concerns ACET raised regarding the current status of TB elimination. The public health community is complacent about TB because the disease no longer serves as a leading cause of morbidity. TB programs primarily focus on bolstering and maintaining the achievements that have been made in TB control over time. Moreover, the current economic recession has resulted in prioritizing other public health issues that are more pressing than TB. Although the 2010 goal was established as a TB case rate of 1/1 million, the current case rate of 3.8/100,000 demonstrates that TB elimination will not be achieved in the near future.

Dr. Castro encouraged ACET to formally express its concerns on TB elimination to the Director of CDC and the Secretary of HHS. For example, ACET could make a compelling argument that CDC's syphilis, hepatitis and measles elimination programs have benefited from sustained support over time. In response to ACET's suggestion, Dr. Castro confirmed that DTBE's future updates and presentations would more clearly demonstrate the role of its ongoing research, data collection and programmatic activities in eliminating TB in the United States.

Update on the Menu of Suggested Provisions for State TB Prevention and Control Laws

Ms. Melisa Thombley, of DTBE, provided a status report on the Menu of Suggested Provisions CDC developed for state TB prevention and control laws. The overarching purpose of the Menu is to provide immediate, flexible and practical value to public health officials and their legal counsel in the enactment, promulgation, amendment or implementation of TB prevention and control laws in a variety of jurisdictions.

The dual goals of the Menu are to capture the types of provisions that are considered to be effective for possible inclusion in state TB control or general communicable disease control codes and also to provide a continuum of optional provisions within each type. The suggested Menu provisions also are applicable to localities, tribes and territories in addition to states.

In the summer and fall of 2009, CDC conducted research on TB prevention and control statutes and regulations in all 50 states, the District of Columbia and New York City. CDC created categories based on these research findings, the 1993 *MMWR* article on state TB control laws, and current issues in TB prevention and control. CDC re-reviewed and categorized TB control laws or general communicable disease control laws in each state, the District of Columbia and New York City.

DTBE and the CDC Public Health Law Program held the "Developing a Menu of Suggested Provisions for State TB Prevention and Control Laws" Workshop on February 4-5, 2010. The purpose of the workshop was for CDC to obtain feedback from the participants on whether provisions should be added or deleted from the draft Menu and for the participants to identify laws that have been effective in their respective jurisdictions. The workshop participants included CDC staff, state and local TB program staff, their legal counsel, and representatives from partner organizations.

CDC revised the draft Menu based on feedback provided during the February 2010 workshop and comments submitted by ACET during the March 2010 meeting. ACET's input was particularly invaluable to CDC in drafting the "Reporting" section of the Menu. This section was the most difficult to develop and accounts for the majority of new, innovative and revised provisions.

In addition to the workshop participants and ACET, CDC also obtained feedback from the APHL TB Steering Committee on the laboratory provisions of the draft Menu. The input and expertise by this group was tremendously helpful to CDC in drafting and revising the "Laboratory Reporting," "Laboratory Testing" and "Screening" sections of the Menu.

After revising the draft Menu based on comments submitted by the three sources, CDC drafted an introduction and descriptive notes to accompany each section. The introduction outlines the development and purpose of the Menu as well as its intended or unintended uses. The descriptive notes explain the importance of each of the TB control laws in controlling and preventing TB cases and also outline specific situations and jurisdictions in which existing provisions have been effective. CDC circulated the revised draft of the Menu to the workshop participants, NTCA Board and ACET for final review.

The 2009 evaluation of local public health practices regarding the isolation of persons with infectious TB local emphasizes the need for the Menu. The online survey of TB control officers in 124 U.S. counties was designed to represent high-, medium- and low-burden counties based on the number of TB cases reported from 2005-2007. The 85 counties represented in the survey reflected a 69% response rate. The purpose of the survey was to characterize and understand practices and barriers encountered at the local level to public health management of TB.

Preliminary findings from the survey are summarized as follows. Enforcement of orders by health officers was problematic. Of all county law enforcement officials responding to the survey, 26% would not enforce an order by a health officer for involuntary isolation and would require a court order. Challenges were identified with facilities for involuntary and long-term

isolation. Of all survey respondents, 20% were unsure of the actual facilities that could be used for either voluntary or involuntary long-term isolation.

Inter-jurisdictional issues are important, but gaps were identified. Of all survey respondents, 90% reported having TB cases that involved multiple jurisdictions, but only 67% reported having written policies for inter-jurisdictional notification. System gaps were noted in four areas: communication between health departments, funding, patient location tracking, and different or conflicting policies between jurisdictions. Costs were found to tax the system and payment sources were not well defined. Of all survey respondents, 37% had no existing agreements to identify specific entities that covered costs of isolation, particularly in cases requiring more resources.

At this time, CDC is respectfully requesting ACET's formal endorsement of the Menu. CDC will make any final revisions recommended by ACET prior to submitting the Menu for internal clearance. CDC is considering a number of options to assure broad implementation and evaluation of the Menu over time.

CDC will distribute the final Menu to its key partner organizations and provide technical consultations and training sessions on utilization of the Menu through webinars and the Regional Training and Medical Consultation Centers (RTMCCs). At the completion of the clearance process, the Menu will be available on the websites of CDC, NTCA and other groups. CDC plans to provide ACET with periodic updates on the implementation and evaluation of the Menu.

ACET commended CDC for its outstanding efforts over a long period of time in drafting the Menu of Suggested Provisions for State TB Prevention and Control Laws. ACET also thanked CDC for implementing an inclusive process to obtain feedback from a wide range of organizations in diverse fields, including the TB control, legal and public health communities.

The ACET members made a number of suggestions for CDC to consider in finalizing and publishing the Menu.

- Dr. Edward Nardell, the ACET liaison to the International Union Against Tuberculosis and Lung Disease (IUATLD), would provide DTBE with historic and recent data on TB transmission and the impact of treatment on communicability of disease. These data focus on protecting persons from TB transmission and most likely would affect state and local TB prevention and control laws.
- CDC should distribute the final Menu to WHO as a model for international countries. The global TB community has been requesting guidance on TB prevention and control laws for quite some time. Other organizations that should receive the final Menu for broader dissemination to their constituents include ASTHO and the National Association of County and City Health Officials (NACCHO). ASTHO also would welcome the opportunity to promote the Menu to state legislative liaisons who are housed in state health departments. Ms. Anna Buchanan, the alternate ACET liaison to ASTHO, offered to serve as the point of contact or technical resource between CDC and state legislative liaisons.

- CDC should refine the supporting data for the Menu to focus on the size of jurisdictions. This data analysis would be particularly helpful to smaller localities.
- CDC should use the Menu as a baseline in a point prevalence study to regularly monitor its implementation in the context of TB law practices over time and inform changes and innovation to future TB prevention and control laws.
- The Menu should be prominently featured in CDC's annual Public Health Law Course to attorneys and distributed to the National Association of Local Boards of Health to provide education on the importance of TB in public health law.

Update by the Division of Global Migration and Quarantine (DGMQ)

Dr. Drew Posey, of the DGMQ Immigrant, Refugee and Migrant Health Branch, was pleased to announce that Dr. Christine Olson recently joined the staff of DGMQ. Dr. Olson has extensive expertise in global health and TB issues due to her previous work on the Afghanistan Health Initiative in the CDC Division of Reproductive Health and her preventive medicine residency in Seattle-King County on a policy assessment of isolation of TB patients.

Dr. Posey reported on DGMQ's ongoing activities in the areas of implementation of the TB Technical Instructions (TBTIs) for immigrants and refugees entering the United States, clinical consultations for panel physicians, the U.S.-Mexico Breakout and Summit, Five Countries Conference, and Electronic Disease Notification System.

DGMQ's implementation of directly observed therapy (DOT) and culture for U.S.-bound immigrants and refugees in 27 countries represents 53% of immigrants and >50% of refugees. DGMQ will implement the 2007 TBTIs in India in 2010. India is the fourth largest source country of immigrants to the United States and accounts for a large burden of domestic TB. ACET and NTCA will conduct an evaluation of the Vietnamese TB screening program in August 2010.

To date in 2010, DGMQ has conducted regional panel physician training sessions in India, Ghana and the Dominican Republic with attendance by 109 panel physicians from 33 countries and 26 consular officers from 14 countries. DGMQ is currently analyzing data and input from the regional panel physician training sessions to make future plans and improvements as needed.

DGMQ is collaborating with DTBE, RTMCCs and SNTC to provide expert clinical consultations to panel physicians to improve the treatment and management of complex TB cases overseas. The RTMCC Clinical Consultation Network is available to overseas panel physicians and treatment programs for this effort.

SNTC developed a web-based form for panel physicians to submit requests for consultations electronically and also created a database for DGMQ to analyze trends and patterns of the requests over time, monitor the effectiveness of its programs and track the quality of panel physicians. After the web-based system was launched on May 24, 2010, the first request was for a consultation to address a refugee with extensively drug-resistant TB (XDR-TB).

The U.S.-Mexico Breakout and Summit were convened during the National TB Conference in June 2010 with presentations by DGMQ and a panel physician from Mexico. These events resulted in the participants proposing two major action items to DGMQ. First, DGMQ should coordinate a meeting with CDC, U.S. Immigration and Customs Enforcement, and the Mexico National Tuberculosis Program to discuss a seamless transition and continuity of care of TB patients who are deported from the United States to Mexico.

Second, DGMQ should participate in evaluations of programs along the U.S.-Mexico border. Data from the Panel Physicians Program in Ciudad Juarez, Mexico show that 101 persons were diagnosed with culture-positive TB from October 1, 2007-May 24, 2010. The vast majority of persons diagnosed with TB in Mexico reported their intention to travel to cities in the United Sates.

The Five Countries Conference (Australia, Canada, New Zealand, United Kingdom and United States) is currently being held in London, England to discuss migration and border health security issues. Australia will present its collaborative efforts with other countries in oversight of immigration screening. These activities will highlight joint activities among Australia, Canada and the United States in Haiti, China and India.

DGMQ is continuing to advance and improve its Electronic Disease Notification System (EDN) to send receiving health departments information on all refugees arriving to the United States and all immigrants arriving to the United States with a Class A or B TB condition. The EDN System provides health departments with a mechanism for entering post-arrival TB evaluation results.

DGMQ and DTBE are exploring the possibility of developing a memorandum of understanding to collaborate on the EDN System. DTBE will use a Public Health Prevention Service Fellow to address EDN data reporting issues. Efforts are underway to coordinate and increase reporting of TB follow-up examinations to the EDN System and provide the National Tuberculosis Indicators Project with access to EDN data.

Preliminary data as of May 25, 2010 show that California, Texas, New York, Hawaii and Washington were the top five states that received B1 notifications of persons suspected of having TB overseas. The percentage of B1 notification worksheets returned by states that indicated follow-up evaluations entered into the EDN System ranged from 87% in Washington to 0% in Hawaii.

Update on Program Collaboration and Service Integration (PCSI) Activities

Mr. Gustavo Aquino is the Associate Director for Program Integration in NCHHSTP. He pointed out that the 2010 NCHHSTP Draft PCSI Plan was distributed to ACET for review. The plan provides a detailed description of the five PCSI objectives, including specific activities, the lead NCHHSTP organizational units, primary contacts and milestones.

NCHHSTP defines “PCSI” as building the capacity of two or more programs to collaborate in a common goal of delivering integrated services. Multiple programs can make small changes to maximize prevention opportunities by seamlessly packaging and delivering comprehensive services to individuals. PCSI is not designed to integrate programs.

NCHHSTP’s key accomplishments in PCSI are highlighted as follows. The 2009 PCSI White Paper was published. An FOA was released for grantees to analyze local epidemiologic data across the four disease areas and collect evidence to demonstrate the effectiveness of PCSI. Of $3.6 million, $2.4 million will be awarded to six jurisdictions to conduct demonstration projects in year 1 in areas that account for ≥80% of HIV, viral hepatitis, STD and TB morbidity. NCHHSTP will make efforts to leverage additional funding to fund 16 jurisdictions in year 2.

The remainder of the funds will be targeted to the development of a state-of-the-art web-based surveillance application across NCHHSTP’s four disease disciplines, training, programming, and capacity building of the PCSI Team in the NCHHSTP Office of the Director. An evaluation plan was developed to assess the effectiveness of PCSI.

The presence of PCSI was enhanced on the CDC website to foster internal collaborations across NCHHSTP, strengthen external collaborations with partners, and provide online resources for NCHHSTP grantees. The PCSI website clearly identifies Project Officers and Program Consultants throughout NCHHSTP and allows users to easily access local sites across disease areas. A PCSI webcast was held on May 20, 2010 with internal and external partners.

NCHHSTP’s core FOAs for TB, viral hepatitis and STD training and surveillance were revised to include language on PCSI and provide grantees with more flexibility to deliver integrated services. The HIV prevention FOA will be recompeted in FY2011 with similar language on PCSI. NCHHSTP plans to use the new HIV prevention FOA to conduct more comprehensive activities on HIV co-infection with TB, STDs and viral hepatitis.

NCHHSTP’s future PCSI activities include a large HIV/HCV research project among MSM and a literature review to identify best practices and determine the effectiveness of PCSI. The PCSI staff and infrastructure will be expanded to increase the focus on surveillance, data collection and evaluation. Funds will be allocated to CDC’s new “Strategic Framework on MSM” and also to NACCHO to present “PCSI success stories” during national conferences.

NCHHSTP’s priorities for PCSI over the next year are integrated programming, training and surveillance. NCHHSTP will take a more methodical approach to assessing its PCSI activities and leveraging opportunities for collaboration and integration. NCHHSTP will develop data security and confidentiality standards across its four disease disciplines based on extensive feedback external consultants provided to CDC during an expert consultation on the previous day. The new standards will be designed to promote data sharing, collaboration and integration of surveillance data across NCHHSTP programs.

