

**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  
October 27-28, 2009  
Atlanta, Georgia**

---

**Record of the Proceedings**

---

# TABLE OF CONTENTS

Attachment 1: List of Participants .....	A1.1
Attachment 2: Acronyms Used In These Meeting Minutes .....	A2.1
Meeting Minutes.....	1
<b>October 27, 2009</b>	
Opening Session.....	1
NCHHSTP Director's Report.....	2
DTBE Director's Report.....	5
Update on the Healthcare Infection Control Practices Advisory Committee .....	8
Update by the Division of Global Migration and Quarantine .....	10
Overview of the Nepal TB Screening and Treatment Program Evaluation .....	12
Overview of the TB Control in Urban Settings Study .....	18
Update by the Foreign-Born Workgroup .....	19
Update by the Transnational TB Continuity of Care Workgroup .....	21
Update by the African American Workgroup.....	22
Update by the BCG Workgroup .....	24
Update on the Food and Drug Administration TB Diagnostic Activities .....	26
Overview of the DTBE Mycobacteriology Laboratory Branch External Peer Review .....	28
Overview of the DTBE Flagship Projects .....	30
<b>October 28, 2009</b>	
Overview of Health Reform .....	36
Update on the TBTC Recompetition .....	38
Update on the Federal TB Task Force .....	40
Panel Presentation on TB Control in U.S. Affiliated Pacific Islands .....	41
CDC Perspective.....	41
Secretariat of the Pacific Community Perspective .....	44
Commonwealth of Northern Mariana Islands Perspective .....	46
U.S. Department of the Interior Perspective .....	48
ACET Business Session .....	52
Public Comment Session .....	56
Closing Session .....	56

## ATTACHMENT 1

### List of Participants

#### ACET Members

Dr. Michael Fleenor, Chair  
 Dr. Iram Bakhtawar  
 Mr. Shannon Jones  
 Mr. Joseph Kinney  
 Dr. Ana Lopez-de Fede [via conference call]  
 Dr. Masahiro Narita  
 Ms. Sirlura Taylor

#### Designated Federal Official

Dr. Hazel Dean, NCHHSTP Deputy Director

#### Ex-Officio and Liaison Members

Dr. Naomi Aronson  
 (Department of Defense)  
 Dr. William Baine (Agency for Healthcare  
 Research and Quality)  
 Dr. Robert Benjamin (National Association  
 of County and City Health Officials)  
 Dr. Amy Bloom (U.S. Agency for  
 International Development)  
 Dr. Jane Carter (International Union  
 Against Tuberculosis and Lung Disease)  
 Ms. Linda Danko  
 (Department of Veterans Affairs)  
 Dr. Antonio Falcon (U.S. Section,  
 U.S.-Mexico Border Health Commission)  
 Mr. Phillip Griffin (National Tuberculosis  
 Controllers Association)  
 Dr. John Halpin (National Institute for  
 Occupational Safety and Health)  
 Mr. Warren Hewitt (Substance Abuse and  
 Mental Health Administration)  
 LCDR Jennifer Jones  
 (Division of Immigration Health Services)  
 Dr. Michael Leonard, Jr. (Infectious  
 Disease Society of America)  
 Ms. Susan Perez (Treatment Action Group)  
 Dr. Lee Reichman (American College of  
 Chest Physicians)  
 Mr. Dan Reyna  
 (HHS Office of Global Health Affairs &  
 the U.S.-Mexico Border Health  
 Commission)

Dr. Max Salfinger (Association of Public  
 Health Laboratories)  
 Ms. Rachel Stricof (Association of  
 Professionals of Infection Control  
 and Epidemiology, Inc.)  
 Dr. Litjen Tan  
 (American Medical Association)  
 Dr. Lornel Tompkins  
 (National Medical Association)  
 Dr. Theresa Watkins-Bryant (Health  
 Resources and Services Administration)

#### CDC Representatives

Dr. Kenneth Castro, DTBE Director  
 Dr. Jose Becerra  
 Ms. Eileen Bell  
 Dr. Peter Cegielski  
 Dr. Sha Juan Colbert  
 Mr. Michael Craig  
 Ms. Ann Cronin  
 Ms. Christine Dubray  
 Mr. Andrew Heetderks  
 Dr. Kashef Ijaz  
 Dr. Dolly Katz  
 Ms. Ann Lanner  
 Dr. Beverly Metchock  
 Ms. Tamara Miller  
 Ms. Bonnie Plikaytis  
 Mr. James Posey  
 Dr. Drew Posey  
 Ms. Sandy Price  
 Ms. Margie Scott-Cseh  
 Mr. Donald Shriber  
 Mr. Phillip Talboy  
 Dr. Andrew Vernon  
 Dr. Elsa Villarino  
 Dr. Wanda Walton

#### Guest Presenters and Members of the Public

Dr. Richard Brostrom (Commonwealth of  
 the Northern Mariana Islands)  
 Dr. Jennifer Flood (California Department of  
 Public Health)

Ms. Belinda Haerum (Association of State  
and Territorial Health Officials)

Dr. Janet O'Connor (Secretariat of the  
Pacific Activities)

Ms. Freddie Poole  
(Food and Drug Administration)

Mr. John Seggerson (STOP TB USA)

Ms. Roylinne Wada

(U.S. Department of the Interior)

Mr. James Watt (California Department of  
Public Health)



IOM — International Organization for Migration

-

-

**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  
October 27-28, 2009  
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 October 27-28, 2009 in Building 8 of CDC's Corporate Square Offices, Conference Room A/B/C in Atlanta, Georgia.



Dr. Hazel Dean, Deputy Director of NCHHSTP and Designated Federal Official of ACET, called the meeting to order at 8:30 a.m. on October 27, 2009. She welcomed the attendees to the proceedings and particularly recognized the alternate *ex-officio* and liaison members. She also acknowledged three guest speakers, Ms. Roylinne Wada and Drs. Richard Brostrom and Janet O'Connor, who would make presentations on TB control in the U.S. Affiliated Pacific Islands (USAPIs).

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 announced that Dr. Diana Schneider, the former ACET *ex-officio* member for the Department of Homeland Security, recently accepted a new position with the HHS Office of the Secretary. The participants joined Dr. Dean in congratulating Dr. Schneider on her new position as the Director of Research and Evaluation in the HHS Office of Population Affairs.

Dr. Michael Fleenor, Chair of ACET, joined Dr. Dean in welcoming the attendees to the meeting and opened the floor for introductions. The list of participants is appended to the minutes as Attachment 1.



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, a new CDC organizational structure was proposed in September 2009 and is expected to become effective on January 1, 2010 pending HHS approval. Under the new organizational structure, Coordinating Centers would be eliminated. A new Center for Global Health and a new Office of Public Health Preparedness and Response would be established. The Global AIDS Program would be transferred from NCHHSTP to the new Center for Global Health.

A Principal Deputy Director and four Deputy Directors would be appointed to report directly to Dr. Thomas Frieden, Director of CDC, from four new offices: the Office of Infectious Diseases; Office of State and Local Support; Office of Surveillance, Epidemiology and Laboratory Services; and Office of Non-Communicable Diseases, Injury and Environmental Health.

Four Associate Directors would be appointed in the areas of programs, science, quality and communications. The National Center for Health Marketing and the National Center for Public Health Informatics (NCPHI) would be eliminated and the functions of these operating units would be transferred to new or existing CDC offices. The Organizational Improvement Team is closely collaborating with acting leaders on the implementation of CDC's new organizational design.

Dr. Frieden established the following priorities for CDC to support the new organizational structure: strengthen surveillance and epidemiology; improve capacity and effectiveness in supporting state and local health departments; provide leadership in the areas of health policies and community prevention to further reduce the burden of the leading causes of preventable illness and death; and extend and intensify CDC's activities in global health.

CDC is continuing to lead the national response to the novel influenza A virus (H1N1) outbreak. Influenza is perhaps the most unpredictable of all infectious diseases and is a tough enemy. The initial H1N1 outbreak occurred very late in the season and showed remarkable heterogeneity across the United States. H1N1 disproportionately affects young persons, causes widespread illness (some severe or fatal) in most states, and is socially disruptive, particularly for schools. Tens of thousands of healthcare personnel (HCP) and others are responding worldwide to the outbreak. Influenza season lasts until May.

Widespread H1N1 influenza activity was reported by state and territorial epidemiologists the week ending September 12, 2009 and further spread to most of the country by the week ending October 3, 2009. The current influenza activity is markedly different than the previous year in

the week ending October 4, 2008. At that time, most states had no H1N1 influenza activity and no states had widespread H1N1 influenza activity.

At the National Center level, the NCHHSTP Office of Health Disparities was officially renamed as the "Office of Health Equity" (OHE) on October 1, 2009. The Office was established in June 2003 with a mission to improve the health of populations disproportionately affected by HIV, viral hepatitis, STDs and TB and to help eliminate health disparities. The new name reflects NCHHSTP's broader focus on eliminating health inequalities within and between populations and health inequities that stem from broader environmental, political and social contexts. To advance its mission, OHE will incorporate and promote a social determinants health approach to achieve health equity.

Efforts are underway to complete the NCHHSTP Strategic Plan as a consensus document with widespread center-wide input. The Strategic Plan would outline a number of key goals for NCHHSTP: program collaboration and service integration (PCSI), promotion of health equity, global health protection and healthy systems strengthening, partnerships for prevention, and workforce development and capacity building. The Strategic Plan would be disseminated to ACET and other external stakeholders in November 2009 with a three-week deadline for review and comment.

NCHHSTP provided key external stakeholders and program consultants with the first draft of the PCSI white paper that outlines the PCSI strategic vision and framework. The reviewers were asked to give NCHHSTP feedback on the PCSI goals, key measures for monitoring and evaluating new progress, and partnership efforts to advance PCSI efforts at national, state and local levels.

The draft PCSI white paper also was unveiled during the National HIV Prevention Conference in August 2009 and was well received by participants. The Health Communication Science Office staff and PCSI Team jointly gathered stories on successful strategies local and state groups have implemented to encourage PCSI. Public health practitioners across the country from North Carolina to Hawaii were interviewed on camera about their PCSI efforts. The interviews would be packaged as online videos and posted on the PCSI website by the end of 2009.

NCHHSTP would operate under a continuing resolution through October 31, 2009 and allocate funding at FY2009 levels. In the FY2010 Congressional appropriations reports, the House encouraged TB grantees to keep administrative costs  $\leq 10\%$ . The House further directed CDC to include county health departments in stakeholder meetings regarding the TB formula.