NCHHSTP recently revised its capacity building FOA to provide training on PCSI and other collaborative activities, such as joint assessments and joint planning. This effort is designed for

trained staff in funded programs to expand and seamlessly deliver integrated services at the local level.

Overall, PCSI will be particularly relevant for TB in three major areas. First, expanded HIV testing has reduced the number of HIV/TB co-infected cases, but ~10% of persons with active TB are still co-infected with HIV. NCHHSTP recognizes the need for its divisions and funded programs at the local level to improve the current HIV testing rate of 67% and identify more HIV/TB co-infected cases.

Second, solid data need to be collected to determine the impact on the epidemic of screening HIV-positive persons for TB at the local level. Third, NCHHSTP needs ACET's expertise and advice on the correlation between TB and diabetes. At this point, NCHHSTP is questioning whether ACET endorses PCSI and if NCHHSTP should focus on additional areas in PCSI over the next year.

ACET commended NCHHSTP on making tremendous progress in PCSI since introducing this initiative in 2007. The members were particularly pleased that NCHHSTP is promoting PCSI to integrate "services" rather than "programs," particularly since an HIV program has the potential to greatly dilute efforts by a TB, STD or viral hepatitis program. ACET made comments and suggestions in three areas for NCCHSTP to consider in finalizing its 2010 Draft PCSI Plan.

First, ACET was concerned that California has not reported its HIV cases since 2004, particularly since this state accounts for the largest number of TB cases in the United States and the incidence of HIV/TB co-infection is ~10% at this time. CDC should use its role as an HIV prevention funding agency to California to address this issue. Second, NCHHSTP should incorporate the PSCI objectives into CDC's national objectives and evaluation metrics that are embedded in agency-wide cooperative agreements.

Third, PCSI promotes service integration, but the initiative appears to have only expanded silos from the division level to the National Center level. For example, PCSI's limited focus across NCHHSTP does not integrate services with other CDC operating units that conduct activities of relevance to TB, particularly tobacco, diabetes and other chronic disease programs.

Update on the Decline in Reported TB Cases

Dr. Thomas Navin is Chief of the DTBE Surveillance, Epidemiology and Outbreak Investigations Branch. He presented provisional data as of February 26, 2010 to respond to the five leading hypotheses regarding the unexpected decline in TB cases. However, he noted that analyses of these data have not been fully vetted and show tremendous differences among states.

Hypothesis 1 proposes an artifact of surveillance as the potential cause for the decline in TB cases. By state, Pennsylvania reported the largest decline in TB cases of 39% in 2009. However, the decrease was due to an unusually large number of TB cases Pennsylvania reported in 2008.

By TB treatment start date, the most significant discrepancies between the number of TB cases in 2008 and 2009 were observed in the early part of the year, while the number of TB cases was virtually the same between 2008 and 2009 at the end of the year. Data analyses were performed to explain statistically significant changes between actual and forecasted U.S. monthly TB cases by therapy start date from 2000-2009.

CDC utilized its BioSense surveillance system to analyze TB trends based on data from RelayHealth, an electronic prescription insurance claims service provider. This data set covers ~50% of the U.S. outpatient anti-infective market (or ~27,000 outpatient community pharmacies). The data set excludes prescriptions that were paid for out-of-pocket, denied coverage, dispensed by public health clinics or ordered from an online pharmacy. Analyses with the RelayHealth data set showed similar declines in TB cases as other data sets. These data analyses rule out surveillance as a potential cause for the decline in TB cases.

Hypothesis 2 proposes underreporting within public health as a potential cause for the decline in TB cases. CDC conducted extensive investigations in California, Georgia, New York City and Pennsylvania and found no evidence of systematic underreporting. CDC administered a survey to its public health laboratory grantees that showed a 5.9% decrease in the number of individual patient clinical specimens received between 2008 and 2009 and a 13.3% decrease in the number of individual patient clinical specimens positive for *M.tb* complex between 2008 and 2009.

CDC conducted an investigation to compare county, state and CDC TB case counts in 11 high-burden counties between 2008 and 2009. All of the identified discrepancies were an artifact of discordance. The number of actual unreported TB cases identified was 1 in 2008 and 0 in 2009. The 11 high-burden county survey assumed a decline of 3.8% per year in the number of culture-positive TB cases based on 2008 reported data. However, the decline in the actual number of cases reported from the field was much greater than the expected decline. These investigations rule out underreporting within public health as a potential cause for the decline in TB cases.

Hypothesis 3 proposes underreporting into public health as a potential cause for the decline in TB cases. CDC's efforts to collect data from Georgia and Pennsylvania to determine whether hospitals, private clinics and commercial laboratories reported each TB case were labor-intensive and difficult. CDC is uncertain whether underreporting into public health is a potential cause for the decline in TB cases.

Hypothesis 4 proposes the failure to diagnose TB as a result of changes in laboratory diagnostic procedures, physicians who are less likely to "consider TB," and patients who are less likely to seek care as a potential cause for the decline in TB cases. CDC does not have data or methodologies at this time to systematically confirm or disprove this hypothesis in an objective manner.

Hypothesis 5 proposes a true decrease in disease based on three scenarios as a potential cause for the decline in TB cases. In terms of demographic changes, the decline in TB cases

was much less dramatic in U.S.-born persons than in FBP in 2008. Based on years of residence in the United States, the percent decline in TB cases was greatest in FBP with <2 years U.S. residency (-25.3%) and lowest in FBP with ≥10 years U.S. residency (-6.9%). These data indicate that a true decrease in TB cases occurred that was largely driven by demographic changes in FBP.

In terms of the impact of the 2007 TBTIs, California data showed a dramatic decline from 2007-2009 in the number of TB cases with B-notifications diagnosed within one year of arrival to the United States. The largest declines in B-notifications were from the Philippines, Vietnam, China, India and Mexico following implementation of the 2007 TBTIs in these countries. However, the total decline of B-notifications in California was <50 TB cases and did not reflect the bulk of the decline.

At the national level, Mexico accounted for the largest decline in foreign-born TB cases following implementation of the 2007 TBTIs, but screening does not identify the majority of TB cases from this country. Moreover, foreign-born TB cases from India significantly decreased by 12.8%, but the 2007 TBTIs have not yet been implemented in this country. These data clearly show that the 2007 TBTIs had an impact on the decline in foreign-born TB cases, but were not completely responsible for the unexpected decline in this population.

In terms of decreased transmission of TB, CDC used genotyping data to identify clusters by genotype matches in the same county and in the same year. CDC determined that its genotyping data could not provide sufficient evidence to confirm decreased transmission of TB as a potential cause for the decline in TB cases, particularly among U.S.-born persons. By age, however, a dramatic decline of 13% in TB transmission among U.S.-born persons was seen in children <4 years of age. The significant numeric decline in TB transmission of 304 cases among U.S.-born persons ≥45 years of age could not be explained.

Overall, data showed a statistically significant decline in the number of TB cases beginning in late 2008 to early 2009. The decline might have been reversed in the fall of 2009. The decline in TB cases as an artifact of surveillance or underreporting is unlikely based on independent analyses with CDC BioSense and public health laboratory data sets.

The largest decline in TB cases was seen in FBP, particularly among persons with <2 years U.S. residency. This finding might be attributable to the economic recession that most likely caused a decrease in the number of persons entering the United States or an increase in the number of persons leaving the United States. The impact of the 2007 TBTIs on the decrease in TB cases needs further clarification.

A modest, but significant decline was seen in U.S.-born TB cases, particularly among persons ≥45 years of age. The factors for this decrease are unclear at this time, but are probably attributable to multiple reasons, such as decreased access to care. CDC plans to collect new data from additional sources to address the unanswered hypotheses.

ACET was impressed by CDC's remarkable and systematic data collection efforts to explore, explain and respond to all of the potential causes for the unexpected decline in TB cases between 2008 and 2009.

The members raised the possibility of ACET crafting and delivering evidence-based messages to publicize the reversal of the unexpected decline in TB cases in late 2009. ACET emphasized the need to present the updated data during World TB Day in 2011 and use the information to increase attention and awareness of this issue among the media and general public.

Dr. Fleenor confirmed that additional updates on the unexpected decline in TB cases would be placed on future ACET agendas after CDC fully analyzed and completed vetted the 2009 provisional data.

Overview of the Affordable Care Act and Public Health

Mr. Andrew Rein is the Associate Director for Policy at CDC. He presented on the Affordable Care Act (ACA) as it relates to public health. The ACA expands insurance coverage to 32 million additional persons. Other mandates in the ACA are highlighted as follows. Persons will be able to buy into state-based competitive insurance marketplaces ("Exchanges") with premium and cost-sharing tax credits. Small businesses that provide insurance coverage to their employees will be offered tax credits. Adult children will be covered under their parents' insurance plans until 26 years of age.

The ACA will make insurance coverage more affordable through Exchanges, incentives and elimination of cost-sharing for certain covered services. The ACA will protect consumers through new insurance market regulations, such as no exclusions for preexisting conditions, no rescissions of coverage, and no lifetime or annual limits on coverage.

The ACA will result in cost-savings by minimizing waste, fraud and abuse based on stiffer penalties and oversight by HHS and Department of Justice Task Forces. Demonstration projects will be piloted that focus on payment reform, including accountable care organizations, payment bundling groups and patient-centered medical homes. The new Centers for Medicare and Medicaid Services (CMS) Innovation Center will develop, implement and streamline new ideas.

The ACA will increase quality of care through a number of mechanisms. The National Quality Strategy will identify high-priority and evidence-based interventions to improve healthcare quality. Public reporting of healthcare-associated infections will also help improve quality of care. Chronic disease management and coordination will be emphasized in many programs.

The ACA will provide a true opportunity for public health because more persons will have access to preventive services. Preventive services will be covered under Medicare and private insurance and covered services will be based on the U.S. Preventive Services Task Force (USPSTF) and the CDC Advisory Committee on Immunization Practices (ACIP)

recommendations. States will also be offered financial incentives to include preventive services under Medicaid. The focus on utilization of services will result in new partnerships and opportunities.

The Prevention and Public Health Fund will provide sustainable funding that is expected to grow from $500 million annually in 2010 to $2 billion annually from 2015-2019. Prevention, wellness and public health activities will be supported in the Prevention and Public Health Fund.

The National Prevention and Health Promotion Strategy will be developed as a blueprint for prevention activities at the federal level. A National Prevention, Health Promotion and Public Health Council will lead development of the National Prevention Strategy. This Council will be chaired by the Surgeon General and represented by Cabinet secretaries and other key federal leaders. An advisory group will be established with experts from various public health disciplines. The National Prevention Strategy is scheduled to be published by March 23, 2011.

The ACA data and programs will provide a number of public health benefits. Data collection and monitoring will be improved through the new Key National Indicators Project and collection of standardized health disparities data. New funds will support a variety of programs, such as the Childhood Obesity Demonstration Project, Teen Pregnancy Prevention Program, Home Visitation Programs and School-Based Health Centers. Grants, technical assistance and data collection support will be offered to small businesses to support employer-based wellness programs.

The ACA's national menu labeling requirement will place information in the hands of consumers. The focus is on posting calories on menus of restaurants with >20 locations nationwide and also on vending machines for companies with $\geq$20 vending machines in operation nationwide. Complete nutrition information and a statement of the recommended calorie intake will also be available.

The ACA gives authority to new programs, though funds are not yet appropriated for these programs. New authorities include Transformation Grants, Epidemiology and Laboratory Capacity Grants, an education and outreach campaign to raise awareness about preventive benefits as well as, diabetes prevention oral health, immunization, and healthy aging programs.

Ms. Ann Cronin is the Associate Director for Policy and Issues Management in DTBE. She agreed with Mr. Rein that the ACA would provide a number of public health benefits overall, but she did not see the specific role of the ACA in addressing TB.

On the one hand, the rigorous evidence base of TB and the strong relevance of TB activities to communities are consistent with the ACA mandate to identify evidence-based interventions to improve healthcare quality in communities. On the other hand, TB would be unable to compete with healthy environments, calorie counting and other interventions that are more "popular" or "well known" to the general public.

Ms. Cronin also noted that the ACA does not appear to address international health issues. Most notably, undocumented persons from other countries account for the majority of TB cases in the United States.

ACET made three suggestions regarding the ACA for CDC to consider.

- CDC should be engaged and provide input during the initial stage of CMS's regulatory process before Notices of Proposed Rulemaking for health reform are released for public comment.
- CDC should explore the opportunity of CMS supporting a small-scale demonstration project in a community and a large-scale project in a state on public health financing of a TB waiver authority.
- CDC should extract, compile and distribute language from the ACA to TB control programs that would be most relevant to TB. For example, the guidance document could describe reimbursable TB services under the ACA that were not covered in the past.

Dr. Castro made remarks in response to Ms. Cronin's comments. First, CDC should clearly and deliberately articulate the critical need to use the ACA to support elimination programs for TB and other diseases in addition to using this law to focus on the leading causes of death and morbidity as a public heath mission. Dr. Castro offered to closely collaborate with his CDC colleagues who oversee other elimination programs in this effort.

Second, CDC should provide leadership in using cost-effectiveness research data to demonstrate the societal benefits of providing care to uninsured and undocumented immigrants for TB, influenza and other diseases at the community level.

Overview of the U.S. Preventive Services Task Force (USPSTF)

Dr. Stuart Berman is the Senior Advisor to the Director of NCHHSTP. He explained that USPSTF was first convened in 1984 as a Congressionally-mandated advisory body sponsored by AHRQ. USPSTF is an independent panel of 16 members from the private sector with expertise in prevention and primary care. The mission of USPSTF is to evaluate the benefits of individual services based on age, gender and risk factors for disease and also to make recommendations on preventive services and specific populations that should be routinely incorporated into primary medical care.

An Evidence-based Practice Center (EPC), typically the Oregon EPC, conducts systematic literature reviews. However, USPSTF has ultimate decision-making authority over the inclusion or exclusion of data in its guidelines. USPSTF guidelines cover preventive measures (e.g., screening tests, counseling and preventive medications), but decisions on immunizations are deferred to ACIP. USPSTF recommendations are graded as A, B, C, D or insufficient evidence.

USPSTF recommendations are important to health care in both public and private settings. For example, PCACA defines "coverage of preventive health services" as group health plans and health insurance issuers that offer group or individual health insurance and, at a minimum, provide coverage for and do not impose any cost-sharing requirements in two areas: (1) evidence-based items or services with an A/B USPSTF recommendation and (2) immunizations with an ACIP recommendation.

PCACA essentially provides USPSTF with an opportunity to mandate government spending on certain services. With the exception of the Vaccine for Children's Program, no policy other than PCACA gives private individuals or entities an opportunity to spend government dollars without Congressional decision-making. USPSTF makes great efforts to be transparent and accountable to the public on its decision-making process. The *USPSTF Procedure Manual* is posted online for access by the public.

The 2007 Sawaya, *et al.* study presented a table to illustrate the process USPSTF uses to assign recommendations a letter grade or statement of insufficient evidence after assessing the certainty and magnitude of net benefit of preventive services. Grades A and B are assigned to preventive services with substantial or moderate net benefit. USPSTF recommends offering or providing Grade A/B services in clinical practice.

Grade C is assigned to preventive services with a small net benefit. USPSTF recommends against routinely offering or providing Grade C services in clinical practice, but acknowledges that considerations may support providing the service to an individual patient. Grade D is assigned to preventive services with a 0 or negative net benefit. USPSTF recommends against offering or providing Grade D services in any circumstance. "Insufficient" is assigned to preventive services with inadequate evidence to assess the balance between benefits and harms of the service.

The 2007 Barton, *et al.* study outlined the contents of USPSTF recommendations: preamble, summary statement, structured rationale, clinical and other considerations, discussion, recommendations of others, references and tables. The 2007 Guirguis-Blake, *et al.* study described USPSTF's procedures for developing a recommendation statement, including the 12 major activities as well as the responsible party and timeline for each activity.

The sequential analytic framework USPSTF uses in its process of developing recommendations considers persons at risk, screening and its potential adverse effects, early detection of the target condition, treatment and its potential adverse effects, intermediate outcomes, a possible association between intermediate and patient outcomes, and the impact of early treatment in reducing morbidity or mortality.

The 2007 Sawaya, *et al.* study presented a table listing the questions USPSTF considers in evaluating evidence related to key questions and assessing the overall certainty of evidence of the net benefit for preventive services. USPSTF considers the research design and quality of studies, capacity to generalize study results to the general U.S. primary care population, the number and size of studies to address key questions, consistency of the study results, and additional factors.

Based on findings from evaluating the evidence, USPSTF ranks its level of certainty regarding the net benefit for preventive services as "high," "moderate" or "medium." A study published in the *Annals of Internal Medicine* in 2005 illustrated USPSTF's assessment of the net benefit of HIV screening and counseling with a three-year hypothetical cohort.

The USPSTF library contains >60 active topics at this time. USPSTF members, organizations, EPCs and individuals can nominate new topics. *Federal Register* notices and announcements to partner organizations are disseminated every two years to solicit suggestions for new topics. The USPSTF Topic Prioritization Workgroup drafts a prioritized list based on two criteria: (1) the public health importance of the topic (*i.e.*, the burden of suffering and potential of the preventive service to reduce the burden) and (2) the potential for a USPSTF recommendation to affect clinical practice based on a gap between evidence and practice or existing controversy.

In addition to evaluating new topics, USPSTF also updates existing topics every five years and reaffirms other topics to keep these issues current. Reaffirmed topics are typically well-established evidence-based standards of practices (e.g., hypertension screening). USPSTF would only change its recommendations based on a very high level of evidence.

USPSTF refers some topics to other evidence-based groups that are in a better position to make accurate and timely recommendations. Other than referring decisions on immunizations to ACIP, USPSTF anticipates that very few topics would be referred to other evidence-based groups. USPSTF's decision to refer topics is reconsidered every five years.

USPSTF recommended against updating the 1996 TB infection screening guidelines to avoid duplicating CDC's efforts, but USPSTF noted that its methods to review evidence might differ from those utilized by CDC. Moreover, the website that USPSTF references is not a direct link to CDC's current TB screening guidelines. CDC has emphasized the need for USPSTF to revise this language with a direct web link and clarify that CDC's TB screening guidelines are much more current than 1996.

CDC is posing several questions to ACET at this time regarding USPSTF's potential role in making recommendations on the TB screening guidelines. Should DTBE take any actions in this regard? Should DTBE seek a Grade A/B recommendation from USPSTF on TB screening? Should DTBE take the first step of nominating TB screening as a USPSTF topic or consider another approach?

Dr. Andrew Vernon is Chief of the Clinical and Health Systems Research Branch in DTBE. In addition to the questions posed by Dr. Berman, he also asked ACET to consider another issue. The 2009 Guyatt, *et al.* study compared the USPSTF and "Grading of Recommendations, Assessment, Development and Evaluation" (GRADE) approaches in making recommendations.

One of the most significant differences is that the GRADE approach does, but USPSTF does not consider cost and cost-effectiveness issues in making Grades A, B or C recommendations. Dr. Vernon asked ACET to consider the potential implications for TB if USPSTF decides to use the GRADE approach to evaluate evidence.

In response to Dr. Vernon's comments, Dr. Hahn noted that ACIP recently announced its plans to pilot the GRADE approach. Because USPSTF defers decisions on immunizations to ACIP, the pilot project might provide a level of confidence of USPSTF accepting the GRADE approach as an evaluation measure.

Dr. Castro was in favor of DTBE making efforts for USPSTF to consider targeted TB screening as a topic. DTBE would continue its collaborative efforts with ACET and external professional organizations to develop TB screening recommendations. Dr. Castro supported this approach because PCACA would cover reimbursement of TB screening services with a Grade A/B recommendation by USPSTF.

Several ACET members supported Dr. Castro's proposal for DTBE to take actions in recommending that USPSTF consider targeted TB screening as a topic. Dr. Fleenor confirmed that ACET would revisit this issue during the business session on the following day.

Panel Presentation: National Tuberculosis Indicators Project (NTIP)

CDC and ACET made a series of presentations to describe recent developments in NTIP. The updates are summarized below.

Ms. Kai Young, of DTBE, reported that NTIP is a performance monitoring system to provide a series of indicator reports. These reports include standardized indicators that are calculated using CDC TB surveillance data. The indicator reports help programs to track their progress toward meeting national objectives, focus program evaluation efforts, and provide national and program performance targets as benchmarks for self-assessment.

NTIP reports describe the national objective, illustrate a performance graph, outline program data that were used to calculate the indicators, and articulate the methodology. The major purposes of NTIP reports are three-fold: (1) facilitate discussion, education and problem-solving by DTBE and program areas, program managers and staff, and program and community partners; (2) enhance capacity to provide guidance and technical assistance; and (3) identify strategies to collaboratively detect and understand barriers and improve program effectiveness.

At the national level, NTIP reports have been incorporated into 2010 cooperative agreement reporting requirements and are used as a tool by Program Consultants during site visits. At the state level, NTIP reports are used to report data back to local jurisdictions, facilitate technical assistance at the local level, and apply data to cohort review sessions.

NTIP improvements will be rolled-out in July 2010 with county-level reports and reports of quarterly trends in addition to yearly trends. Across the United States, ~168 counties have reported $\geq$15 TB cases over the past three years on average. In the near future, NTIP will be enhanced with biweekly data reporting and provision of a line list of cases that did not meet the national performance objectives.

Ms. Kimberly Field is the ACET liaison to NTCA. She presented the NTIP-Focused Program Evaluation Pilot Project. Cohort reviews of TB programs were initiated in New York City as a systematic review of all cases reported in a cohort period to ensure that each case was given appropriate care.

Cohort reviews demonstrate promise in enhancing outcomes for case management, prioritize contact investigations at the same level as case management, establish accountability, and provide opportunities for training and education. New York City's cohort review model has been adopted by numerous TB programs at state, city and county levels with high, medium and low TB incidence.

The Washington State cohort review was based on the New York City model and implemented in 2003. The Washington State cohort review form was extensively revised to obtain additional information on timeliness measures, laboratory turnaround times and genotype clusters. At the Washington State level, a one-day quarterly cohort review was conducted nine to 12 months after a TB case was reported. The state level quarterly cohort review traditionally was performed in a half-day with a review of 30-40 cases per quarter. At the Seattle-King County level, a weekly case review was conducted within the first three months of case management.

In preparation of the cohort review, Washington State case managers completed presentation forms for all TB cases and presented a mock cohort review two months in advance of the actual cohort review. During the cohort review, a case presentation was made and feedback was obtained from medical directors and program managers. Cohort reviews focused on diagnosis and treatment of TB, case management, timeliness measures, laboratory turnaround times and contact investigations. A summary was provided at the next cohort review meeting.

Ms. Young presented challenges identified in the Washington State cohort review. Seattle-King County staff believed case reviews and cohort reviews were duplicative processes and were not a productive use of staff time. Preparation time for the cohort review was perceived as an additional burden. Attention and focus on the program were perceived to be lacking due to overemphasis on medical issues. The staff noted that feedback on program performance was not immediately provided.

DTBE funded the project to pilot NTIP in a cohort review to achieve four key objectives: (1) bring data to staff in the field; (2) take advantage of a local cohort review session or program staff meeting to discuss implementation of NTIP; (3) help programs to advance from monitoring to evaluating activities; and (4) use NTIP to provide performance trend data as a cohort summary, select cases for review, and engage staff in the process of evaluating programs and mobilizing efforts for improvement.

In a traditional cohort review, individual cases are reviewed; efforts are made to ensure objectives are met for each case; and a performance summary is shared at the end. In the enhanced NTIP-focused program evaluation, the performance summary is shared at the beginning; emphasis is placed on programmatic and systematic challenges (*i.e.*, policies, procedures and opportunities to support staff); and cases are selected for discussion.

In the NTIP-focused program evaluation, field staff input data into the surveillance system and the state sends data to CDC. CDC runs the NTIP analysis and provides the program with the line list of cases that did not meet the national objectives. The program cleans and returns the corrected data to CDC. The final line list of cases that did not meet the national performance objectives are shared with staff and a few cases are selected for discussion. The timeline between cohort reviews is ~3 months.

In the NTIP-focused program evaluation, NTIP reports are used to introduce 10-15 cases selected for discussion. Case managers and disease investigators share success stories and challenges. The majority of the time during the program evaluation is spent on the program using anecdotes to identify challenges, discover opportunities and describe issues. The discussion is used to focus on broad themes rather than small details, such as different approaches that might have been taken, strategies for the program to improve support to staff, and strategies for CDC to enhance support to the program.

CDC learned multiple lessons in piloting NTIP in the Washington State cohort review. From a programmatic perspective, the NTIP-focused program evaluation provided a valuable opportunity to communicate national objectives and priorities; helped staff to understand its contributions to a larger mission by connecting case discussion with performance; focused on programmatic opportunities and concerns; engaged staff in contributing to problem-solving; encouraged program evaluation beyond quality assurance; and included a wider audience, such as disease investigators.

From a data perspective, the NTIP-focused program evaluation provided a mechanism for improving data quality. The approach of providing a listing of cases enabled field staff to identify errors in Report Verified Case of TB (RVCT) forms. This process is time consuming, but was found to be worthwhile to programs.

CDC acknowledges that facilitating a productive discussion is a challenge in the NTIP-focused program evaluation. To address this issue, CDC is exploring the possibility of adding focus group facilitation skills to the process and plans to refine other methods to facilitate discussions. CDC also intends to identify approaches to systematically capture and document meetings to provide evidence and feedback to CDC via cooperative agreement progress reports.

CDC will expand topics and include other programmatically relevant activities in the NTIP-focused program evaluation, such as the TB Genotyping Information Management System, Class B immigrants and refugees, and laboratory activities. CDC will continue to improve the NTIP national objectives by obtaining feedback from state partners and local field staff.

CDC recognizes that the NTIP-focused program evaluation has several implications for practice. Effective cohort reviews address both process and outcome assessments, but most programs focus on the process and spend minimal time on understanding barriers and challenges. NTIP is an effective tool to help programs focus on these issues and improve evaluation of their performance.

If case reviews are not currently an ongoing process, however, CDC acknowledges that a review of all cases during the cohort review process will continue to be an essential component. CDC will continue to use NTIP to help programs make a greater impact by prioritizing and focusing efforts.

Dr. Masahiro Narita is an ACET member and Director of the TB Control Program in Seattle-King County Public Health. He proposed the following recommendations on NTIP. Specific indicators should be developed to evaluate program performance and assess quality control and improvement.

A cohort review is an important program evaluation activity, but the NTIP-focused program evaluation is a more efficient and effective tool than the traditional cohort review. ACET should formally endorse and emphasize the importance of NTIP. DTBE should include the NTIP-focused program evaluation as an additional option in the cohort review process.

ACET made several comments and suggestions for CDC to consider in its ongoing efforts to refine NTIP.