ACET expressed support of NCHHSTP's PCSI activities overall. ACET members who reviewed the draft PCSI white paper also commended NCHHSTP on developing a solid, positive and well-written document. However, some ACET members expressed concerns with the PCSI activities and also made comments and suggestions on OHE and the proposed FY2010 budget for NCHHSTP.

In terms of PCSI, the ACET members recalled that during the August 2007 PCSI Consultation, many partners and stakeholders expressed their concerns to NCHHSTP about the minimal

attention given to TB compared to other infectious diseases. For example, the ACET members pointed out that the draft PCSI white paper was unveiled during the National HIV Prevention Conference and not at a TB event. The ACET members further noted that all of the public health practitioners featured on the videos described their PCSI efforts from an HIV perspective.

The ACET members conveyed that because NCHHSTP has not gathered perspectives on PCSI from the TB community, professionals in the field believe CDC views TB as a “stepchild.” The ACET members advised NCHHSTP to consider three suggestions in refining its PCSI activities.

- NCHHSTP to strike an appropriate balance between PCSI activities and a categorical focus on TB to ensure capacity is maintained and a resurgence in TB does not occur.
- NCHHSTP should leverage opportunities for TB to be alongside rather than in the background of HIV.
- NCHHSTP should administer a survey to collect solid data on the knowledge, attitudes and practices of PCSI among front-line workers in the field.

In terms of OHE, ACET was pleased with the new name and the broader focus on health equity. However, some ACET members emphasized the critical need for NCHHSTP to continue to focus on racial/ethnic populations. Data show that TB would be exclusively a “minority” disease in the United States in the future. The ACET members advised OHE to provide leadership at both the CDC and NCHHSTP levels in incorporating the principle of health equity in all activities.

In terms of the proposed FY2010 budget, the ACET members advised NCHHSTP to show strong support for the proposed language in the House appropriations report. The requirement for TB grantees to keep indirect costs  $\leq 10\%$  would dramatically impact many states. Most states have indirect costs of 20%-30%, but a few states have indirect costs as high as 70%. The exorbitant indirect costs have served as a significant barrier to programs delivering effective TB control services on the front line. The 10% limit on indirect costs would result in a huge increase in funding front-line TB control activities.

Dr. Dean made clarifying remarks and provided additional details in response to ACET’s comments and suggestions on PCSI and OHE. NCHHSTP has made strong efforts over the past two years to equally include HIV, viral hepatitis, STDs and TB in its PCSI activities and not exclude any of these disease entities. The presentation of the draft PCSI white paper at the National HIV Prevention Conference was solely opportunistic. This agenda item was not originally planned and was only included after the draft was completed in time for the Conference. Moreover, the PCSI Team conducted the video interviews in conjunction with ongoing activities by OHE.

Dr. Dean offered to place Dr. Kathleen McDavid Harrison, Associate Director for Health Equity in NCHHSTP, on a future agenda to provide an update on the PCSI activities. NCHHSTP and the National Association of County and City Health Officials (NACCHO) have discussed the possibility of administering a national survey to collect data from the field on PCSI. As an initial effort, NACCHO made a commitment to survey its membership to systematically gather PCSI data.

Dr. Dean emphasized that NCHHSTP has taken a number of actions to support OHE's broader focus and scope, while maintaining a focus on health disparities in racial/ethnic populations. Several masters-level and doctoral-level students have been recruited to staff OHE on both short- and long-term bases. The center-wide Health Disparities Workgroup and CDC personnel who are deployed to OHE also conduct a variety of health equity/health disparities activities. OHE closely collaborates with the Office of Minority Health and Health Disparities that directly reports to Dr. Frieden.

NCHHSTP serves on both the CDC-wide Health Equity Workgroup and the CDC/Agency for Toxic Substances and Disease Registry Minority Initiatives Coordinating Committee. NCHHSTP is the only CDC National Center that has established an Office of Health Equity. NCHHSTP's model would provide a foundation for other National Centers to conduct activities specifically focused on health equity.

In response to Dr. Fleenor's question, Dr. Dean reported that no decision has been made at this time on the future of the Board of Scientific Counselors (BSC). The BSC was established to provide scientific advice and recommendations to the Coordinating Center for Infectious Diseases (CCID), but all Coordinating Centers would be eliminated in CDC's new organizational structure.

Dr. Dean noted that the four BSC Workgroups would convene meetings on November 4, 2009. The BSC Workgroup for NCHHSTP primarily would focus on a review of the Strategic Plan. As the ACET representative on this workgroup, Dr. Dean urged Dr. Fleenor to use the upcoming meeting as an opportunity to raise concerns and provide comments on strategies NCHHSTP plans to implement to continue to obtain external input on TB activities from a wider audience.

Dr. Kenneth Castro, Director of DTBE, proposed a process for ACET to address its concerns regarding PCSI and OHE. ACET could adopt a formal resolution to inform CDC of its support for PCSI and emphasize the critical need to retain a categorical TB focus. ACET also could approve a formal recommendation to advise CDC of the need to maintain health equity in all of its priorities and activities.

Dr. Fleenor closed the discussion by describing ACET's next steps in providing guidance to NCHHSTP. The draft PCSI white paper would be distributed to ACET by the end of the day for ACET to formally respond to the document during the business session on the following day. ACET would use its formal response to the PCSI white paper to inform the development of a resolution on the NCHHSTP Strategic Plan during the first meeting in 2010.



Dr. Castro prefaced his report by announcing that CDC's organizational improvements highlighted in Dr. Dean's update would result in the transfer of full-time equivalents and funding from CCID to NCHHSTP. He covered the following areas in his update.

NCHHSTP was the first National Center to undergo CDC's new quarterly performance review (QPR) process on October 20, 2009. During the QPR, DTBE informed Dr. Frieden of its key initiatives: the National TB Indicators Project; recompetition of both the TB Trials Consortium (TBTC) and the TB Epidemiologic Studies Consortium (TBESC); genotyping methods for TB aberration detection and response to improve TB control and prevention; and rollout of molecular testing of drug resistance for more rapid assessment.

During the QPR, DTBE introduced two flagship projects that were designed to address high priorities and engage various DTBE branches and external partners. The flagship projects focus on the interruption of transmission and prevention of future TB cases as well as an effective response to multidrug-resistant/extensively drug-resistant TB (MDR/XDR-TB). Each of the two flagship projects would be funded in the range of ~\$1.25-\$1 million.

The flagship project to prevent future TB cases would target vulnerable U.S.-born populations, such as substance abusers and homeless persons. The new resources would be used to demonstrate improvement in the two project areas, inform the creation of future cooperative agreements, and apply data to develop policy recommendations for states. An overview of the two flagship projects would be presented later in the meeting.

During the QPR, DTBE summarized its major accomplishments and most significant challenges. In terms of accomplishments, the TB case rate has decreased to 2/100,000 in U.S.-born persons and 20/100,000 in foreign-born persons (FBPs). New discoveries have been made for the diagnosis of latent TB infection (LTBI). Genotyping has allowed better characterization of circulating strains. Drug-resistant TB can be more rapidly identified and promising drug regimens have been developed for shortened treatment. The Federal TB Task Force published the *Plan to Combat Extensively Drug-Resistant Tuberculosis* in February 2009. Surveillance data and slides were released on TB cases reported in the United States in 2008.

In terms of DTBE's challenges, resources are extremely limited to address the changing TB epidemiology and trends. State and local health department infrastructures for TB services are continuing to weaken. Efforts to accelerate the decline of TB in U.S.-born persons and FBPs by relying on research advances for new diagnostics are extremely challenging, particularly while attempting to implement the use of shorter, safer and more effective treatment regimens. Capacity needs to be scaled-up for implementation research to evaluate and rollout promising new drugs and diagnostics for use in the field.

DTBE is continuing to transition from the Tuberculosis Information Management System (TIMS) to the National Electronic Disease Surveillance System Base System (NBS). The TB Program Area Module of NBS was designed, developed, tested and deployed in all 16 NBS states. All NBS states are currently in production and are sending 2009 data to CDC on the revised Report Verified Case of TB (RVCT) form.

DTBE and NCPHI used Health Level 7 standards for data transmission to jointly design, develop and deploy a TB Public Health Information Network (PHIN) message for states that opted to use systems other than NBS. The data quality standards incorporated >250 TIMS data entry checks. All commercial, NBS, electronic RVCT and state-developed systems would use

this messaging standard for data exchange. DTBE is currently assisting reporting areas with the implementation of PHIN messaging for states that opted for state-designed solutions.

Because the vast majority of American Recovery and Reinvestment Act (ARRA) dollars allocated to CDC were targeted to chronic diseases, NCHHSTP did not receive any ARRA funding to address infectious diseases. However, DTBE is collaborating with internal CDC partners on two projects with ARRA funding.

DTBE partnered with NCPHI to draft the ARRA Information Technology Initiative to strengthen the collection, management and exchange of public health surveillance data. DTBE is partnering with the CDC Division of Diabetes Translation to address the extraordinarily high incidence of diabetes in the USAPIs. Diabetes in this population is expected to be a significant risk factor for progression to TB disease.

DTBE incorporated the 2010 TB funding formula into the FY2010 TB cooperative agreement. The competitive continuation application process allowed DTBE to continue to support current grantees rather than recompute the cooperative agreement among new applicants. DTBE submitted its funding recommendations to the CDC Procurement and Grants Office and also partnered with the National Tuberculosis Controllers Association (NTCA) to establish base funding of \$100,000 for USAPIs that report  $\geq 5$  TB cases.

DTBE established the TB Program Evaluation Network (TB PEN) to build program evaluation capacity at state and local levels. DTBE convened the first TB PEN Conference in July 2009 in conjunction with the TB Education and Training Network. DTBE would soon initiate assessments of CDC-funded TB projects on the U.S.-Mexico Border beginning with Cure TB. The interferon gamma release assay (IGRA) guidelines were cleared, reviewed by both companies and are being submitted to the *Morbidity and Mortality Weekly Report (MMWR)* for publication.

DTBE would hold meetings to increase involvement by the Regional Training and Medical Consultation Centers (RTMCCs) in international projects funded by the U.S. Agency for International Development (USAID). To support this effort, a World Health Organization (WHO) Regional TB Center was established in the Philippines. A needs assessment was performed to determine training and education needs for TB infection control in Mexico. An MDR-TB Expert Network would be created in Mexico. Although the RTMCCs were not funded to establish a laboratory component, the possibility exists for DTBE to link the RTMCCs' new international activities to laboratory projects in the future.

The recompetition of TBTC was completed, but DTBE is requesting ACET's participation in this review. TBESC is continuing to conduct activities under existing and new task orders. Task Order 2 is an immunogenetic study of TB contacts that is in the final stages of data collection through registry matches, data cleaning and data analysis. Task Order 29 is designed to improve TB and LTBI testing in HIV-infected persons at Health Resources and Services Administration (HRSA) clinics.

Task Order 30 is designed to quantify the risk of premature death in TB survivors by assessing both the total and average years of life remaining after TB diagnosis and treatment. Task Order

31 is an evaluation of IGRA in overseas examinations of immigrant children in moderate and high-burden countries (*i.e.*, Mexico, the Philippines and Vietnam). Task Order 32 is an evaluation of the current cost of TB in urban U.S cities (*i.e.*, Washington, DC, Seattle, Newark, San Antonio and Miami).

To support the recompetition of TBESC, DTBE sponsored the third meeting of the Strategic Planning Workgroup on October 2, 2009 to discuss three potential research focus areas for the new TBESC cycle. Final recommendations would be submitted for decisions to be made on programs and research of relevance to TBESC in the future, but DTBE expects FBPs to be one of the research focus areas. DTBE anticipates developing the request for application for new TBESC sites in March 2010.

The DTBE Health Systems Team is staffed with only one individual at this time. DTBE is currently discussing the functions of and potential restructuring options for the Health Systems Team. DTBE acknowledges that capacity to apply decision analysis, meta-analysis, health econometrics and other prevention effectiveness methods would increasingly become important as TB rates continue to decline.

DTBE responded to several requests for assistance to outbreak investigations from May-October 2009 in Georgia, Indiana, Florida, Texas and the Republic of the Marshall Islands. DTBE provided technical support in the following areas: isoniazid (INH) resistance in a homeless population, TB outbreaks in a homeless population and adult psychiatric residence, use of genotyping data for cluster assessment and aberration detection, and the emergence of MDR-TB.

DTBE is continuing to refine its TB Genotyping Information Management System (TB-GIMS). This promising technology allows states to detect clusters of certain TB strains by county and conduct follow-up activity to improve TB prevention and control at the local level. DTBE will rollout TB-GIMS in 2010 as a prominent component of its aberration detection mapping capacity system.

Dr. Theresa Watkins-Bryant, the ACET *ex-officio* member for HRSA, informed ACET of a new interagency project. CDC and HRSA allocated funding to Primary Care Associations in Maryland, New Jersey and South Carolina to target African Americans (AAs) in implementing quality initiatives with a demonstrated track record of success in improving health outcomes of patients. The Primary Care Associations are funded to build infrastructure between state and local health departments and HRSA-funded health centers and also to provide TB and hepatitis C training to as many primary care providers as possible.

ACET was pleased that DTBE is considering the possibility of linking U.S. laboratories to the RTMCCs' future international activities. A funding stream from the RTMCCs would be useful because U.S. laboratories are prohibited from using state funds to support international projects.

ACET advised DTBE to take advantage of the existing relationship between HRSA and the Division of Diabetes Translation. DTBE could utilize this partnership to leverage opportunities to address diabetes in the context of its progression to TB disease among AAs.



Ms. Rachel Stricof is the ACET liaison to both HICPAC and the Association of Professionals of Infection Control and Epidemiology, Inc. She explained that her update primarily would be devoted to HICPAC's recent activities on infection control of H1N1 in healthcare settings.

CDC issued initial guidance on H1N1 in April 2009 in response to early reports of a high case fatality rate among persons who had the H1N1 virus in Mexico. HICPAC convened conference calls each day on infection control for H1N1 beginning on April 27, 2009. CDC issued an interim guidance document in May 2009 with recommendations in the following areas: respiratory hygiene and cough etiquette, placement of patients in a private room with a closed door, and airborne infection isolation rooms (AIIRs) for aerosol-generating procedures.

CDC's interim guidance document emphasized that precautions would apply to all febrile respiratory illness if novel H1N1 was present in the community. Precautions would be predicated on the travel history or history of exposure if novel H1N1 was not present in the community. CDC's interim guidance document also provided recommendations on limiting the entry of HCP to the room; using standard and contact precautions in terms of gowns, gloves, eye protection and fit-tested N-95 respirators while caring for patients; and continuing precautions for seven days or the duration of symptoms, whichever would be longer.

N-95 respirators or a higher level of respiratory protection were recommended for all contacts with suspected or confirmed H1N1. As a result, some healthcare facilities in areas with a high incidence of H1N1 depleted their supplies of N-95 respirators and were required to use local health department stockpiles. Overall, the hospital epidemiology and infection prevention control communities, physicians and nurses questioned CDC's interim guidance.

In response to this controversy, CDC convened a seven-member workgroup in June 2009 with HICPAC and organized labor representatives. In July 2009, the full HICPAC membership voted on the proposed recommendations developed by the workgroup and called for droplet precautions, the use of surgical masks for routine care, and AIIRs and N-95 respirators for aerosol-generating procedures.

Based on a meeting between CDC leadership and labor union stakeholders later in July 2009, an Institute of Medicine (IOM) panel was convened in August 2009. The IOM panel issued a report that recommended N-95 respirators for all suspected and confirmed novel H1N1 cases. In response to the IOM report, CDC posted new guidance on its website on October 14, 2009 with the following recommendations.

CDC emphasized the hierarchy of controls (*i.e.*, elimination of potential exposures, engineering and administrative controls, and personal protective equipment). CDC recognized that vaccination is the most effective prevention strategy. CDC continued to recommend the use of N-95 respirators for all contact with suspected or confirmed 2009 H1N1 patients. The Occupational Safety and Health Administration (OSHA) stated that CDC's guidelines established a legally enforceable standard of care. Healthcare facilities would be required to

comply with CDC's guidelines because OSHA would enforce the guidelines under the General Duty Clause and General Industry Respiratory Standard.

CDC clearly acknowledged the supply issue with N-95 and other respirators and advised healthcare facilities to prioritize respirators for the highest risk situations if supply was an issue. CDC recommended that healthcare facilities determine "highest risk" situations as performing aerosol-generating procedures, caring for patients with *Mycobacterium tuberculosis (M.tb)* and other infections requiring airborne precautions. CDC provided healthcare facilities with specific advice on complying with the guidance, including performing an assessment, documenting the current supply of respirators, estimating future needs throughout the influenza season, documenting efforts to obtain the estimated supply need, and establishing plans, if necessary, based on availability.

CDC noted that plans of healthcare facilities should outline prioritization of aerosol-generating procedures currently and throughout the influenza season and consider extended use or reuse of respirators. A priority use mode was described in the guidance for healthcare facilities that would not have sufficient supplies. CDC clearly stated that its guidance only applied to patients with suspected or confirmed 2009 H1N1 during the 2009-2010 influenza season.

Ms. Stricof noted that in addition to H1N1, HICPAC also is continuing to provide expert advice to CDC on other important infection control issues. HICPAC has a strong focus on injection safety due to the shift in the delivery of care from healthcare settings from the acute care to ambulatory settings and the lack of infection control oversight in these alternate, ambulatory settings. Outbreaks of hepatitis B and C virus and other infections are increasingly recognized in ambulatory settings. In 2006, 14.9 million procedures were performed in ambulatory surgery centers.

HICPAC is providing expert advice to CDC on its \$40 million ARRA appropriation that is being allocated to state health departments to implement the HHS Healthcare-Associated Infection Action Plan. HICPAC is providing expert advice to CDC on nontuberculous mycobacteria (NTM) control in response to reports of contaminated water with rapid NTM growers in older buildings and NTM pseudo-outbreaks in laboratories. HICPAC is updating its *Infection Prevention and Control in Healthcare Personnel Guideline*. HICPAC will solicit ACET's expertise and rely on ACET's recommendations to provide updated guidance on a number of issues in the TB section of the guideline, including BCG vaccine and XDR-TB.



Dr. Drew Posey, of the DGMQ Immigrant, Refugee and Migrant Health Branch, reported on DGMQ's ongoing activities related to the TB Technical Instructions (TBTIs), international adoptees, IGRAs and Electronic Disease Notification (EDN) system. In terms of the TBTIs, all immigrants and refugees who apply for U.S. immigration are required to undergo TB screening. The 1991 TBTIs only relied on sputum smears, but the 2007 TBTIs require tuberculin skin testing (TST) for children 2-14 years of age, sputum smears and culture for persons with

abnormal chest x-rays (CXRs), drug susceptibility testing (DST) on culture-positive isolates, and directly observed therapy (DOT) in accordance with U.S. guidelines for persons with laboratory-confirmed TB.

Since 2007, DGMQ has implemented the TBTIs in 25 countries. At this time, ~52% of U.S.-bound immigrants and >50% of U.S.-bound refugees are screened with the new TBTIs. By March 2010, DGMQ would implement the 2007 TBTIs for immigrants and refugees in Cambodia, Egypt, India, Malaysia, Nepal and Thailand. By May 2010, DGMQ would complete initial or follow-up site visits to China, Guatemala and Russia.

In January-May 2010, DGMQ would provide training to panel physicians in the Dominican Republic, Ghana and India on TB and other aspects of the overseas examination. DGMQ also would provide training to panel physicians in seven additional countries throughout 2010. DGMQ would continue to recruit experts from ACET and NTCA to evaluate implementation of the TBTIs in overseas countries because guidance from these efforts has been extremely valuable.

DGMQ most recently implemented the TBTIs in Haiti in September 2009. Haiti serves as the seventh largest source country for immigrant visa entrants and accounted for 15,127 immigrants arriving to the United States in 2008. The Haitian Group for the Study of Kaposi's Sarcoma and Opportunistic Infections operates the laboratory in Haiti with assistance from the National Laboratory Directory. DOT programs are affiliated with two panel physicians.

The 12,000 international adoptees that entered the United States in FY2009 were subject to the TBTIs and overseas screening. Immigration law considers international adoptees as "immigrant applicants." DTBE first implemented the TBTIs in Ethiopia and China in April and July 2009, respectively, due to the sizeable adoptee populations of these countries. DGMQ has received inquiries regarding TB culture requirements for young children.