- CDC should acknowledge the challenges of TB programs in striking a balance between devoting additional staff time and effort to collecting and reporting NTIP data versus delivering care to patients and conducting contact investigations in the field.
- CDC should institutionalize the engagement of independent RTMCC medical experts in discussions during NTIP-focused program evaluations. However, CDC should leverage funds to reimburse RTMCC experts for their participation in these discussions.
- CDC should explore the option of utilizing separate forums, such as conference calls, to engage local treating physicians in program evaluation discussions. The Idaho TB Program found that this approach facilitated more questions, comments and honest critiques among program staff.
- CDC should take caution in eliminating the review of all TB cases in the NTIP-focused program evaluation. The original New York City model of focusing on every single TB case in traditional cohort reviews has been beneficial in many areas.

Ms. Field appreciated ACET's concerns regarding the NTIP-focused program evaluation, but she provided a field perspective on this initiative. Data from cohort reviews and performance summaries have played a critical role in advocacy for TB control at the local level. For example, cohort review data have allowed the Washington State TB Program to demonstrate the impact of furloughs and other staffing issues on the ability of staff to meet national TB objectives and outcomes.

Panel Presentation: Efforts to Modernize TB Control

Dr. Thomas Navin is Chief of the DTBE Surveillance, Epidemiology and Outbreak Investigations Branch. He reported that CDC funds two laboratories in California and Michigan under the National TB Genotyping Services (NTGS). TB laboratories may submit isolates for

genotyping at no charge. Genotype results are posted on CDC's TB Genotyping Information Management System (TB GIMS) website.

CDC's universal genotyping goal is to genotype isolates from every culture-positive TB case in the United States and link genotyping data to TB surveillance data. CDC attempts to achieve 100% coverage, but actual coverage has increased from 50% in 2004 to ~80% in 2007-2009. CDC launched TB GIMS in March 2010 to allow TB officials to access current reports, maps and patient information. TB GIMS has the capacity to support >3,000 users, but only 300 users are active at this time.

Ms. Smita Chatterjee, of DTBE, presented case studies on the detection of TB aberrations. Aberration detection involves rare and common genotypes that are geographically clustered and dispersed. The log-likelihood ratio (LLR) measures differences between observed and expected geospatial concentrations. The higher the LLR, the greater the chance of unexpected geographic clustering that might indicate recent transmission. The alert level in TB GIMS allows TB controllers to prioritize and assess genotype clusters at state or local levels.

In early 2009, CDC identified an unusual group of TB cases in the PCR02118 cluster in Jefferson County, Kentucky. An LLR >10 is characterized as high, but CDC found that the Jefferson County cases were extremely high with an LLR of 20.3 from 2006-2008. In the fall of 2009, state and local TB programs in Kentucky requested CDC's assistance to evaluate the cluster. Raw data from TB GIMS from December 2004-December 2008 indicated 16 TB cases with matching genotypes.

All of the cases in the PCR02118 cluster were U.S.-born, 81% were non-Hispanic whites, 63% were 45-64 years of age, 44% were homeless in the past year, and 38% consumed excess alcohol. CDC deployed a two-person team to Kentucky to provide onsite assistance from November 30-December 4, 2009. Because TB GIMS was not launched until March 2010, the investigators were limited to manual data analysis.

If TB GIMS had been available at the time of the Kentucky investigation, local TB controllers and CDC would have benefited from more tools and information to respond to the PCR02118 cluster much earlier. TB GIMS would have provided TB controllers with the following resources and data from 2000-2009: a national map, national distribution report and epidemiologic curve of the PCR02118 TB cluster; a county list with the alert level for all polymerase chain reaction types; a surveillance summary report; and a county map of the PCR02118 cluster in Kentucky.

Ms. Chatterjee concluded her presentation with a live demonstration of TB GIMS to illustrate the key features of the system to ACET. However, CDC acknowledges that TB GIMS is not a substitute for TB investigations in the field.

Dr. Adam Langer, of DTBE, presented outcomes of CDC's technical assistance site visit to address the PCR02118 TB cluster in Jefferson County, Kentucky. The objectives of the site visit were to review known information on the PCR02118 cluster; assess whether transmission of TB disease was occurring; prioritize ongoing contact investigations; and provide the local community with recommendations to prevent transmission of *M.tb* in the future.

During the technical assistance site visit, CDC received an update on TB clusters from state and local officials as well as recorded and reviewed data from multiple sources: RVCT data from all known cases, NTGS data, data from the metropolitan Louisville, Kentucky electronic TB system, medical charts of patients who were being treated at the time of the investigation, and contact investigation records for all patients.

CDC established the following definitions for purposes of the investigation. A "case" was defined as persons diagnosed with TB from 1998-2009 in the metropolitan Louisville, Kentucky area. A "confirmed case" was defined as a culture-confirmed TB case with isolates that were genotyped and matched with the PCR02118 cluster. A "probable case" was defined as a TB case that had no genotype information available, but was epidemiologically linked to a confirmed case.

Results of CDC's investigation of the PCR02118 cluster in Jefferson County, Kentucky are summarized as follows. More probable cases were identified in the early stages of the outbreak because universal genotyping became available in the middle of 2000, but the investigation covered TB cases beginning in 1998.

Based on data CDC obtained from contact investigations and conversations with public health investigators and nurse managers, CDC characterized Patient 1 as a "super spreader" in the social network diagram. This patient was originally diagnosed with TB in 1998 and re-diagnosed TB in 2005. Other characteristics of Patient 1 included numerous TB risk factors, considerable delays in seeking care, extensive sociable relationships within the community, and non-adherence to TB treatment initially.

Demographic data showed that U.S.-born white males 46-49 years of age accounted for the vast majority of patients with TB in the PCR02118 cluster in both the 2000-2004 and 2005-2009 time periods. In 2000-2004, 11% of patients in the cluster were homeless versus 35% in 2005-2009. Excess alcohol use, injection and non-injection drug use, HIV infection and tobacco use ranged from 11%-67% among patients in the PCR02118 cluster in 2000-2004 and from 15%-80% in 2005-2009.

Overall, CDC documented recent transmission within the PCR0218 cluster. The potential for new patients in the cluster was high, but the limited spread of cases geographically provided an opportunity to halt community transmission. Geographic clustering of a rare genotype resulted in an aberration detection alert.

Dr. Langer presented outcomes of the multi-state MDR-TB outbreak within the PCR10515 cluster in Alaska, California and Washington State. From March-October 2008, the California Department of Public Health identified two MDR-TB cases in two unrelated adults who resided in two California counties. Both patients were born in foreign countries on different continents and had resided in the United States for more than five years. Both patients had the matching rare PCR10515 genotype and matching drug-susceptibility results. In a routine contact investigation, the local health department identified two additional pediatric clinical cases associated with one of the adult cases.

The rare PCR10515 genotype is <0.01% of all genotyped isolates in the United States. Because the adult cases reported no shared epidemiologic links during repeated interviews, TB control investigators in California searched for additional PCR10515 cases outside the state and asked CDC to use TB GIMS to rapidly query the NTGS database.

California investigators contacted TB controllers in Alaska and Washington State. The Alaska case was diagnosed in 2006 at a seafood processing facility in Aleutians. The Washington State case reported travel to Alaska before diagnosis in 2008. During re-interviews, the California patients reported working at the same facility as the Alaska case who was diagnosed in 2006. During a re-interview, the Washington case was unable to confirm working at the facility, but company records listed the patient as an employee in 2006. All four patients were linked back to the source case in Alaska.

The investigation showed that TB in foreign-born persons is not always a reactivation of remotely acquired TB infection. TB is not always local. Migration of infected contacts can result in a geographically dispersed outbreak. Genotyping can help establish links between cases, particularly those with rare genotypes.

Dr. Navin described CDC's current approach to incorporate risk factor data into TB aberration detection. Aberration detection involves the use of statistical analyses to identify deviations from expected patterns. TB GIMS is applied to ensure unusual clusters are flagged for attention. CDC's current approach to aberration detection focuses on more cases than expected for a particular time and place, but does not include risk factor data. Risk factors are predictive of poor outcomes or subsequent cluster growth.

TB experts have flagged a number of risk factors associated with poor outcomes (e.g., MDR, children <5 years of age and HIV) and risk factors associated with cluster growth (e.g., drug or alcohol abuse, homelessness and incarceration). Risk factors for cluster growth are strongly associated with large clusters that have the highest clustering scores. In the top 30 county-based clusters by LLR, 64% of participants in these clusters met SDH criteria.

CDC performed an analysis with 2005-2008 data to automate its understanding of the role of risk factors on cluster growth. Clusters included in the analysis were clusters in which the first case could be identified, clusters that grew to at least three cases, clusters in which growth of the third case occurred before January 2008 and could be identified, clusters with a significant concentration of cases based on SatScan results, and clusters with genotype coverage $\geq$50%. TB cases in 2005 were excluded from the analysis.

Of 933 clusters that SatScan identified as significant, 451 had genotype coverage $\geq$50%, 325 had no cases in 2005, 185 had at least one case in 2006, 87 had $\geq$3 cases, and 65 had a third case before 2008. Of the 65 clusters included in the analysis, 36 had growth in the subsequent 12 months after the third case and 29 had no growth in the subsequent 12 months after the third case. The chance of cluster growth was 92% if any case among the first three cases in the cluster was homeless. Other risk factors associated with cluster growth included substance abuse (78%), no high school education (76%), Asian race (31%) and female gender (28%).

CDC used a computer program to develop a decision tree that ranked the risk factors from most to least importance in impacting cluster growth. Of the 65 clusters, 55% grew and 44% did not grow. Homelessness was the most distinguishing single risk factor. Of 13 clusters that had at least one homeless case, 92% grew. Of clusters with no homeless cases, low education based on neighborhood zip code was the most distinguishing single risk factor and accounted for a 67% chance of cluster growth. The chance of cluster growth without these two risk factors was only 24%.

CDC is proposing to incorporate risk factor data into TB GIMS reports. The format would be revised for TB controllers to list the characteristics of a cluster in their jurisdictions and for TB GIMS to calculate the likelihood of cluster growth to at least a fourth case. Inclusion of risk factor data would be helpful in identifying specific clusters that need additional investigation.

CDC's next steps in this effort will be to repeat the decision tree analysis with its current June 2010 data set. Results will be incorporated from expanded *Mycobacterium* interspersed repetitive units (MIRU) reports into a MIRU2 analysis. CDC's existing manual alert system will be refined and automated to identify clusters that reach a critical threshold and flag cluster growth.

Overall, CDC has identified an algorithm with the capacity to estimate the chance of cluster growth with estimates that are independent of LLR. Aberration detection algorithms can be used to inform decisions on resource allocations. However, the algorithm requires further study to determine changes in estimates over time.

CDC acknowledges that TB GIMS, genotyping and aberration detection are not substitutes for epidemiology in the field by experienced TB controllers. However, these technologies provide tools that facilitate data manipulation and generation of reports and maps. These technologies also provide a common language to describe TB transmission. CDC welcomes input and expertise from ACET on sharing *M.tb* genotype data across states.

ACET understood the legal responsibility of TB controllers to protect the confidentiality of patients, but several members emphasized the critical need for CDC to at least allow neighboring jurisdictions to share *M.tb* genotype data. The exchange of these data would drive improvements in TB prevention and control.

Dr. Castro raised the possibility of CDC collaborating with ACET and NTCA to develop data sharing guidelines while continuing to safeguard the confidentiality of patients.

Update by the BCG Workgroup

Dr. Edward Nardell is the ACET liaison to IUATLD. He presented the update on behalf of Dr. Barbara Seaworth, an ACET member and chair of the workgroup, who was unable to attend day 1 of the meeting.

During the March 2010 meeting, ACET agreed to include the following language in the "TB Prevention and Control Measures for U.S. Healthcare Workers and Volunteers Serving in High Risk Setting for Exposure to *Mycobacterium tuberculosis*" Guidelines:

> BCG vaccination of workers who will be exposed in high-risk settings should be recommended as an option after an evaluation of (1) the risk of transmission of TB, (2) the prevalence of serious drug resistance, and (3) consideration of the safety and efficacy of BCG for a particular individual.

The workgroup made a number of advancements following the March 2010 ACET meeting. Dr. Ford von Reyn, of the Dartmouth Medical School, and Drs. Eddy Bresnitz and John Grabenstein of Merck were as added as new members. Industry made a commitment to continue to produce BCG and provide input on the guidelines. During its last conference call, the workgroup discussed the responsibility of sponsors of U.S. healthcare workers, students, researchers and other volunteers to identify risk characteristics of sites and partner with sites in high-burden countries to improve infection control as much as possible.

The workgroup added an executive summary to the guidelines and edited the draft multiple times to improve its flow. The current iteration of the guidelines was distributed to ACET for review and comment. The workgroup is now requesting ACET's formal endorsement to submit the draft guidelines to CDC to initiate the clearance process. However, the workgroup is interested in retaining its membership to provide ongoing advice on implementation issues, such as a training video on administering BCG.

Dr. Fleenor confirmed that the workgroup's request for ACET's formal endorsement of the draft guidelines would be discussed during the business session on the following day. ACET made two key suggestions before the document was called for a vote.

First, the new language of recommending BCG as an option should be revised with stronger and clearer guidance. Quality of evidence ratings should be assigned to this and other recommendations. Second, the following new language should be included in the guidelines: "An assessment of the capacity of a site to diagnose and effectively treat TB might be the most important action to take in protecting persons serving in high-risk settings."

Dr. Castro offered to collaborate with the workgroup to revise the title of the guidelines to clarify its intent. The document is meant to provide guidance for persons who might be exposed to serious drug-resistant TB while serving in high-risk settings overseas.