To address these issues, DGMQ expanded the membership of the TBTI Workgroup to include pediatric experts to address international adoptee issues. The workgroup developed an addendum regarding travel clearance, but did not recommend changes to the existing screening algorithm for TBTIs. The workgroup issued the following guidelines for travel clearance of applicants  $\leq 10$  years of age in the addendum.

Applicants  $\leq 10$  years of age may travel while culture results are pending if none of the following conditions exist: positive sputum smears, CXRs with findings of cavities or extensive disease, forceful and productive cough, and contact to an infectious MDR-TB case. Following the release of these guidelines, CDC convened a meeting in October 2009 with a diverse group of adoption stakeholders, including adoption advocacy organizations, U.S. Department of State (DOS) and Department of Homeland Security staff, adoption clinic physicians and TB physicians.

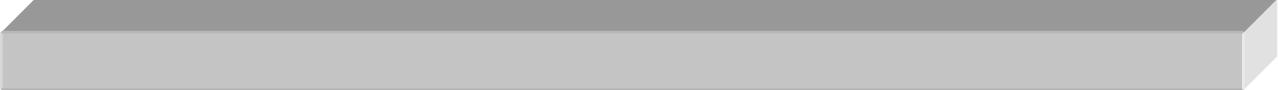
The purpose of the meeting was to build rapport with the adoption community by initiating dialogue regarding TB and other health issues related to international adoptions. The meeting was successful and was followed by a briefing later in October 2009 in which CDC and

advocacy organizations made presentations to >40 Congressional staffers. The CDC meeting and Congressional briefing have led to increased awareness and understanding of CDC's role in preventing the spread and transmission of TB from children adopted overseas.

DGMQ finalized the TBTI document with the following revisions: (1) updated language for consistency with the new DOS forms completed by overseas panel physicians; (2) changes to the 2007 TBTIs based on recommendations by the Philippines Evaluation Team and the TBTI Workgroup; and (3) inclusion of the addendum regarding travel clearance of international adoptees. The updated TBTI document became effective on October 1, 2009.

In terms of IGRA, DGMQ had extensive discussions with DTBE and the TBTI Workgroup and decided that IGRA should be allowed in screening of immigrants where TST is currently required. For panel physicians implementing the TBTIs, IGRA could be used for applicants 2-14 years of age in countries with a TB rate of  $\geq 20/100,000$  beginning on October 1, 2009. For civil surgeons implementing the technical instructions, IGRA could be used for applicants  $\geq 2$  years of age beginning on November 1, 2009.

In terms of EDN, DGMQ increased its staff to 19 personnel on both day and night shifts to decrease the data entry backlog. The increased staff allowed DGMQ to eliminate the data entry backlog from July-October 2009 and update the EDN system with new data and transmission of the new DOS forms. The EDN Team is performing technical modifications to further improve the EDN system and also is continuing to participate in monthly meetings with the NTCA EDN Workgroup.



Dr. Jennifer Flood is a former ACET member and Chief of the Surveillance and Epidemiology Section of the TB Control Branch at the California Department of Public Health. She represented NTCA on the Evaluation Team that conducted the site visit of the TB screening and treatment program for U.S.-bound Bhutanese refugees in Nepal. Dr. Flood's overview of the site visit is summarized below.

After ACET passed a recommendation to evaluate and review overseas medical screening programs to assess implementation of the 2007 TBTIs, evaluations were conducted in Thailand and the Philippines. Nepal was selected for the third evaluation due to the large number of Bhutanese refugees scheduled to resettle to the United States.

Since 1980, >100,000 refugees have been in camps in Southeast Nepal. The refugees are Nepalese descendants who moved to Bhutan in the 19<sup>th</sup> century. The Buddhist Nepalese perceived the growing population of Bhutanese refugees as a threat and restricted their rights. The United States agreed to resettle ~60,000 refugees. DOS funds the International Office of Migration (IOM) to provide medical screening.

The objectives of the evaluation were to provide recommendations to IOM for screening, diagnosis and treatment of TB in U.S.-bound refugees; provide guidance to CDC to improve the effectiveness and practicality of the 2007 TBIs; and identify model practices for implementation by other refugee or immigrant screening programs.

The Evaluation Team observed all steps of the screening and treatment process; conducted structured interviews with both refugee patients and public health staff; reviewed >20 case records and associated CXRs; and interviewed staff in the Nepal National TB Program (NTP), regional WHO Office and the Association of Medical Doctors of Asia (AMDA).

Dr. Flood summarized the Evaluation Team's findings and observations. In Damak, the IOM facility performs TB screening and treatment, refugee camps collect sputum and administer DOT, the Magic Mountain facility isolates infectious TB and MDR-TB patients, and the Lifeline Hospital provides acute care. The IOM Transit Center performs pre-departure screening in Kathmandu.

The Evaluation Team found the TB screening process to be extremely efficient with a fairly strict protocol, clear direction and motivation among patients and staff. Each day, refugees are transported from camps in the early morning, triaged in a waiting area, registered and given identification cards. All refugees are photographed, fingerprinted and tracked at each step of the screening process to prevent fraud.

The medical component of the screening process includes vital signs, intakes, medical histories and blood draws of each refugee; TST for refugees <14 years of age; CXRs for adult refugees; and an examination by a panel physician. Refugees with abnormalities are referred to panel physicians. IOM completes the entire process in one day and screens ~300 refugees each day.

IOM nurses place and read TST results and have performed >4,000 TSTs to date. Of the Bhutanese refugees who have been screened to date, 15% of children <14 years of age had TST results of at least 10 mm versus ~60% of refugees >14 years of age. The Evaluation Team was impressed with IOM's placement and reading of TST results. The technique was excellent, did not deviate from the CDC procedure, and had high concordance with readings by the Evaluation Team.

A radiologist is onsite at the IOM facility seven of eight weeks. Films are electronically transferred and read in Thailand when the radiologist is absent. Digitized and hard-copy films are available and CXRs are immediately read. Prior films are compared, but a systematic quality assurance program for radiology has not been implemented at this time. The Evaluation Team reviewed >50 CXRs and reports and found IOM's imaging technique to be excellent. No significant differences were observed in the interpretation of films between the Evaluation Team and IOM radiologist.

Laboratory technicians wear N-95 respirators to collect sputum at refugee camps and observe and guide the sputum collection process. The laboratory generates a patient list and labels with identification. A photograph of each patient is placed on the collection slip. Patients are given clear instructions the day before and the day of sputum collection. Names on the list and

photographs on the collection slip are used to confirm the identification of patients. Sputum production occurs in a covered space with sidewalls and an open space at the top for ventilation. The quality of specimens is checked.

The laboratory performs acid-fast bacilli (AFB) smear, culture and rapid testing as well as first- and second-line DST. The laboratory uses the MTBDR-plus assay on all initial smear-positive sputum specimens and TB isolates. The Evaluation Team found this intervention to be tremendously useful for the laboratory to identify drug-resistant TB early. The laboratory carefully, meticulously and efficiently performed the labeling, processing, smear and isolation steps. A second technician checked positive slides. Quality control indicator reports were routinely produced and reviewed. The performance on external quality assurance measures for smears and DST was excellent.

Instead of sending separate e-mail messages to physicians for their individual patients, laboratory results were reported via group e-mail messages to all physicians. The rapid DST MTBDR-plus assay results were reported with the following language that suggested the test was not definitive: "This test assay has not been validated by US FDA. Therefore, these results are not definitive, but can be considered in the overall clinical evidence. The definitive results by validated culture testing will be provided as soon as possible." Results of conventional DST occurred only after confirmatory testing and resulted in delays in treatment. The records did not clearly indicate when a clinician learned of a positive culture or susceptibility results. Treatment changes were only made after the final conventional DST results were known.

The Evaluation Team reviewed >20 records of TB patients, including smear-positive/smear-negative cases, culture-positive/culture-negative cases, and INH-/multidrug-resistant cases. Charts also were reviewed of TB patients with cavitory disease, patients who had specific adverse events (*i.e.*, persistently sputum smear-positive), and one patient who had died. The Evaluation Team was impressed with the clinical management of TB patients. Individualized regimens were used in accordance with American Thoracic Society (ATS) guidelines. Physician examinations, smears and cultures were meticulously performed each month. CXRs were performed at three and six months at a minimum.

Prior TB treatment history in refugee camps was based on the patient report and was not available to IOM physicians. Therapy was not initiated until culture confirmation when symptoms were present and CXR findings suggested TB. Doses and treatment regimens were appropriate for the patient's weight and DST. Documentation on the patient's progress and response to treatment was extremely detailed. The duration of treatment was adjusted for cavitory disease and delayed culture conversion. Hepatitis and other complications of TB were successfully managed. Strong linkages to local specialty care providers and hospitals have been established to rapidly make appropriate referrals for patients with adverse events.

IOM procures second-line drugs from the Nepal NTP to manage MDR-TB cases only after conventional DST confirms MDR-TB and the patient is reviewed by the NTP Office. The Green Light Committee's (GLC) standardized MDR-TB regimen is used: ofloxacin, kanamycin, ethionamide, and cycloserine with pyrazinamide and ethambutol if the patient is sensitive.

Physicians conduct baseline and monthly visits at the IOM facility. The length of MDR-TB treatment and monitoring was consistent with the ATS guidelines and *MDR-TB Survival Guide*.

IOM has identified six MDR-TB cases to date and its experience in this area is limited. The treatment regimen includes at least five drugs for all MDR-TB cases. The Evaluation Team determined that IOM had outstanding attention to detail in monitoring MDR-TB patients and responding to complications. However, the Evaluation Team noted that the current second-line drug regimens are limited by the NTP regimen. Drug procurement steps IOM is required to take have resulted in delayed initiation of MDR-TB treatment.

IOM contracts with AMDA staff to deliver DOT in refugee camps. Patients bring TB drug cards with their photographs to confirm identification. The staff dispensed and observed each patient swallowing the drugs. Patients were queried about drug side effects periodically rather than regularly. DOT doses were recorded in a log in the refugee camps, but the log was not consistently used to transfer the dose record to the refugee clinical form. A systematic and routine quality assurance mechanism to monitor DOT has not been developed. Patients were in close proximity with no separation between infectious and non-infectious patients. Patients wore masks for the duration of DOT regardless of their infectious status.

The 2007 TBTIs call for evaluation of household and named contacts of active TB cases and recommend LTBI treatment only for patients <4 years of age or immunosuppressed. IOM identified TB contacts if named by the case or if the contact had the same household or family number as the case. IOM maintains a database of contacts. Because contact investigations are limited to known U.S.-bound refugees, the Evaluation Team was concerned about contacts of refugees who would not be resettled and evaluated by IOM. The contact investigations resulted in the identification of six active TB cases and 27 child contacts with LTBI who were treated with INH by DOT.

The Evaluation Team found the IOM staff to be fluent in the 2007 TBTIs and ATS guidelines. However, the staff has no in-depth or longstanding TB management experience and skills. The IOM director and staff emphasized the need for continuing education, more clinical training, regular case conferences and ongoing mentoring, particularly to address complicated TB scenarios. The refugees received education on expected outcomes in the destination country, the screening process, TB diagnosis and cough etiquette. However, knowledge of infection control issues was unclear because refugees who were no longer infectious continued to wear masks.

In 2007, 237 TB cases were identified in the Nepal refugee camps with a TB rate of 221/100,000. The diagnosis depended on clinical presentation and positive smears. Many cases were missed because CXRs and cultures were not performed for a diagnosis. Drug resistance was detected only after months of unsuccessful treatment. The NTP treatment protocol differed from the IOM protocol due to the absence of rifampin (RIF) in the continuation phase, an eight-month treatment regimen, and only two months of DOT.

IOM and AMDA jointly applied for additional DOS funding to support a harmonization project that would be designed to improve TB treatment of refugees prior to the screening examination

and provide the same standard of care to both resettling and non-resettling refugees. IOM and AMDA would use the one-year funding to identify persons with TB by signs and symptoms; collect sputum; perform smears, culture, DST and CXRs; administer DOT; and provide all TB patients with supplementary food. Records would be passed to IOM to maintain prior treatment histories of resettling refugees.

The Evaluation Team noted that the Nepal harmonization project should be replicated and broadly disseminated to other overseas TB screening and treatment programs to build capacity and enhance skills of panel physicians in other countries with large populations of resettling refugees or immigrants and a high burden of TB.

In terms of TB screening from December 2007-July 2009, IOM screened 19,914 refugees and identified 129 active TB cases. Of the 129 TB cases, 73% that were on treatment were smear-negative/culture-positive and would not have been identified with the 1991 TBTIs. Of the 129 TB cases, 2% had MDR-TB, 3% were INH-resistant, and 5% were polydrug-resistant and did not have MDR-TB.

In terms of TB treatment outcomes from December 2007-July 2009, 78% of the 129 TB cases demonstrated sputum conversion in the first month and 97% of 129 TB cases had converted by the second month. No treatment failures have been documented to date. Of 87 cases with final treatment outcomes, 91% were cured, 6% discontinued treatment due to non-TB diagnosis, 1% transferred from the program, and 1 patient died. The Evaluation Team was impressed with these outstanding treatment outcomes.

Dr. Flood reviewed the Evaluation Team's key findings of the Nepal TB screening and treatment program. Many outstanding practices were observed and a number of key areas could serve as models for other programs. The exemplary TB case detection and treatment components should be replicated, widely disseminated and published. Clinicians and staff had an impressive level of TB knowledge, consistently adhered to both the 2007 TBTIs and the ATS guidelines, and vigilantly monitored complex patients.

WHO views the Magic Mountain Isolation Centre as a major accomplishment that should serve as a model for other sites. IOM was applauded on its rapid DST use and harmonization project to detect TB and reduce the spread of disease. The IOM laboratory was found to serve as an excellent resource for the region. IOM has established solid linkages with partner organizations. The number of smear-negative/culture-positive TB cases detected demonstrated the benefit of culture. Successful treatment outcomes reflected the impact of individualized treatment based on DST and meticulous clinical management.

Dr. Flood highlighted the Evaluation Team's recommendations to IOM in the following areas. For radiology, a fulltime radiologist should be recruited and hired. A systematic quality assurance program should be developed for CXR readings. For the laboratory, the language should be changed to report rapid DST results for clinicians to quickly respond. Physicians should be notified of results for their individual patients in separate rather than group e-mail messages. The date test results are reported to clinicians should be indicated.

For clinical management, information on prior TB treatment should be systematically captured in existing electronic medical systems. Empiric treatment should be initiated in high TB suspects. Treatment should be modified at the time of the rapid DST report. Direct procurement of second-line drugs should be considered for rapid and individualized MDR-TB treatment. Expert consultation should continue to be pursued for complicated clinical scenarios. For DOT, quality assurance should be enhanced.

For infection control, directly observed preventive therapy (DOPT) for children should be separated from DOT of infectious cases. Additional education should be provided to staff and refugees on the use of masks. For contact investigations, AMDA should be encouraged to evaluate contacts of refugees who are not scheduled for resettlement. For education and training, case conferences and in-service training should be offered on a regular basis. Comprehensive TB training should be provided to the nursing and DOT clinic staff.

For capacity building, a transition plan should be created for the IOM laboratory to extend services to the surrounding community. The AMDA partnership should be continued to apply culture and susceptibility testing to all refugees to prevent the spread of MDR-TB. Results of the Nepal TB screening and treatment program should be published to inform other overseas medical screening programs of these model practices and outcomes.

Dr. Flood highlighted the Evaluation Team's recommendations to CDC in two areas. For the TBTIs, a description of rapid drug-resistant assays should be included and indications for empiric therapy should be clarified in the next iteration of the TBTIs. Steps for programs to build regional capacity and benefit from other high-burden communities should be explicitly outlined. Collaborations should be established with NTPs and WHO in efforts to implement international standards. For training and education, support should be provided for ongoing training and education of panel physicians and staff.

Dr. Flood presented a series of photographs throughout the overview of the Evaluation Team and technical consultants, the environment and living conditions in Nepal, the IOM Damak staff and screening facility, the sputum collection site at a refugee camp, the Magic Mountain Isolation Centre, administration of DOT to patients and contacts, the Kathmandu Transit Center, and the water supply and purification system to prevent illness in the refugee camps and Kathmandu Transit Center. The full evaluation report could be viewed on the NTCA website.

ACET and CDC commended the Evaluation Team on conducting a rigorous, thorough and comprehensive evaluation. Dr. Castro particularly agreed with the Evaluation Team's finding to expand the Nepal harmonization project to improve NTP activities in other areas overseas. To support this effort, he raised the possibility of presenting the harmonization project to the WHO Stop TB Team.

In response to a request by Mr. Jones, Dr. Castro explained that CDC invested ~\$35,000 for per diem and other travel costs for CDC staff and external consultants to evaluate the Nepal TB screening and treatment program.



Dr. Masahiro Narita is an ACET member and Director of the TB Control Program in Public Health-Seattle & King County. He described a study that is underway to better understand TB control in urban settings and ultimately increase knowledge of the essential components of TB control at the national level. The landscape of TB control is constantly changing. Although TB control in urban settings has unique aspects, a global approach is needed to benefit all populations affected by TB.

Because Seattle-King County had its highest number of TB cases in 2007 since 1969, the public health department partnered with DTBE and the NACCHO Infectious Disease Committee to develop and implement a study on TB control in urban settings. The literature review for the study showed that urban environments might affect population health, particularly the dynamics of TB control. Population density and large marginalized populations in urban environments also might be linked to poor health.

The study methods included selecting the 100 most populated U.S. cities according to the 2000 census; analyzing 48 cities that reported at least 20 TB cases each year from 2000-2007; and applying the Joinpoint regression model to determine significant trends in TB case rates in each of the 48 cities from 2000-2007. Dr. Narita's summary of the general findings of the study is outlined below.

The 48 cities included in the study ranged in population from 207,000-8.1 million persons based on population projections in 2000. The average number of annual TB cases for the 48 cities was 111 with a median of 66 cases in each city and a range of 26-1,075 cases among the cities. The average TB rate of the 48 cities was 12.8/100,000 with a median of 11.5/100,000 in each city and a range of 4.5-32.1/100,000 among the cities. The average incidence rate in the United States excluding the 48 cities was 5.1/100,000 over the same time period.

The sum of TB case counts in the 100 most populated U.S. cities represented 41% of the U.S. TB case burden, but only 20% of the U.S. population. The 48 cities included in the study represented 36% of the U.S. TB case burden, but only 15% of the U.S. population. None of the 48 cities demonstrated a statistically significant increasing TB case rate from 2000-2007 and 19 cities showed a significantly decreasing TB case rate. The remaining 29 cities showed no significant change in TB case rates. Differences between the 19 cities with success in decreasing TB case rates and the 29 cities with no significant change in TB case rates need further study.

Of the TB patients in the 48 cities, 63% were male, 35% were AAs, 28% were Hispanic, 24% were Asian, 56% were foreign-born, and 21% had HIV co-infection. Compared to the remainder of the United States, the 48 cities experienced a rate of decline in TB case rates that was three times faster and the same rate of decline in TB case counts. A decline in TB case rates is a significant indicator of successful TB control efforts, while the case count impacts the burden to TB control programs.

Bivariate analyses were performed and showed that cities with decreasing case rates had significantly higher numbers of foreign-born, Asian and AA populations, TB/HIV co-infection, injection drug use and MDR-TB. Cities with decreasing case rates had significantly lower numbers of homeless persons, incarcerated populations and excessive alcohol use. Positive sputum smear results and evidence of cavitory disease on CXR were two major indicators of advanced TB disease.

Both the cities with decreasing and non-decreasing TB case rates had a 45.9% proportion of sputum smear-positive cases. Cities with decreasing TB case rates had a 23% proportion of cavitory disease compared to a 28.6% proportion in cities with non-decreasing TB case rates. The use of DOT and completion of TB therapy were lower in cities with decreasing case rates. These data indicated that cities with success in decreasing TB case rates might use DOT more judiciously and place more emphasis on community engagement and other TB control activities.

ACET commended CDC, NACCHO and the Seattle-King County researchers for developing and implementing the well-designed study of TB control in urban settings. The ACET members made two key suggestions to consider in refining the study.

First, CDC and the researchers should consider the possibility of expanding the study to include mixed areas with high-density urban and low-density rural populations. Second, CDC and the researchers should perform a cluster analysis with genotyping to determine differences in sputum smear-positive cases and cases with evidence of cavitory disease between the cities with decreasing and non-decreasing TB case rates.