Before initiating the clearance process, Dr. Castro suggested distributing the guidelines to a group of Peace Corps medical directors and volunteers, travel medicine clinicians, and representatives of academic institutions that send students overseas for work. These reviewers could provide an end-user perspective on whether the document is clear and identify gaps in the guidelines.

Dr. Castro advised ACET to use the Infectious Disease Society of America's rating system of categories I-III to rate the strength of the evidence and categories A-E to recommend the

standard of care if a decision is made to rank the recommendations in the guidelines in the future. He noted that the DTBE Communications, Education and Behavioral Studies Branch and DGMQ's travel medicine advisory group would play a key role in rolling-out the guidelines to key target audiences.

With no further discussion or business brought before ACET, Dr. Fleenor recessed the meeting at 5:30 p.m. on June 29, 2010.

Panel Presentation: Pediatric TB Issues

Dr. Dean reconvened the ACET meeting at 8:35 a.m. on June 30, 2010 and yielded the floor to the first presenter.

A panel of speakers made two presentations on efforts that are underway to develop a pediatric TB research agenda. The presentations are summarized below.

Dr. William Burman is the Medical Director of the Infectious Diseases Clinic at Denver Public Health and Chair of the Tuberculosis Trials Consortium (TBTC) Science Planning Committee. He presented data to describe the past, current and future efforts in involving children in TB drug development trials.

Based on 2008 data, children 0-14 years of age accounted for 6.1% of all TB cases (or 786 total cases) in the United States. Children typically are not included in international data sets, but are estimated to account for 11% of all TB cases (or ~1 million cases per year) globally and ~40% of active TB cases in high-burden settings. Estimates have shown that TB is the cause of 150,000 deaths per year among children globally. In the first 60 years of TB drug development, children were involved in only five underpowered clinical trials. The inability to involve children in TB drug development trials has resulted in a number of consequences.

Age-specific dosing of first-line TB drugs is uncertain overall, but children have been under-dosed with key TB drugs for 40 years. The 2006 WHO guidelines did not differentiate between adults and children in recommending first-line anti-TB drugs: isoniazid (INH), rifampicin, pyrazinamide and streptomycin. The WHO recommendations distinguished between adults and children for ethambutol dosing, but the guidance was not supported by data. Most notably, the WHO guidelines ignored the 2003 Kearns study and a number of other published studies that demonstrated the requirement for children to have higher doses of hepatically-metabolized drugs than adults.

The 2009 Schaaf study recommended increasing the rifampin (RIF) dose from 9.6 mg/kg to 16-20 mg/kg in children. The conclusion was based on 50% of children in the study with a sub-optimal maximum concentration (Cmax) of RIF <4. The 2009 McIlleron study recommended increasing the INH dose from 5 mg/kg to 10 mg/kg in children. The conclusion was based on a Cmax of INH less than the suggested range for 70% of children in the study.

TBTC data were used to describe doses of rifapentine that would be required to achieve the same serum concentrations in adults and children. For example, a dose of 15 mg/kg in adults would need to be doubled for children 2 years of age to achieve the same pharmacokinetics (PK) outcomes.

Because child-friendly formulations of TB drugs have not been developed to date, TB clinics take several actions to overcome this barrier. Tablets are cut or crushed and capsules are opened in an effort to obtain the correct dose. Ground-up pills and opened capsules are placed in non-standardized liquids and foods (e.g., applesauce, pudding or syrup). No standards have been developed to determine the accurate length of time to hold extemporaneous formulations in liquids or foods.

The 2008 Weiner study compared children who were given rifapentine by whole tablets or extemporaneous crushed-tablet formulations and adults who were given rifapentine by whole tablets. The study showed that children who were given rifapentine in an extemporaneous crushed-tablet formulation in chocolate syrup had substantially lower PK values than children who were given whole tablets. This finding was statistically significant.

The lack of appropriate pill sizes has resulted in less accurate dosing of TB drugs to children. Moreover, the lack of standardized preparations has led to uncertainties about the effects of tablet disruption and the vehicle to deliver extemporaneous formulations to children. These factors have resulted in even greater differences in drug exposure to a population that already has inherently larger variances in PK parameters than adults.

WHO presented data on its recent drug formulation studies. The perception is that young children require suspension formulations. New formulations might be extremely expensive to develop. Based on experiences with HIV therapy to pediatric populations, providers and families prefer solid dosage forms due to their greater stability and easier dosing. Crushable mini-pills are needed for accurate weight-based dosing.

TB drug development trials that are underway on fluoroquinolones, enhanced rifamycins and other novel drugs show great promise in markedly improving TB treatment for active disease, MDR-TB and latent TB infection (LTBI). Clinical trial data published in 2008 used a mouse model to show that daily and higher doses of rifapentine could shorten the entire regimen to three months.

Clinical trial data published in 2009 used a mouse model that indicated higher doses of INH or RIF could reduce the duration of treatment for drug-susceptible TB to four months. Data from a pilot trial published in 2009 showed dramatic initial results of higher culture conversion among patients who were given TMC207/optimized background regimens for MDR-TB than patients who were given placebos/optimized background regimens.

Children are not significantly involved in current TB drug development trials. No pediatric plans have been announced for clinical trials on moxifloxacin, high-dose rifampin, TMC207, OPC67683 or PA824. However, recruitment efforts are underway to enroll >1,000 children >2 years of age in a large randomized trial of rifapentine.

A study published in 2008 identified a number of reasons for excluding children from clinical trials: infrequent transmission of TB from children to others, infrequent culture-confirmation of active TB as a result of paucibacillary disease, frequency of extrapulmonary TB in children, the lack of effective therapy for drug-susceptible TB in children, concerns about side effects in the pediatric population, and uncertainties regarding the appropriate time and optimal trial design to involve children in TB drug development trials.

Regulatory requirements are engendered by the inclusion of children in trials. Concerns have been raised about dividing limited resources for TB drug development research between adults and children. However, none of these challenges should prevent children from being involved in TB drug development trials.

To address these concerns, the necessity of involving children in TB drug development trials should be clearly articulated to funders, regulatory agencies, investigators and patients. A standard should be developed to determine the appropriate time to involve children in TB drug development trials. The traditional approach of completing research on adults and then involving children in trials is no longer appropriate. The exclusion of children from drug development programs should be monitored and widely publicized.

The involvement of children in TB drug development trials is associated with trial design issues. Although obtaining a culture-confirming TB diagnosis in children is difficult, induced sputum and other new technologies can be used to yield better specimens. Clinical definitions and radiographic systems can be used to diagnose TB and determine the patient's response to therapy. Children should not serve as the population for definitive trials of new regimens due to limited capacity to distinguish between differences in the efficacy of various potent regimens. Tolerability and PK should be the primary endpoints of pediatric TB trials.

Efforts are underway to improve methodologies for PK studies in very young children. Current methods require a sophisticated infrastructure (*i.e.*, centrifuge and a -70° freezer) and limit sampling due to difficulties involved with repeated venipuncture. Innovative strategies include sparse sampling with population PK analysis in which young children are randomized to be sampled at different time points. Dried blood spot sampling with a heelstick or fingerstick that currently is being developed will improve sparse-sampling studies, markedly simplify processing and storage at study sites, and expand the number of sites to perform PK sampling.

A large study that will be published in the near future analyzed the efficacy of INH therapy in HIV-infected children 3-25 months of age in high-burden settings. The trial design of randomizing children to be sampled at different times allowed characterization of a full PK curve at three points in treatment with very limited sampling of each infant. The study suggested that the appropriate INH dose is 15 mg/kg rather than 5 mg/kg as recommended by WHO. The study also showed the predominant effect of the NAT2 genotype and served as a model to use sparse sampling to assess PK in key subgroups, such as infants.

A study published in 2008 proposed a number of suggestions on the appropriate time to involve children in TB drug development trials. Emphasis should be placed on potential child-friendly formulations in Phase 2A. Initial PK single-dose or multi-dose studies should be conducted in

children with TB in Phase 2B. Randomized comparisons between new and standard TB drugs or regimens should be made in Phase 3. Additional studies should be conducted with key subgroups in Phase 4 to validate age-specific dosing recommendations (e.g., children <3 years of age, HIV-infected children and children with extrapulmonary involvement, particularly meningitis).

Regulatory incentives and disincentives should be offered to ensure the involvement of children in drug development trials. A six-month patent extension should be given for obtaining a pediatric indication, but this incentive would not be relevant to TB. FDA now requires all drug sponsors to include a pediatric assessment of trials unless a waiver or deferral is granted. The European Medicines Evaluation Agency requires submission of a pediatric implementation plan for all new drugs for diseases that affect children. The complete plan is binding on the sponsor and must be filed immediately after the completion of relevant PK studies in adults.

The involvement of children in TB drug development trials increasingly is being recognized as an ethical imperative. Efforts are underway to develop standards for the appropriate time and strategies to involve children. Vigorous advocacy, monitoring and earmarked funding for children have increased over time. TB researchers are strengthening their working relationships with pediatric HIV clinical trials groups and investigators. Innovative methodologies for PK studies are being developed. Research is continuing to improve specimen quality and *M.tb* detection.

Antiretroviral (ARV) therapeutics serve as a model of involving children in drug development trials, conducting PK studies to determine age-specific dosing, and developing child-friendly formulations for most drugs. This approach resulted in prompt and dramatic decreases in pediatric HIV-related morbidity and mortality soon after the availability of potent ARVs. Data from these trials led to FDA approving ARVs in children 2 weeks to 18 years of age. These trials had small cohorts ranging from 80-182 children.

Three major goals have been established for TB drug development by 2015: a three-month regimen for LTBI treatment, a three-month regimen for treatment of active TB, and much more effective treatment for MDR-TB. Two key pediatric goals have been established in these same areas for 2015: fully evaluate LTBI and active TB regimens in HIV-positive and HIV-negative children of all age groups and gather PK and tolerability data on MDR-TB in children.

Dr. Mamodiko Makhene is the ACET *ex-officio* for the National Institutes of Health (NIH) and a Medical Officer in the NIH National Institute of Allergy and Infectious Diseases (NIAID). She explained that NIAID has lead responsibility for TB research at NIH. Her summary of domestic and international efforts that are underway to involve children in TB research is outlined as follows.

The major challenges in pediatric TB research are that the disease spectrum varies by age, a solid reference or gold standard has not been developed to diagnose TB in children, and gaps exist in the use of TB therapeutics for children. Disseminated and extrapulmonary TB, including central nervous system involvement, is more common in children.

Similar to adults, the diagnosis of TB in children includes a medical history, physical examination and relevant tests (e.g., TST, chest x-ray and sputum smear microscopy and culture). Sputum culture is the gold standard for a definitive diagnosis of TB in adults, but cultures are not positive in the majority of cases involving children.

The collection of adequate sputum specimens is difficult in children and bacillary loads are lower in pediatric populations. Positive cultures in asymptomatic children who were recently exposed to TB do not necessarily signal actual disease and might indicate infection. A referenced standard has not been developed to compare and evaluate new TB diagnostics.

Gastric aspirate is a standard method of sputum collection in young children, but efforts are underway to improve the yield with other methodologies (*i.e.*, induced sputum, the string test and nasopharyngeal aspirate). The 2005 Zar study compared induced sputum and gastric lavage for microbiological confirmation of pulmonary TB in infants and young children. The study found that one induced sputum produced a yield equivalent to three consecutive gastric aspirates.

NIAID is sponsoring the Hatherill study in Cape Town, South Africa to compare the diagnostic yield of induced sputum and routine sputum collection in HIV-infected and HIV-uninfected patients with suspected TB. The cohort includes 600 persons $\geq$12 years of age with suspected pulmonary TB. A higher yield with induced sputum regardless of HIV status is one of the anticipated findings of the study.

NIH will continue to fund the TB Research Unit (TBRU) at Case Western Reserve University through 2014. The consortium of research institutions in TB endemic countries conducts clinical studies to establish markers to identify those at highest risk for progression to TB disease; characterize correlates of response to therapy and vaccination; and contribute to the identification of improved therapeutics, vaccination strategies and diagnostic strategies.

TBRU is conducting a study on novel CD8+ T-cells diagnostics for childhood TB. The study is designed to determine whether CD8+ T-cells directed toward *M.tb* proteins could distinguish between 92 young children <5 years of age with intrathoracic TB and 50 children with pneumonia or other lower respiratory tract infections. The study also will evaluate the sensitivity and specificity of five different antigen combinations in children.

NIAID will continue to fund the TB Clinical Diagnostic Research Consortium (CDRC) through 2016. CDRC includes pediatricians at experienced study sites in TB-endemic countries. The purpose of CDRC is to assess early-stage investigational TB diagnostics in the context of existing clinical management algorithms, conduct feasibility studies to validate a proof of principle, and provide preliminary data to support test development. CDRC has not planned pediatric studies at this time.

WHO held a meeting on the evaluation of TB diagnostics in children in May 2010 in Geneva. A Pediatric TB Expert Panel was convened to initiate dialogue and reach consensus on an accepted reference standard for evaluating TB diagnostics in children. The panel also is

charged with developing standardized protocols to allow testing in a range of settings and populations.

Participants at the WHO meeting emphasized the need to standardize definitions and treatment outcomes and also to clearly distinguish between a clinical case definition for clinical management and a reference standard for children. The possibility was raised of including children ≥10 years of age with pulmonary TB in adult studies. The potential use of statistical approaches due to the absence of a perfect reference standard was discussed. Discussions on the evaluation of TB diagnostics in children will be continued at the 2010 IUATLD meeting in Berlin.