Dr. Dolly Katz, of DTBE, informed ACET of FBWG's progress on revising CDC's 1998 "Recommendations for Prevention and Control of Tuberculosis Among Foreign-Born Persons. ACET recommended establishing the FBWG to revise the guidelines because TB rates have only modestly decreased in FBPs since CDC first began tracking TB incidence by country of origin in 1986. However, TB rates have significantly declined in U.S.-born persons since that time.

The differential success of decreased TB rates between U.S.-born persons and FBPs is primarily due to TB control strategies in the United States. The most successful strategies have focused on recent transmission, including early diagnosis and treatment of TB disease; screening and treatment of recently infected contacts; and targeted testing and treatment of persons at high risk for LTBI.

CDC acknowledged the need for a new approach to TB control in FBPs because the two most broadly implemented strategies have not significantly impacted the incidence of TB among FBPs. Moreover, LTBI treatment has not been widely implemented for FBPs. Most foreign-born TB cases are due to reactivation of infection acquired prior to arrival to the United States. The 6.9 million FBPs with LTBI must be addressed to achieve TB elimination.

FBWG convened a meeting in July 2009 with key members of its writing group to reach consensus on the major recommendations in the revised guidelines. The ten-member consensus panel agreed on issues in three major categories. One, what FBPs should be screened? The consensus panel agreed that each individual born in a TB-endemic country should be screened at least once for LTBI.

This recommendation would include all persons born in every foreign country with the exception of Australia, Canada and Western Europe. The consensus panel further recommended conducting screening primarily as part of routine health maintenance for persons seeking medical care in primary care settings rather than during health department outreach efforts.

Two, what methods should be implemented to screen FBPs? The consensus panel agreed that IGRAs are the preferred screening method for most FBPs due to their higher specificity in persons who have received BCG vaccination.

Three, what FBPs should be treated after LTBI has been tested and identified? The consensus panel agreed that the following FBPs should be treated for TB: FBPs who have been in the United States for less than five years; FBPs  $\leq 35$  years of age; FBPs living in universities or other institutional/congregate settings; foreign-born members of national groups (*i.e.*, FBPs from Ethiopia and Somalia) with extremely high TB rates even years after arrival to the United States; and FBPs at high risk of disease progression due to other medical risk factors, such as diabetes or end-stage renal disease.

The consensus panel also reached agreement on two other areas of the revised guidelines. For FBPs who have LTBI and lack other risk factors, the decision for physicians to provide or not provide treatment should be based on an individualized decision after consultation with the patient, discussion of the risks and benefits of treatment, and the likelihood of the patient completing treatment. For foreign-born patients physicians elect not to treat, education should be provided about the symptoms of TB, future risk of developing active TB, and the development of diabetes or other situations in which the decision should be reevaluated.

Dr. Katz concluded her update by noting that FBWG only needs to conduct two key activities before finalizing and submitting the revised guidelines to the CDC clearance process. Input would be obtained from ACET. The process to edit and compile supporting sections (*i.e.*, descriptions of procedures for overseas examinations of immigrants and refugees) would be completed. The revised guidelines were distributed to ACET for review.

ACET commended FBWG on its tremendous progress in further revising and improving the updated guidelines on TB control in FBPs. The ACET members asked FBWG to consider and engage in additional dialogue to clarify the following issues before the revised guidelines are finalized:

- The recommendation to treat FBPs  $\leq 35$  years of age for TB.
- Roles and responsibilities in both the public and private sectors for educating providers and the community on the revised guidelines.

- A process to determine the competency, skills and knowledge of physicians in treating FBPs for TB.
- The need to develop a health screening policy, including TB screening, for foreign-born students who attend universities in the United States.
- The need to develop an implementation guide for the revised guidelines.



Mr. Dan Reyna is the General Manager of the U.S. Section of the U.S.-Mexico Border Health Commission (BHC). He explained that the Workgroup was established in 2002 with an initial focus on TB cases under the jurisdiction of Immigration and Customs and Enforcement (ICE). Since that time, the Workgroup's focus and scope have been expanded to include cross-jurisdictional and transnational issues. The Workgroup's informal membership includes >50 persons and a Legal Issues Subgroup.

Mr. Reyna summarized the Workgroup's key accomplishments to date. Collaborations were established with several groups to create policies and procedures to address transnational TB continuity of care for ICE detainees: the Division of Immigration Health Services (DIHS), state and local TB programs, the Migrant Clinicians Network to implement the TBNet Program, and the San Diego County Health Department to implement the CureTB Program. These procedures were incorporated into national guidelines and plans.

Outreach was provided to state and local TB control programs on collaborative efforts to facilitate continuity of care for TB patients in ICE custody, particularly those housed in local jails or contract detention facilities without DIHS staffing. Collaborations were established among the four U.S. states that border Mexico to gain understanding of cross-jurisdictional legal issues and help identify solutions for patients who cross-jurisdictional boundaries.

Collaborations were established with BHC to gain understanding of the legal issues for patients, including those who are repatriated, who move between the United States and Mexico. A U.S. Border State Legal Issues Forum was co-sponsored in partnership with BHC in October 2007. A proposal has been submitted to co-sponsor a Binational Legal Issues Forum in 2010 in partnership with BHC.

The Workgroup is focusing on four priority issues at this time. One, solutions are being identified to address for MDR-TB and other medically complex patients who are scheduled for repatriation and are not good candidates for treatment and case management in their countries of nationality. These patients might be eligible for requesting a stay of removal, but not for retention in custody. Options would be limited in these instances if state or local jurisdictions are unable or unwilling to continue treatment after the TB patient is released in their jurisdictions.

Two, outreach is being provided to more local jurisdictions where DIHS has no presence to facilitate continuity of care for ICE detainees housed in local jails nationwide. Three, collaborations regarding cross-jurisdictional TB case management, including legal issues,

between the United States and Mexico. Four, collaborations are being continued with BHC on these issues.

Mr. Reyna highlighted several issues that need to be addressed related to the transition of the Workgroup. Dr. Diana Schneider formerly chaired the Workgroup, but has left employment with DIHS for a position HHS. The Workgroup requested guidance from ACET to ensure its continuity and identify a new chair or co-chairs. The Workgroup also asked for a DTBE staff member to serve as a co-chair.

The role and responsibilities of the Workgroup chair or co-chairs are to convene meetings via conference call; prepare and disseminate meeting summaries or minutes; maintain current participant and distribution lists; coordinate or delegate leads for special projects; and serve as the point of contact for communications among the participants.

In response to Mr. Reyna's request for guidance, Dr. Fleenor confirmed that ACET would revisit the transition of the Workgroup at a future meeting.



Dr. Sha Juan Colbert, of DTBE, reported on AAWG's efforts to develop a "Strategic Plan to Reduce Racial/Ethnic Health Disparities in Tuberculosis." TB rates among Asians, AAs and Hispanics are 23.4, 8.1 and 7.5 times higher than those of non-Hispanic whites, respectively. In an effort to address these health disparities, AAWG is developing a Strategic Plan with three major components.

The "community awareness and outreach" component would include the following activities. A council or advisory board would be established with representatives from all sectors of the community in states with high rates of TB in AA populations. Culturally appropriate standards of care and other products for the medical community would be created and widely disseminated. Television and radio media campaigns would be launched to raise awareness on TB/HIV disparities. Best practices from other disease programs would be replicated. Celebrities and other noted figures would be recruited to educate the public on TB in the AA community.

In the "research" component, data would be collected on the epidemiological impact and consequences of socioeconomic status (*i.e.*, poverty and employment), segregation and unstable housing. Data also would be gathered on the impact of education and educational attainment on health literacy and disparities.

The "protocol and guidelines" component would include the following activities. Culturally appropriate and appealing fact sheets would be disseminated. CDC's screening, diagnostic and treatment algorithms for TB and LTBI as well as other appropriate materials would be distributed to providers and other sectors of the medical community in target areas.

The “Working Together to STOP TB Toolkit” would be developed and broadly distributed to AA providers and others who serve the AA community. The toolkit would include posters to be placed in physician waiting rooms and other targeted settings; fact sheets for specific project areas; and templates and other resources to raise awareness to educate and mobilize communities. Products developed by the Chicago, Georgia and South Carolina project sites would be disseminated to areas with high rates of TB in the AA community.

Several activities are underway and additional projects have been proposed to advance the development of the Strategic Plan. In the current activities, the toolkit is being designed to help communities build group discussions and coalitions to more effectively reduce TB disparities in the AA community. The Southeastern National TB Center is evaluating the current version of the toolkit.

DTBE is continuing to widely disseminate TB fact sheets and also maintain and update the “Stop TB in the African American Community” website and electronic mailing list. All of the current activities are consistent with findings in two TBESC task orders: Task Order 11: “Addressing TB Among African Americans in the Southeast: Identifying and Overcoming Barriers to Treatment Adherence for LTBI and TB Disease” and Task Order 23: the “National Study of Determinants of Early Diagnosis, Prevention and Treatment of TB in the African American Community.”

In the proposed activities, a research study would be conducted to determine TB diagnostic decision-making of physicians who treat AA patients. The mixed method study design would include an evaluation of provider behaviors to identify factors contributing to misdiagnosis or delayed diagnosis, focus groups and key informant interviews. A “National TB Educational Campaign for Physicians” would be launched by making presentations at national, state and local conferences (*i.e.*, National Medical Association, Black Nurses Association and HRSA-funded community health clinics) and also developing and distributing educational materials.

Dr. Colbert emphasized that TB in U.S.-born populations requires sufficient and responsible attention, but a significant amount of time is needed to develop the proposed projects and products. Moreover, dedicated staff and follow-up are lacking in ongoing efforts to address TB in U.S.-born populations.

ACET advised AAWG to take a number of actions to inform the development of the Strategic Plan to Reduce Racial/Ethnic Health Disparities in Tuberculosis.

- AAWG should use the NCHHSTP PCSI Initiative to engage other partners (*i.e.*, child and maternal health programs, chronic disease programs and community coalitions) in more effectively addressing TB issues that are persistent in and unique to the AA population. These programs could be extremely useful in leveraging opportunities to include TB screening as a routine part of care when providers screen AA patients for chronic diseases or other infectious diseases (*i.e.*, HIV, STDs, hypertension or diabetes).
- AAWG should collect data from other sources to enhance the research component of the Strategic Plan. First, TB-specific and age-specific mortality rates among AAs >45-50 years of age in the ongoing mortality study would be extremely useful. Second, a

graphic display of TB-GIMS data by location would be helpful in identifying and quantifying TB clusters among AAs in specific communities. Third, mapping data and cross-matching data from diabetes and other state registries would be valuable in determining relationships among TB, HIV, and other infectious and chronic diseases. These data also could play an important role in locating high-risk patient groups and their healthcare providers. Fourth, the latest version of the Joinpoint analytic software would make a significant contribution to analyzing important trends in TB case rates and making comparisons between U.S.-born minority populations.