The Stop TB Partnership Workgroup on New Diagnostics was convened to promote the development of new diagnostics. A Pediatric Subgroup was formed in December 2009 with four major tasks: (1) catalog current pediatric TB diagnostic research activities and promising pilot studies; (2) incorporate diagnostic test strategies into pediatric TB studies for vaccines, drugs and contact studies; (3) develop a roadmap for improved diagnostic testing that is needed for surveillance, case finding, and drug and vaccine trials in children; and (4) potentially fund promising pilot studies.

Several gaps need to be filled in TB diagnostics for children. Validated point-of-care diagnostic tests are needed and should be widely available in high-burden countries for paucibacillary disease. These tests ideally should be non-invasive, based on the collection of urine or saliva rather than sputum, and have capacity to accurately diagnose all forms of pediatric TB infection and disease by age, spectrum, HIV/non-HIV infection status, clinical presentation, resistance and disease localization. Scoring systems need to be validated to aid in the diagnosis of TB. A logical roadmap needs to be developed to advance the field of TB diagnostic studies in children.

Other issues that need to be addressed in the area of pediatric TB drugs include poor characterizations of exposure response profiles for first-/second-line drugs, new drugs and combination regimens; the lack of pediatric formulations; the absence of efficacy and safety data by age group; uncertainties regarding the optimal duration and dosing frequency; the absence of PK data to guide age-appropriate dosing; limited data on drug-to-drug interactions with ARVs; and overdosing or under-dosing of children.

NIAID and the Stop TB Partnership Workgroup on New Diagnostics co-sponsored a workshop in July 2009 to develop guidelines on involving children in TB drug development trials. The participants included funders, drug developers, regulatory officials, investigators and advocates. The meeting was held in conjunction with the FDA "Clinical Trials for Drug-Sensitive TB Workshop." The purpose of the meeting was two-fold: (1) discuss key issues to consider in involving the pediatric population in the development of drugs to treat TB and (2) generate consensus and points for consideration on the best and most efficient strategies to study anti-TB drugs in children.

Pediatric formulations were a key topic of discussion during the meeting. The most desirable properties of pediatric dosage forms identified by the participants were minimum non-toxic

excipients, easy administration, palatability, minimal manipulation before use, low bulk and weight, capacity to be transported, stability in different climates, and affordability.

WHO convened the "Expert Committee on Selection and Use of Essential Medicines" in 2009 to obtain guidance on pediatric formulations. The committee determined that the most suitable dosage for children in terms of stability, dosing and administration was a flexible oral solid form. The solid form was found to have benefits over liquid dosage. The committee recommended fractionation of a solid form to half tablets only and administration of the dosage to once or twice daily.

The NIH National Institute of Child Health and Human Development (NICHD) is responsible for establishing pediatric drug testing and development programs under the Best Pharmaceuticals for Children Act. NICHD solicits nominations from the broader pediatric community on drug, biologic or medical devices that need further study in children and therapeutic areas proposed for analysis for a specific pediatric condition, subpopulation or setting of care. NICHD publishes the "Annual Priority List of Needs in Pediatric Therapeutics" and has expressed an interest in conducting research on formulations for TB drugs in children.

NICID released the "Pharmacokinetics Research in Pediatric HIV/TB" FOA with an August 24, 2010 deadline for applications. Grantees will be funded to evaluate PK of TB drugs and assess PK drug interactions of TB/HIV drugs and their impact on treatment outcomes in children with TB/HIV co-infection. NICHD is involved with TBTC Study 26 to determine the effectiveness and tolerability of a weekly regimen of rifapentine for three months versus a daily regimen of INH for nine months for LTBI treatment in HIV-infected and HIV-uninfected children.

The NIAID Division of AIDS funds the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) that is currently conducting a trial on immediate versus delayed INH prophylaxis in HIV-infected pregnant women in high-risk areas. The IMPAACT sites have a global reach and strong capacity to conduct pediatric TB trials. NIAID will sponsor the "TB Research in Underserved Maternal and Pediatric Populations with HIV" meeting in July 2010.

The Stop TB Partnership Childhood TB Subgroup was convened to promote research, policy development, formulation and implementation of guidelines, mobilization of human and financial resources, and collaboration with partners to decrease childhood TB morbidity and mortality. Based on a literature review of the published evidence on dosage, toxicity and PK of ethambutol, the subgroup recommended revision of daily dosing of this drug for children.

By age group, the incidence of TB is higher and the disseminated form is more common in young infants than in older children with "adult type" TB. The Code of Federal Regulations specifically addresses the appropriate time to extrapolate adult efficacy data to pediatric populations. The regulations state that FDA may approve drugs for pediatric use based on adequate and well-controlled studies in adults with other information.

FDA approval is based on if the course of disease and effects of the drug, both beneficial and adverse, are sufficiently similar in pediatric and adult populations to allow extrapolation to

pediatric patients from adult efficacy data. Federal regulations prohibit extrapolation of adult efficacy data to children in the following situations.

The disease process is not similar in adults and children based on a different rate of disease progression, extent of dissemination and susceptibility. Concentration response relationships differ because blood levels are not expected to correspond with efficacy. Efficacy is expected to differ between adults and pediatric age groups. The disease predominantly or exclusively affects the pediatric population. To guide the decision-making process of extrapolating adult efficacy data to children, a "Pediatric Study Decision Tree" is available on the FDA website.

The 2010-2015 Global Plan to Stop TB has been updated with four key goals targeted to the pediatric population. An overall research agenda should be prioritized to include children in TB research to improve surveillance, prevention, case detection, treatment outcomes, operational research and health systems strengthening research.

Fast-tracked and targeted research should be conducted on TB diagnostics, vaccines and drugs in the pediatric population, including HIV-infected children. Rapid, accurate, affordable and cost-effective diagnostic tools for all forms of TB infection and disease in children should be widely available. Safe, effective and child-friendly shortened drug regimens should be created to prevent and cure all forms of TB in children.

Dr. Castro acknowledged that the discussion was primarily devoted to ACET asking questions and obtaining clarification on pediatric TB issues. He noted that after ACET had an opportunity to consider the extensive data Drs. Burman and Makhene presented, the members were welcome to adopt a formal resolution supporting the continuation of ongoing activities in pediatric TB and endorsing future efforts to involve children in TB drug development trials.

Overview of Preliminary Data on MDR-TB Transmission Studies

Dr. Edward Nardell, of the Harvard Medical School and Brigham and Women's Hospital, is the ACET liaison to IUATLD. He presented preliminary data to demonstrate the impact of treatment on MDR-TB transmission. These studies show that transmission of TB, including reinfection, is a key driver of the MDR-TB epidemic.

The effectiveness of MDR-TB treatment on transmission is virtually unknown, but new observations indicate a rapid and profound treatment effect that is similar to drug-susceptible TB. Unsuspected and untreated patients spread TB and have implications for hospital and ambulatory treatment, public health law and transmission control priorities. Emphasis is needed on rapid diagnosis and effective treatment.

Community-based treatment of MDR-TB was introduced by Partners in Health in Peru in 1996, but has since been expanded to Lesotho, Karachi, Cambodia and other sites. At this time, only ~10% of MDR-TB patients are hospitalized in Lima. Although community-based treatment has

been highly effective and provides less opportunity for institutional transmission, these countries are extremely concerned about the possibility of community transmission of MDR-TB.

A conference was held in South Africa in May 2010 to discuss decentralized management of MDR-TB and establish a policy framework for South Africa. Data were presented on patient load and the availability of beds in nine centers in South African provinces. The 1,824 beds that were available for 4,552 registered patients in the Republic of South Africa in 2008 caused a deficit of 2,728 beds.

Questions have not been answered to date regarding the actual point where transmission occurs and the actual point in treatment where transmission stops. The appropriateness of using chest x-ray, smear, culture or other surrogate markers also has not been determined. Transmission of MDR-/XDR-TB, particularly in institutional settings and to high-risk individuals, is important to public health due to the threat to communities, morbidity and mortality of individual patients, the emergence of more resistant and deadly strains, and the requirement of extensive resources.

In an effort to fill these data gaps, ACET established a workgroup in 2008 to develop evidence-based "Guidelines for Discontinuation of Isolation for Patients with Multidrug-Resistant Tuberculosis." The workgroup's charge was to summarize existing guidelines; systematically review the evidence on transmission of MDR-TB; identify advantages, disadvantages and supporting data to change the current guidelines on discontinuation of isolation of MDR-TB patients; and draft recommendations for ACET's review and comment.

The workgroup conducted a comprehensive literature review of existing guidelines on discontinuation of airborne infection isolation of patients with drug-susceptible TB. Current guidelines included in the literature review were developed by CDC, the United Kingdom Department of Health, New York City Bureau of Tuberculosis Control, and Public Health Agency of Canada.

Most of the existing guidelines recommended a minimum of 14 days for TB treatment and three negative cultures or smears, but did not mention a minimum number of days for treatment of MDR-TB due to the lack of data. The literature review led the workgroup to question the availability of data to support MDR-TB isolation guidelines, the availability of data to discontinue isolation after a specific duration of time, and the availability of data to support microbiologic criteria for isolation discontinuation.

Of 720 potentially relevant citations the workgroup initially identified, 28 articles were ultimately included in the review. Of the 28 selected articles, only eight mentioned MDR-TB therapy. The workgroup reached the following conclusions based on its review of the 28 articles. Culture negativity appeared to be the standard to deem cases non-infectious. The most conservative guidelines recommended three negative cultures. Overall, the literature search yielded minimal evidence, but existing policy and guidelines may serve as a basis to inform ACET's guidelines. Other indices of response to therapy should be studied.

Based on the workgroup's findings, ACET engaged NTCA and other key stakeholders in a discussion to review the advantages and disadvantages of developing more stringent guidelines on the discontinuation of isolation of MDR-TB patients. ACET presented various approaches to DTBE leadership, but progress was not made in formulating the ACET guidelines by the June 2009 deadline due to the lack of data.

Based on 2008 WHO data, >50% of MDR occurs in patients not previously treated and many previously treated cases are reinfected. Of 53 XDR-TB patients in Kwazulu Natal, South Africa, 55% had no previous TB treatment, 67% had been hospitalized, 100% had HIV co-infection, and 100% died 16 days from TB diagnosis on average. This outbreak emphasized the critical need for improved infection control.

The 2007 Glemanova, *et al.* and Bull WHO retrospective study described the importance of transmission in Tomsk, Siberia. Substance abuse was found to be a strong predictor of non-adherence, but non-adherence was not associated with MDR-TB. The study further showed that MDR-TB occurred more among adherent TB patients who had been hospitalized in the course of therapy than in persons with TB treated as outpatients.

The 1986 Nardell, *et al.* study used phage typing to analyze exogenous reinfection of drug-resistant TB in a Boston homeless shelter, but genotyping has been used in more recent studies to prove exogenous reinfection. The Sonnenberg, *et al.* study found a 52% reinfection rate in a high HIV setting in South Africa, while the Gao, *et al.* study found a 62% reinfection rate in a low HIV setting in Shanghai, China. In institutional settings, the 2005 Dimitrova study found that the TB risk among healthcare workers in Russia was ten times more than the general population and had serious implications for the global TB workforce.

The 1966 Bull WHO study reported the experience of conducting the first clinical trials of ambulatory TB treatment in Madras, India. The trials found no more household conversions after the start of treatment. Most household contacts had been exposed for months before diagnosis and treatment. Susceptible contacts were already infected and patients were no longer infectious.

The 1973 Brooks, *et al.* study reported the results of 107 TST-negative subjects living with 21 patients with positive sputum. After 23 days of hospitalization, 19 smear-positive patients were discharged. All of the patients did not become negative on culture after five months. No TST-negative subjects in contact with patients after the beginning of treatment converted their skin tests.

The 1974 Gunnels, *et al.* study reported the results of contacts of 155 patients who were discharged one month after treatment in hospitals. Of 69 culture-negative patients and 86 culture-positive patients, 52 patients were smear-/culture-positive. The study found no difference in the infection rate among 284 contacts of culture-positive cases versus 216 contacts of culture-negative contacts.

The 1974 Riley and Moodie study reported the results of 70 household contacts of 65 new TB cases on domiciliary treatment with a non-RIF regimen. A series of six consecutive TSTs

showed no transmission among TST-negative contacts after the start of treatment. Most household contacts were infected in the first or second month before diagnosis and treatment.

The 1976 Rouillon, *et al.* study found a correlation between sputum smear/culture positivity and transmission before, but not during therapy. Discordance was observed between the effect of treatment on culture and smear. The study confirmed that smear and culture-positive TB patients on therapy did not infect close contacts. The study concluded that less than two weeks of treatment appeared to be effective in stopping transmission among drug-susceptible patients.

These early studies led to the development of a series of policies by CDC and the American Thoracic Society on TB treatment in general hospitals and communities as well as the discharge of patients. The classic Riley experiment was first published in 1959 in which hundreds of sentinel guinea pigs sampled the air from a six-bed TB ward in Baltimore. The initial Riley study included a cohort of strongly smear-positive patients with cavitary TB. Of 77 patients, three produced 73% of guinea pig infections that were cultured. All of the patients had drug-resistant *M.tb* and were on inadequate therapy. During a four-month period, no infections occurred when drug-susceptible patients on therapy were admitted to the ward.

The second Riley two-year study included untreated patients. The relative infectivity of all smear-positive patients in context to the amount of time spent on the ward was analyzed in 61 untreated patients and 29 treated patients with susceptible TB and six untreated patients and 11 treated patients with drug-resistant TB. Treatment was ~98% effective in stopping transmission among drug-susceptible TB patients and also had an effect in stopping transmission among drug-resistant TB patients.