- AAWG should collaborate with AA coalitions and other stakeholders that are currently making efforts to ensure racial/ethnic health disparities are a prominent component in the National HIV/AIDS Strategy. This approach could help to increase awareness and provide education on TB in the AA population at the high level of the White House Office of National AIDS Policy.
- DTBE should advise the Southeastern National TB Center to use the evaluation of the toolkit as an opportunity to determine whether this resource could be used to build and sustain community coalitions over time.

During the next meeting of the NCHHSTP Health Disparities Workgroup, Dr. Dean advised Dr. Fleenor to raise the possibility of CDC developing TB screening guidelines for U.S.-born minorities at high risk for TB, particularly AAs and Hispanics. Dr. Dean agreed with AAWG's approach to replicate and apply best practices and lessons learned from other disease programs in the community awareness and outreach component of the Strategic Plan. She noted that the HIV community has been extremely successful in establishing solid partnerships to more effectively address HIV in high-risk subgroups of the AA community.

Dr. Dean advised AAWG to ensure that the TB Health Disparities Strategic Plan was consistent and aligned with the NCHHSTP Strategic Plan. She pointed out that the "Health Equity" section also emphasizes social determinants of health.



Dr. Elsa Villarino, of DTBE, reported that the Workgroup convened its latest conference call in September 2009. She provided an update on the Workgroup's progress in developing guidelines for "TB Prevention and Control Measures for U.S. Health Care Workers and Volunteers Serving in High-Risk Settings for Exposure to *Mycobacterium Tuberculosis*."

ACET and the CDC Advisory Committee on Immunization Practices (ACIP) published joint guidelines in 1996 on the use of BCG in the following situations: (1) prevention of TB in children continuously exposed to MDR-TB and (2) prevention of TB in HCP in the United States when a high percentage of TB patients are infected with MDR-TB; transmission of drug-resistant TB to HCP and subsequent infection are likely; and infection control measures are implemented, but are not successful in preventing TB transmission.

ACET established and charged the Workgroup with conducting the following activities. The Workgroup would review the 1996 BCG vaccine guidelines due to changes in TB epidemiology globally as a result of the increasing incidence of MDR-/XDR-TB. The Workgroup would review the 1996 BCG vaccine guidelines because of increased humanitarian efforts and university research programs that support activities by HCP, volunteers and students in high-risk populations overseas.

The Workgroup would consider four key issues in its review of the 1996 BCG vaccine guidelines: (1) inadequate or incomplete implementation of infection control measures; (2) transmission of TB in healthcare facilities among HCP and patients; (3) the role of HIV in amplifying TB; and (4) the availability of IGRA as a diagnostic tool for LTBI in eliminating concerns of false-positive TST results due to BCG.

Dr. Villarino summarized the overall structure and specific sections of the guidelines for TB prevention and control measures for U.S. HCP and volunteers serving in high-risk settings overseas. The guidelines would propose BCG vaccination as only one of several interventions. The background section would provide only a minimal amount of information to identify the problem and update previous BCG recommendations.

Most of the guidelines would focus on the evaluation, education and management of persons considered at risk for exposure. The risk for TB among HCP and the epidemiology of TB and MDR-TB globally would be discussed. An update would be provided on the efficacy of BCG, strategies to obtain the vaccine and methods to administer the vaccine.

Specific action steps would be described for the management of TB among at-risk HCP and humanitarian volunteers overseas. These approaches would cover *M.tb* screening prior to the overseas trip, education, fit-testing of respirators, infection control strategies that are likely to be available in low-resource countries, suggestions on minimizing personal risk in these areas, and BCG risks and benefits. Providers would be informed of necessary elements in an appropriate evaluation of travelers after their return to the United States, (*i.e.*, treatment of LTBI if the traveler has newly positive TB based on TST or IGRA results and consideration of risks for exposure to drug-resistant TB).

Dr. Villarino announced that the draft guidelines were submitted to the *MMWR* for publication. The Workgroup would distribute this version to ACET for review and comment by the first meeting in 2010. The Workgroup has established December 2010 as the deadline to publish the guidelines.

ACET fully supported the Workgroup's shift from the narrow focus on BCG vaccination to the broader scope of TB prevention and control measures for U.S. HCP and volunteers serving in high-risk settings overseas. ACET noted that the guidelines would serve as a valuable resource in providing HCP and volunteers with effective strategies and interventions to protect themselves from TB and other respiratory viruses in overseas high-risk settings.

Because the guidelines could be extremely beneficial at this time, ACET questioned whether the Workgroup could accelerate its efforts to compile data, finalize the guidelines and publish the

document prior to December 2010. ACET urged DTBE to dedicate a full-time staff member to assist the Workgroup in more quickly finalizing and publishing the guidelines.

Based on ACET's comments, Dr. Castro encouraged the Workgroup to expedite the publication of the guidelines before December 2010. He pointed out that an article was published in 2008 in the *Journal of Travel Medicine* documenting the excess risk for TB among Peace Corps volunteers who returned to the United States. He conveyed that the 2008 article emphasizes the timeliness of the guidelines and the critical need to publish the document as soon as possible.



Ms. Freddie Poole is the Associate Director of the Division of Microbiology Devices in the FDA Center for Devices and Radiological Health, Office of *In Vitro* Diagnostic Device Evaluation and Safety. She explained that FDA's mission is two-fold: (1) promote public health by promptly and efficiently reviewing clinical research and taking appropriate actions in marketing regulated products in a timely manner and (2) protect public health by reasonably ensuring the safety and effectiveness of devices intended for human use.

FDA's regulatory authority is from the 1938 Food, Drug and Cosmetic Act; the 1976 Medical Device Amendment; the 1990 Safe Medical Devices Act; and the FDA Modernization Act. FDA has regulatory authority over three categories of devices. Class I devices include general controls, such as good manufacturing practices, registration, listing and record-keeping. Test results of Class I devices do not support life, prevent impairment of health, or present unreasonable risks for illness or injury.

Class II devices include general controls that are insufficient and require specific controls, such as guidance documents, labeling regulations and required standards. Class III devices include tests that are critical to the diagnosis of disease and test results with a risk for misdiagnosis leading to illness or injury. Class III devices require valid scientific evidence, such as well-controlled clinical trials.

In May 1980, FDA classified *M.tb* immunofluorescent reagents as Class I devices based on the findings of its advisory panel. The recommendation was based on general controls outlined in Class I devices, clinical experience of the FDA advisory panel with the type of device, and the potential of these reagents to mitigate risks to health.

In July 1994, FDA received its first nucleic acid amplification test (NAAT) for detection of *M.tb*. In September 1994, the Director of the FDA Center for Devices and Radiological Health made a decision to characterize NAATs as Class III devices due to potential safety and effectiveness issues; the substantial importance of NAATs in the diagnosis and treatment of life-threatening illnesses; and the ability of NAATs to test and target new populations with polymerase chain reaction-positive tests in asymptomatic persons.

The rationale for FDA's pre-market approval (PMA) of Class III devices is outlined as follows. New safety and effectiveness issues were raised that were not present in previous DNA probe tests, such as AccuProbe and SNAP *M.tb* Complex. NAATs were used as cultured isolates from symptomatic patients and were based on specimens collected directly from patients or asymptomatic patients. Bronchial aspirates, bronchoalveolar lavages, tracheal aspirates and other types of specimens could be used if sputum specimens were not available. Data had not been produced in the past to evaluate these types of specimens for the significance or presence of *M.tb*.

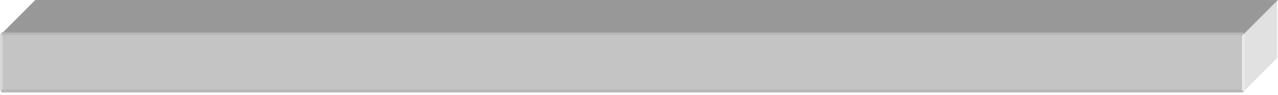
FDA decided to require PMA for Class III devices because previous Class I and II data showed that NAATs were safe, effective and equivalent to FDA legislation. However, Class III devices are a significant improvement over Class I and II devices due to the requirement for well-controlled clinical trials, the need for the device to stand on its own and compare to standard reference methods, and a history of reasonable safety and effectiveness evidence (*i.e.*, the impact of erroneous results on patient management). PMA must demonstrate that the subject device has clinical utility as a diagnostic tool, can serve in another capacity, or can provide data to measurably contribute to a diagnosis of disease or condition.

For Class III devices, the PMA process requires manufacturers to pass pre-approval inspections of their Bioresearch Monitoring Programs, adhere to good manufacturing practices, and comply with annual reporting requirements to notify FDA of failures or changes to devices. Moreover, manufacturers are required to conduct clinical studies to demonstrate the safety and effectiveness of Class III devices; support the intended use, conditions for use and indications of these devices; and validate that the probable benefit of the test results would outweigh any foreseeable misdiagnosis. Clinical trials for Class III devices must be conducted under a unified multi-site study protocol and Declaration of Helsinki ethical principles for foreign research if applicable.

PMA is further required for the detection of *M.tb* directly from clinical specimens with NAAT. FDA has collaborated with manufacturers that have developed Class II NAATs from cultured isolates and also has developed a pre-investigational device exemption process to facilitate the review process. FDA reviews each request and provides recommendations in a timely manner.

Dr. Max Salfinger is the ACET liaison to the Association of Public Health Laboratories (APHL). He emphasized the need for FDA to reverse its 1994 decision to characterize NAATs as Class III devices. Based on the collection of recent, solid and valuable data, CDC now recommends universal NAAT for respiratory testing and WHO now recommends line-probe assays to test for drug resistance on smear-positive specimens. Dr. Salfinger noted that the FDA requirement places a tremendous burden on public health laboratories because NAAT methods and equipment for TB versus those for gonorrhea or chlamydia are different.

In response to Dr. Salfinger's comments, Ms. Poole explained that APHL or other professional organizations, industry and citizens are free to submit a petition to FDA to change the classifications of devices based on the availability of valid supporting data.