Treated patients were immediately admitted to the ward at the time treatment was initiated and generally were removed before sputum became completely negative. The study concluded that the effect of stopping transmission was prompt and striking. Drug therapy appeared to be effective in reducing the infectivity of patients with drug-resistant TB, but the lack of data did not permit a detailed analysis of the problem.

To determine the effectiveness of treatment in stopping MDR-TB transmission, the Airborne Infection Research (AIR) Facility was established in the Republic of South Africa with funding from CDC, NIH, the National Institute for Occupational Safety and Health, and U.S. Agency for International Development. The six-bed ward includes two beds in each of the three patient rooms and two chambers that can house up to 180 guinea pigs each for air sampling.

To date, investigators have completed a pilot study and three experiments at the AIR Facility. The pilot study included 26 smear-positive patients who were coughing, had cavitary disease, and were admitted to the ward over a four-month period to start therapy. The pilot showed that >100 guinea pigs were infected in the first month and 74% were infected over the entire four-month period.

In experiment 1, only nine guinea pigs in the control arm that breathed air from the ward and had no interventions were infected over a three-month period. In experiment 2, 53% of guinea pigs in the control arm were infected over a two-month period. In experiment 3, only one guinea

pig in the control arm was infected over a three-month period. Due to these unexpected results, drug-susceptibility testing was performed with findings from the pilot study and showed that only XDR-TB patients transmitted infection.

To determine the level of treatment upon admission, results from experiment 2 were reviewed and a 10% infection rate was observed. On average, 24 patients included in the experiment had approximately one half-day of treatment upon admission. Data on treatment duration are currently being gathered for the pilot study, mask studies, and ultraviolet 2 and 3 studies, but these results are likely to be similar to the current findings.

Results from the pilot study and three experiments conducted at the AIR Facility showed that drug-resistant or drug-susceptible patients with unsuspected or untreated TB on a general medical, orthopedic, obstetrics or psychiatric ward of a hospital in a developing country will transmit infection. MDR-/XDR-TB patients with unsuspected or drug-resistant TB in a TB hospital will transmit infection. XDR-TB patients with unsuspected or untreated TB on an MDR-TB ward will transmit infection.

These findings emphasize that rapid diagnosis and initiation of therapy are the most effective strategies to stop transmission of infection. Similar to drug-susceptible TB, MDR-TB is highly susceptible to transmission of infection with a standardized regimen. These observations need to be refined, but the studies show great promise in terms of the role of initiating therapy and ruling out XDR-TB to increase the safety of therapy in both inpatient and outpatient settings.

Studies conducted at the AIR Facility in the future will be designed to better define treatment upon admission. Only XDR-TB patients will be admitted to assess the impact of XDR-TB treatment on transmission. Novel approaches to transmission control will be utilized, such as inhaled dry powder antibiotics.

ACET and CDC thanked Dr. Nardell for sharing preliminary data on MDR-TB transmission studies. Instead of solely focusing on MDR-TB versus XDR-TB, ACET advised the investigators to analyze susceptibility with and without fluoroquinolones. This approach would help to identify key components in a treatment regimen that would be successful in stopping transmission of infection. ACET also encouraged the investigators to utilize nucleic acid amplification testing data from cohort reviews to measure the effectiveness of treatment in smear-positive or smear-negative TB patients and their contacts.

ACET noted the need to engage Dr. Nardell in follow-up discussions to address two important issues: (1) the importance of conducting early drug-resistance testing and (2) the need to focus on ethical/logical issues and the tremendous implications of providing MDR-TB treatment in rudimentary homes or other outpatient settings overseas. Most notably, the HIV status of contacts in homes overseas would play a major role in providing MDR-TB treatment in outpatient settings globally.

Dr. Castro advised the investigators to reproduce and link preliminary data from the studies Dr. Nardell presented to rapid drug-susceptibility testing. These data could be used to inform

revisions of existing guidelines on the discontinuation of isolation of MDR-TB patients in a practical and actionable manner.

Update on Stop TB USA Activities

Dr. Randall Reves is the Medical Director of the Denver Metro Tuberculosis Control Program in the Denver Public Health Department and former Chair of Stop TB USA. He presented an overview on "A Call to Action on the Tuberculosis Elimination Plan for the United States."
The 2010 TB elimination goal ACET established in 1989 will not be met and the 2035 TB elimination goal IOM established in 2000 also is unlikely. The 2035 IOM goal was based on rapidly accelerating the development and implementation of new tools to decrease TB rates by 10% each year. Another barrier to reaching the TB elimination goal is that based on 2000-2008 data, TB is projected to be an "exclusively minority" disease in the next 42 years, but efforts have not been adequately targeted to these populations.

Of IOM's five TB elimination goals for 2000, success has been fully achieved in two areas: maintain TB control despite the decline in cases and increase U.S. involvement in global TB control. Of IOM's five TB elimination goals for 2000, success has been achieved to some degree in two areas: develop new TB diagnostics, treatment and prevention tools and mobilize and sustain public support. Of IOM's five TB elimination goals in 2000, no progress has been made in the area of accelerating the decline by increasing targeted testing and treatment of LTBI.

A case study of a patient reported by the California Department of Public Health emphasizes the critical need to increase the focus on TB elimination. The patient was a previously healthy elementary school teacher in the United States who was diagnosed with pneumonia as a result of coughing for three months. After the failure of outpatient treatment, a chest radiograph showed left lung lesions and cavitary disease. Sputum was positive for TB and MDR-TB was diagnosed after weeks of standard treatment. With the exception of international travel to Asia and Mexico, the patient had limited exposure to TB. The completion of curative TB treatment was successful for the patient.

The patient experienced adverse physical, mental and social effects routinely associated with MDR-TB treatment: weeks of hospitalization; initial weeks of inadequate treatment while waiting for laboratory results indicating drug resistance; daily treatment with intravenous medication for at least 4-6 months potentially leading to hearing loss; 3-4 other types of pills causing nausea, depression and other side effects for 18-24 months; intrusive DOT on a daily basis causing the inability to work for months; rejection by friends, coworkers and others; and intensive health department investigations in home, school and social settings.

Of all 31 children in the patient's elementary class, 68% were found to have a positive TST with a 10% risk of developing MDR-TB. Of the patient's 111 "other school" contacts, 14% were found to be infected. Treatment for MDR-TB was recommended, but the benefit of this approach was unproven. Based on non-consent by parents, only 26 of 36 infected contacts

were started on two medications daily for 12 months. The investigation required full-time efforts by two health department staff members for one year. As of February 2010, no additional TB cases had occurred.

The case study of the elementary school teacher in California illustrates that the TB control community is being forced to administer TB treatments abandoned 50 years ago. In the modern era of TB control, a TB diagnosis should have been promptly made and drug susceptibility results should have been rapidly obtained.

The patient should have been approved to safely return to work in 2-4 weeks and given a cure of TB with a six-month short-course regimen, but ideally a two- or four-month regimen. The protection of contacts with a nine-month treatment regimen should have been shortened to 2-4 months. Overall, U.S.-born persons should have the ability to safely travel around the world without the potential of exposure to MDR-TB.

In addition to adverse effects to individual patients, TB also places a tremendous societal burden on the United States. The cost to treat one drug-susceptible patient is $4,000 with DOT. Hospitalization costs $19,000 per person and accounts for 50% of patients. In the United States each year, 1,200 persons with TB die before a diagnosis is made or during the course of treatment. MDR-TB treatment costs range from $28,217 to ~$1.3 million for each patient. XDR-TB treatment costs are >$600,000 for hospitalization only. The death rate is >40% in a large patient series.

The case study illustrates that TB disparately affects racial/ethnic minorities, but every American remains at potential risk for TB due to the global burden of disease, including drug-resistant TB strains requiring treatment for up to two years. Recommendations in the Call to Action will benefit every American and persons globally who have the same urgent need as the United States for new tools to better diagnose, treat and prevent TB. The benefits of TB elimination by 2035 are 253,000 fewer active TB cases, 15,200 fewer TB-associated deaths and $1.3 billion less in TB treatment costs.

The full Call to Action, including an Executive Summary, tables of recommendations and an initial communication tool, are available on the Stop TB USA website and also were discussed during the National TB Conference in June 2010. The key chapters address TB in U.S.-born persons, FBP, low-incidence areas and new tools.

The Call to Action is not intended to replace the IOM plan for TB elimination and emphasizes that the IOM plan and recommendations continue to be valid. The Call to Action serves as a foundation to make specific action plans to implement the 2000 IOM recommendations and encourages involvement by stakeholders. A number of groups will need to be engaged in the effort to eliminate TB in the United States: policymakers at all levels of government, the public health sector, medical practitioners, professional societies, community-based organizations and voluntary organizations.

Dr. Anthony Fauci, Director of NIAID, noted the importance of transforming traditional methods to diagnose, treat, prevent and control TB through biomedical research and public health

measures to the same extent as HIV/AIDS. The 11% decline in TB cases and rates in 2009 might indicate that acceleration of TB elimination is feasible. As a result, a proactive systems approach to TB elimination should be taken rather than diverting program resources if the 11% decline is sustained.

The Comprehensive TB Elimination Act of 2007 was signed in 2008 and authorized up to $210 million per year to DTBE, but the legislation does not address appropriations. Moreover, concerns have been raised regarding the $1 million decrease in funding for DTBE in the FY2011 budget and the impact of this budget cut on existing cooperative agreements between states and local jurisdictions.

HHS Secretary Kathleen Sebelius has made several remarks in response to these concerns. The funding decrease would not have a negative impact on existing cooperative agreements between states and jurisdictions. The cost-savings would improve the effectiveness of the TB program and other CDC programs agency-wide. CDC would continue to provide domestic and international leadership and assistance to prevent, control and eliminate TB. However, HHS and other federal government agencies should clearly articulate their commitments to TB elimination.

Stop TB USA calls for a renewed and expanded commitment to TB elimination in the Call to Action and describes five key action steps. A commitment should be made to implementing the 2000 IOM recommendations and the HHS Secretary should conduct periodic reviews on the progress toward elimination. New timelines and interim goals for TB elimination should be developed.

With assistance from national, state and local voluntary and professional organizations, necessary funding for infrastructure should be obtained to enable Stop TB USA to collaborate with CDC and engage its members and partners in generating political will to implement the 2000 IOM recommendations and the action plans in the Call to Action.

The federal funding gap should be addressed by obtaining an independent assessment of the extent to which increased funding levels authorized in the Comprehensive Tuberculosis Elimination Act of 2007 could accelerate the development and implementation of new tools for diagnosis, treatment and prevention of TB. Policymakers, the public health sector, medical practitioners, professional societies, community-based and voluntary organizations at federal, state and local levels should be engaged to commit to TB elimination.

To implement the Call to Action, Stop TB USA is encouraging its members and other groups to access the plan on its website. Efforts are underway to leverage funds to print and distribute the document to Congressional members, their aides and policymakers at the state level. Specific communication and advocacy tools will be developed and posted online. Stop TB USA is now requesting ACET's endorsement, advice and participation in implementing the Call to Action.

ACET commended the members of the writing committee, reviewers and consultants for their roles in developing, reviewing and providing technical expertise to produce the excellent Call to

Action. ACT also thanked Stop TB USA for taking leadership to develop the document. Several members were in favor of ACET taking a proactive approach to help disseminate and publicize the value of the Call to Action.

ACET suggested other groups for Stop TB USA to systematically engage in implementation of the Call to Action: persons with first-hand knowledge of the previous practice of admitting a TB patient to a sanitarium, persons with family members who had TB, college student groups and other young persons for advocacy of TB elimination, and persons outside of Congress, the TB community and the affected population.

Dr. Fleenor confirmed that ACET would have further discussion to frame a strategy to provide advice and participate in the implementation of the Call to Action.

ACET's Progress Report Toward TB Elimination

Dr. Fleenor explained that the report on ACET's progress toward TB elimination over the past four years would be distributed to the HHS Secretary. The major purposes of the report are highlighted as follows. ACET's 81 resolutions and recommendations are articulated to assist the HHS Secretary in identifying next steps in TB elimination. Of these resolutions, 68% were fully implemented and 20% were partially implemented.

The report serves as a complimentary document to the IOM report and the Stop TB USA Call to Action to formulate TB policies in the United States. The report would be placed in the public domain and could serve as an advocacy tool by professional organizations, stakeholders and communities. The report documents ACET's completed activities and future directions.

The national TB rate in the United States has both decreased and increased from 1980-1990, but a decline in rates typically is associated with a decrease in funding. ACET's 81 resolutions and recommendations were designed to frame success in six key domains. Domain 1 is "surveillance, reporting and program coordination." ACET recommended surveillance of special populations, improved electronic reporting, enhanced coordination and collaboration with other federal, state and local public health agencies, and efforts to leverage TB program resources.

Domain 2 is "policy." ACET recommended cross-communication within CDC (e.g., chronic disease and emergency preparedness), coordination of immigration and public health laws, scalable redesign and implementation of overseas TB screening programs, enhanced TB efforts along the U.S.-Mexico border, development of a legal toolkit for public health enforcement, and implementation of model practices and practice standards.

Domain 3 is "professional and community education." ACET recommended an expanded role of RTMCCs to challenge current practices, promulgate best practices, serve as model centers that are nationally replicable, and expand beyond clinical models to include education of policymakers, community leaders and educators.

Domain 4 is “program evaluation.” ACET recommended a quality improvement process and outcome analysis. Domain 5 is “clinical research.” ACET recommended the development of new drugs, diagnostic testing and vaccines.

Domain 6 is “consistent and adequate funding.” ACET agreed that gaps in the Patient Protection and Affordable Care Act (PCACA) need to be addressed, particularly for patients at highest risk for TB. ACET also agreed on the need to emphasize distinct and adequate CDC funding for state and local program activities that will not be covered under PCACA. In a response to ACET’s recent letter, HHS Secretary Sebelius confirmed her awareness of these gaps.

The intersection among mega determinants of health (*i.e.*, education, personal behavior, socioeconomic status and environment), their combined role in TB elimination, and use of a business model to apply the determinants of health to TB elimination will be key components in ACET’s vision and imagination.

Ongoing success will depend on ACET’s ability to strike an appropriate balance between its vision and imagination of TB elimination. The structural elements of assessment, alignment and action also will be critical factors in ACET making a transformation to TB elimination and continuing to provide leadership. ACET’s true success in leadership is retrospective and is an actual measure in preparing the next generation to build on its existing foundation.

Dr. Fleenor confirmed that based on suggestions proposed during the meeting, he would revise ACET’s progress report toward TB elimination and initiate the CDC review process. CDC would forward the final cleared report to the HHS Secretary. He explained that ACET’s discussion would be divided into two major parts: feedback on the content of the progress report and input on ACET’s strategic planning process, including the transition to new leadership with the incoming Chair, ACET’s vision for TB elimination and future directions.

ACET commended Dr. Fleenor for his excellent leadership as the Chair and also for compiling ACET’s numerous recommendations in a succinct and clear progress report to the HHS Secretary. The members were pleased that time would be devoted to discussing ACET’s strategic planning process. ACET’s comments and suggestions on these two issues are outlined below.

ACET’s Progress Report Toward TB Elimination

- Efforts should be made for PCACA to fully fund treatment as primary and secondary prevention of active TB and LTBI without shared costs, co-pays and deductibles. This benefit should be available to U.S. citizens as well as documented and undocumented persons.
- The report should recommend overseas screening for all visa applicants who will remain in the United States for $\geq$6 months.
- The message at the beginning of the report noting an expectation of a gradual decline in TB should be combined with language at the end of the report expressing concern about the reversal in the anticipated decline without additional resources.

- Language should be added to the "Epidemiological Surveillance and Reporting" section in the Executive Summary to clarify the disproportionate burden of TB in the AA community.
- Language should be added to the "Clinical Research" section in the Executive Summary advising CDC to collaborate with its federal counterparts at NIH, FDA and industry to expand the available therapeutic armamentarium for treatment, diagnosis and cure of TB.
- ACET should explore the possibility of combining its efforts with those of other TB advisory bodies in HHS agencies to have a collective voice in emphasizing the need for HHS to make a strong commitment to TB elimination at the department level. ACET also should present the progress report to U.S. Surgeon General Regina Benjamin due to her strong interest in racial/ethnic disparities.
- Language on pediatric TB should be added to the "Special Populations" section.
- ACET's recommendations on TB should be framed in the context of priorities the HHS Secretary has established for the department: obesity and healthy weight, tobacco and smoking cessation, and hepatitis.
- A new recommendation should be added to the Executive Summary for the HHS Secretary to re-categorize Class III diagnostics as Class II to make these products widely available, less expensive and more easily cleared by FDA. Products for drug resistance have been developed, but cannot be used in the United States due to the absence of FDA clearance.
- The Executive Summary should begin with ACET's recommendations that were fully implemented rather than incomplete activities.
- Organizations outside of TB should be engaged in using ACET's progress report as an advocacy tool, such as the American Diabetes Association, professional groups representing HIV/AIDS and rheumatology, and alcohol detoxification programs.

ACET's Strategic Planning Process

- ACET should identify and prioritize interim steps in its long-term vision and goal of achieving TB elimination. For example, ACET could immediately begin to engage other healthcare providers, TB patients and impacted communities in its dialogue and activities. ACET could devise an action plan to ensure that its recommendations and resolutions are applied to actual practice in the field. A strategy could be formulated to use ACET as a vehicle to advocate and obtain political will for TB issues throughout CDC and HHS. A formal mechanism could be developed for ACET to continuously communicate between face-to-face meetings (e.g., an e-mail exchange system, limited-access website or webinars).
- ACET should take concrete actions to increase its visibility and prominence in the future. For example, ACIP, the Healthcare Infection Control Practices Advisory Committee and CDC's other high-profile advisory groups convene their meetings at CDC Headquarters, while ACET meets at the more "isolated" Corporate Square Campus. The change in venue would be easier and more attractive for CDC leadership at the highest levels and internal partners from other CDC programs to attend ACET meetings.
- Future agendas should be changed to devote the entire second day of ACET meetings to the strategic planning process and business session. To decrease the amount of time that is spent on presenting updates during face-to-face meetings, newly published

papers, activities in DTBE, issues in other CDC programs of relevance to TB, and other recent developments could be circulated to ACET via e-mail on an ongoing basis between meetings.

- CDC should make efforts to extend Dr. Fleenor's term until the draft Foreign-Born Guidelines are finalized and cleared for publication by CDC. Some members were concerned that the change in ACET's leadership might stall progress in releasing the guidelines to the field. The guidelines are a critical need for TB control programs because TB elimination cannot be achieved without improvements in FBP. Moreover, states have been requesting national leadership and technical assistance to strengthen refugee health screening to decrease the number of TB cases in this population.
- ACET should use its vision as a starting point in the overall strategic planning process and then conduct specific activities to achieve the vision. For example, activities that would need to be conducted to achieve the vision of "a world free of TB" include identifying funding sources, clearly defining roles and responsibilities of various federal agencies, and establishing and sustaining strong relationships between CDC and external partners over time.
- Consideration should be given to amending ACET's charter to include permanent *ex-officio* members from CDC programs with oversight and responsibility for tobacco, obesity/diabetes, and healthcare-associated infections.
- An ad hoc group of former ACET members should be assembled to serve as a "brain trust" and advise ACET on strategic directions for TB elimination.

Dr. Castro made several remarks in follow-up to ACET's discussion. In terms of ACET's progress report toward TB elimination, Dr. Fleenor should attempt to brief the HHS Secretary in person. The request for the face-to-face briefing could be supported by the change in ACET's leadership as a result of the expiration of Dr. Fleenor's term as Chair and ACET's requirement under the Comprehensive TB Elimination Act of 2007 to provide periodic progress reports to the HHS Secretary.

In terms of ACET's strategic planning process, Dr. Castro reminded the members that CDC ratified and signed ACET's amended charter on June 4, 2010. ACET is chartered to provide advice and recommendations regarding TB elimination to the HHS Secretary, Assistant Secretary for Health, and CDC Director. ACET shall make recommendations regarding policies, strategies, objectives and priorities; address the development and application of new technologies; provide guidance and review on CDC's TB prevention research portfolio and program priorities; and review the extent to which progress has been made toward TB elimination.

Dr. Castro agreed that the bulk of ACET's time and effort are devoted to its advisory role for CDC's TB prevention research portfolio and program priorities, while minimal attention has been given to its strategic planning role. He confirmed that CDC would assist ACET in striking a better balance between its roles in these two areas in the future.

Dr. Castro was pleased that ACET extensively discussed its strategic planning process. ACET's 1999 *MMWR* article made a recommitment to TB elimination ten years following the

publication of the original TB Strategic Plan that promised the world TB would be eliminated in the United States in 2010.

Dr. Castro raised the possibility of ACET using its strategic planning process to formally acknowledge the failure in meeting the 2010 TB elimination goal, reinforce its commitment to this effort, reassess the TB landscape since 1999, and describe necessary resources to eliminate TB in the United States.

ACET Business Session

Dr. Fleenor opened the business session and called for ACET's formal action or consideration of the following topics.

TOPIC 1: A motion was properly placed on the floor and seconded by Mr. Joseph Kinney and Dr. Susan Dorman, respectively, for ACET to approve the previous meeting minutes. ACET **unanimously approved** the March 2-3, 2010 Draft Meeting Minutes with no changes or further discussion.

TOPIC 2: Dr. Castro reminded ACET that a suggestion was made after the "New TB Diagnostics Workshop" in June 2010 to use the next ACET meeting as a forum to review Class I, II and III regulatory criteria for new TB diagnostics. If action is taken on this suggestion, he emphasized that the next ACET meeting would need to be convened in the metropolitan Washington, DC area.

Two suggestions were made if the next ACET meeting would be held in Washington, DC. First, appropriate FDA officials should be invited to discuss Merck obtaining FDA approval to develop a subcutaneous version of a TB drug. Second, the face-to-face briefing with the HHS Secretary on ACET's progress report toward TB elimination should be held in conjunction with the meeting.

TOPIC 3: **ACET unanimously approved the following resolution by the workgroup:** "Be it resolved that ACET endorses the draft guideline, *Prevention Measures for Reduction of Multidrug Resistant and Extensively Drug Resistant TB Risk in U.S. Healthcare Workers and Volunteers Who Serve in High Risk International Settings*, and recommends to CDC their publication and full implementation." Agreement was reached to publish the prevention measures in the *MMWR* as ACET recommendations.

TOPIC 4: The following motion was properly placed on the floor and seconded by Dr. Susan Dorman and Mr. Joseph Kinney, respectively: "ACET recommends that states and local jurisdictions, acting in accordance with local regulations and statutes, provide county-level *Mycobacterium tuberculosis* genotype data in the TB GIMS database, for access by designated public health officials for the purpose of facilitating and improving tuberculosis control." **ACET tabled the motion until the next meeting.**

Dr. Dorman and CDC would use the time to draft and incorporate more explicit language into existing memoranda of understanding. The new language would recommend sharing state-level *M.tb* genotype data to facilitate, improve and optimize inter-jurisdictional TB control.

TOPIC 5: The following motion was properly placed on the floor and seconded by Drs. Michael Fleenor and Christine Hahn, respectively: "ACET authorizes its Chair to work with DTBE to include language in Department of Defense contracts for construction activities using workers from the U.S.-Affiliated Pacific Islands in Guam to ensure proper TB screening of these workers prior to employment." **ACET unanimously approved the motion.**

Dr. Fleenor confirmed that the standards of care associated with this resolution and approved by ACET during the March 2010 meeting would be a part of the recommendation. He confirmed that Dr. Naomi Aronson, the ACET *ex-officio* for the Department of Defense, committed to providing assistance in properly wording this motion.

TOPIC 6: The following motion was properly placed on the floor and seconded by Drs. Masahiro Narita and Barbara Seaworth, respectively: "ACET endorses the Menu of Suggested Provisions for State TB Prevention and Control Laws." **ACET unanimously approved the motion.**

TOPIC 7: The following motion was properly placed on the floor and seconded by Drs. Masahiro Narita and Iram Bakhtawar, respectively: "ACET endorses Stop TB USA's document, *A Call for Action on the Tuberculosis Elimination Plan for the United States*, and recommends the dissemination and implementation of its content." **ACET unanimously approved the motion.**

TOPIC 8: The following motion was properly placed on the floor and seconded by Drs. Iram Bakhtawar and Masahiro Narita, respectively: "ACET recommends PCSI to (a) expand the program to chronic disease programs with established epidemiological associations to TB (e.g., diabetes control and tobacco cessation); and (b) collaborate with DTBE to support and assist TB programs to integrate TB screening in other programs under NCHHSTP and chronic disease programs." **ACET unanimously approved the motion.**

TOPIC 9: The following motion was properly placed on the floor and seconded by Drs. Fleenor and Susan Dorman, respectively: "ACET recommends that Dr. Fleenor, as Chair, have ultimate discretion in considering the suggestions proposed by ACET during the meeting to revise and finalize the *ACET Progress Report Toward TB Elimination* to the Secretary of HHS." **ACET unanimously approved the motion.**

TOPIC 10: The following motion was properly placed on the floor and seconded by Drs. Masahiro Narita and Iram Bakhtawar, respectively: "ACET recommends that DGMQ develop a plan to incorporate individuals coming to the United States on long-term work or study visas (*i.e.*, more than six months) in overseas TB screening under the existing TB Technical Instructions." **ACET unanimously approved the motion.**

TOPIC 11: The following motion was properly placed on the floor and seconded by Drs. Iram Bakhtawar and Masahiro Narita, respectively: "ACET recommends elevation of the prioritization of pediatric TB in the overall national research agenda." **ACET unanimously approved the motion.**

Public Comment Session

Dr. Fleenor opened the floor for public comments; no participants responded.

Closing Session

October 26-27, 2010 and November 2-3, 2010 were proposed as two potential dates for the next ACET meeting. Dr. Christine Hahn would provide Ms. Margie Scott-Cseh, Committee Management Specialist for ACET, with a link to the "Doodle Quick Meeting Planner" software. This technology is more efficient than an e-mail poll and would allow the ACET members to quickly enter their dates of availability on an electronic calendar.

The participants joined Dr. Fleenor in applauding Dr. Barbara Seaworth for being named as the "Clinician of the Year" by NTCA during the National TB Conference in June 2010.

Dr. Fleenor reiterated his privilege and honor to serve as both an ACET member and Chair over the past few years. He emphasized that he would have been unable to serve in these roles without ACET's expertise as well as strong technical and administrative support by DTBE leadership and staff, particularly Mr. Phillip Talboy, Deputy Director of DTBE, and Ms. Scott-Cseh.

Dr. Fleenor confirmed that he would remain in contact with his ACET and DTBE friends and colleagues. He wished ACET and CDC the best of luck and success in achieving the important public health goal of TB elimination in the United States.

With no further discussion or business brought before ACET, Dr. Fleenor adjourned the meeting at 2:33 p.m. on June 30, 2010.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

_____
Date

_____
Michael E. Fleenor, M.D., M.P.H.
Chair, Advisory Committee for the
Elimination of Tuberculosis