**Dr. Fleenor** chaired the panel that conducted the external peer review of the DTBE Mycobacteriology Laboratory Branch (MLB) in August 2009. He reported that MLB staff presented its ongoing activities and accomplishments over the past few years. The panel then met in a closed session to discuss MLB's successes and recommend actions that MLB should take to improve performance in achieving DTBE's goals and objectives.

The panel formulated recommendations for the external peer review in four major categories: the alignment between MLB's activities and DTBE's mission, goals and objectives, MLB's strengths, MLB's weaknesses, and MLB's activities that need to be modified. The panel advised MLB to use this structure as an ongoing and iterative quality improvement model for external peer reviews in the future.

The panel also focused on three key questions to develop recommendations for the external peer review: (1) Is MLB conducting appropriate activities with the best methods or approaches? (2) Is MLB's structure primarily driven by function or form (*i.e.*, inherent bureaucracy)? (3) Has MLB's laboratories activities been fully integrated into DTBE's mission, goals and objectives for TB control, TB research and TB elimination in the United States?

The panel found MLB's strengths to be in the areas of outbreak investigations; support to states, public health laboratories and other partners across the country; provision of education to communities; genotyping and applied research; establishment of linkages between TBESC epidemiological research and laboratory activities; molecular antibiotic research and improved laboratory capacity.

**Ms. Bonnie Plikaytis** is the Acting Chief of MLB. She presented MLB's formal response to the panel's recommendations in the other three categories: the alignment between MLB's activities and DTBE's mission, goals and objectives, MLB's weaknesses, and MLB's laboratory activities that need to be modified.

MLB was transferred to DTBE in 2004. The Global Laboratory Activity was formed in 2008 with new leadership in MLB and additional organizational changes were made in 2009. NTM services were transferred from DTBE to the Division of Healthcare Quality and Promotion. Molecular detection of drug-resistant services for isolates were evaluated, implemented and made available to U.S. public health laboratories. A cohort was formed with three TB laboratory consultants.

MLB leadership reviewed and made an effort to align all laboratory activities and the laboratory research agenda with DTBE's mission, goals and objectives. MLB's internal process included a methodical review of each topic, engagement of the DTBE Office of the Director and other branches as appropriate, and prioritization of the most critical topics. MLB would develop metrics to measure the effectiveness of these changes over time.

The panel's major recommendation was for MLB to undergo a strategic process to fully align its laboratory activities with DTBE's mission, goals and objectives. The panel also advised MLB to become more of a full partner with DTBE, apply the peer review recommendations to actual practice, develop process and outcome metrics to measure the effectiveness of changes over time, and more fully engage external partners in laboratory activities.

In response to these recommendations, a new DTBE policy was developed, vetted and implemented in September 2009 for engagement with MLB. The policy formalized interactions between DTBE branches and MLB; defined MLB's scope of work and funding sources; and allowed MLB to prioritize its laboratory activities according to DTBE's mission, goals and objectives.

The panel made recommendations for improvement of MLB in four distinct categories. The category 1 recommendations focused on personnel and funding resources. The panel determined that MLB has leveraged limited financial and personnel resources for maximum return. The panel emphasized the need for adequate resources to facilitate MLB's full integration with DTBE and alignment with DTBE's mission, goals and objectives.

In response to the category 1 recommendations, MLB has identified and communicated its resource needs to the DTBE Office of the Director. MLB acquired significant additional funding and personnel in 2009. In the future, MLB would continue to communicate its personnel and funding needs; justify requests for resources that are linked to DTBE's mission, goals and objectives; and monitor performance and remain accountable for all resources entrusted to MLB.

The category 2 recommendations focused on linkages. The panel advised MLB to form broader internal collaborations with CDC professionals and improve external relationships with the wider laboratory community in the United States, including private laboratories, APHL, and public health TB programs and clinicians. The panel advised MLB to communicate and coordinate with other global laboratory activities.

In response to the category 2 recommendations, MLB would encourage staff to continue to participate in CCID initiatives and collaborative research with other CDC laboratories. MLB would use its cohort of TB laboratory consultants to enhance linkages with U.S. public health laboratories and state TB control programs. CDC and APHL recently launched a joint project to survey public and private services to strengthen jurisdictional laboratory networks. MLB would make stronger efforts to define and clarify its support of global activities and research. MLB would communicate these initiatives to DTBE and others involved in global laboratory activities.

The category 3 recommendations focused on capacity building. At the internal level, the panel advised MLB to develop a succession plan and create individualized personnel development plans. At the external level, the panel advised MLB to offer training and educational programs to build capacity in commercial and state public health laboratories. The panel encouraged DTBE to allocate funds to support MLB's training activities.

In response to the category 3 recommendations, MLB would develop a succession plan and use CDC's individual learning accounts to create individualized personnel career plans for staff through internal or external training opportunities and conferences. MLB senior personnel would continue to provide mentoring to and include junior staff on laboratory projects to enhance management skills.

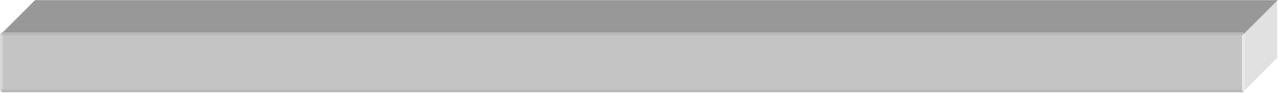
For external capacity building, MLB would conduct a course on the laboratory aspects of TB in early 2010 in conjunction with the National Laboratory Training Network. MLB also would broadcast webinars on pertinent laboratory topics, including molecular diagnostics for drug resistance. DTBE identified training as a core function of MLB and included funds for training activities in the annual MLB budget. The DTBE budget has a line item to support travel of one representative from each state laboratory to attend the annual NTCA meeting.

The category 4 recommendations focused on research. The panel advised MLB to ensure its research is explicitly linked to DTBE's "Translating Research into Practice" (TRiP) Initiative. The panel advised MLB to fully align its research efforts with DTBE's goal of effectively reducing and eventually eliminating TB in the United States. The panel advised MLB to reexamine its other research efforts, particularly vaccine research, as a function of MLB. If these research efforts remain part of MLB's scope of work, the panel noted that the activities should be cost neutral and funded through external sources.

In response to the category 4 recommendations, MLB would ensure that its primary research emphasis remains directly linked to DTBE's TRiP Initiative, particularly in the areas of genotyping, mechanisms of drug resistance and molecular diagnostics. CCID, DTBE and MLB have made substantial investments in vaccine research. The Georgia Research Alliance is allocating funding to support MLB's current vaccine research projects. Principal investigators also are seeking additional funds from external sources.

Ms. Plikaytis thanked the panel for conducting an external peer review that was extremely informative and useful to MLB in determining its future directions. She confirmed that the peer review report would serve as a valuable resource for MLB's future advocacy efforts.

ACET commended MLB on providing its formal response to the external peer review in a timely and efficient manner. Several ACET members noted that the changes MLB has made over the past year in terms of its organizational structure, improved laboratory support and services, and formation of the cohort of TB laboratory consultants have been tremendously beneficial to the field. The ACET members also pointed out that MLB's changes have played a critical role in strengthening relationships between TB programs and laboratories at the state level.



**Prevention of Future TB Cases.** Dr. Colbert reported that this flagship project is being proposed to address one of DTBE's five priorities: interrupt transmission and prevent future cases of TB. The project hopefully would address another DTBE priority to reduce TB in U.S. racial/ethnic minorities.

The LTBI Workgroup was established in May 2009 with representatives from each DTBE branch, DTBE field staff and NTCA. The Workgroup reviewed an inventory of current DTBE initiatives to identify existing gaps and determine activities that would be appropriate for the proposed project. This effort provided the Workgroup with an opportunity to identify completed activities and efforts that should not be replicated. The Workgroup continues to hold weekly meetings.

The Workgroup developed the concept for the project by first conducting a comprehensive literature review. Data show that 9-14 million persons in the United States have LTBI at this time. Poor completion rates among persons who are prescribed LTBI treatment play a major role in the conversion from LTBI to TB disease. A 2006 study showed that of 91.2% of 1,723 LTBI patients who were offered and accepted treatment, only 38.6% actually completed treatment. Data CDC collected in 2006 showed that of 72% of smear-positive contacts with an LTBI diagnosis who started treatment, 66% completed treatment.

Because patients are challenged by taking medication for an asymptomatic condition, the Workgroup designed the project to achieve four key objectives. Assistance would be given to providers in targeting patients who might benefit from enhanced adherence. LTBI treatment completion rates would be increased. The needs of hard-to-reach populations would be addressed. Dialogue would be initiated to explore strategies to address non-adherence to LTBI treatment.

The Workgroup proposes to conduct the project in multiple phases over five years. Phase 1 would focus on building infrastructures of the project sites in year 1 (2010). The funded project sites would be required to develop a strategic action plan to identify persons with LTBI who are at high risk for converting to TB disease. The project sites also would be required to test for LTBI, administer treatment, develop strategies and tools to ensure adherence, and conduct follow-up through outcome assessments.

Phase 2A would focus on performing an adherence risk assessment in year 2 (2011). This phase would be designed to create a more systematic approach to understanding enhanced adherence techniques in programs. A tool also would be developed to better assess the likelihood of persons not adhering to LTBI treatment. Prospective and retrospective cohort study designs would be used to validate the tool. The tool would be designed as a helpful resource to assist TB control programs in allocating resources. During this phase, other tools would be developed to create patient-centered and patient-tailored enhanced interventions for LTBI treatment.

Phase 2B would focus on implementing an adherence intervention in high-risk groups in years 2-5 (2011-2014). This phase would be designed to achieve two key outcomes. Local health department capacity would be expanded and strengthened to identify populations at high risk for LTBI and groups with high rates of non-adherence to LTBI treatment (*i.e.*, homeless persons and substance abusers). Medication adherence services would be provided for persons who are candidates for LTBI treatment and have substance abuse disorders.

Phase 3 would focus on administering a shorter medication regimen in years 3-5 (2013-2014). This phase would be designed to compare adherence rates among high-risk groups based on the availability of funding and short-course LTBI treatment.

Dr. Colbert concluded that the proposed project is providing the Workgroup with a solid opportunity to focus on special populations (*i.e.*, non-adherent, substance abuse and homeless populations). The project also serves as a model of strong internal and external collaborations, effective communications and efficient teamwork. She requested ACET's input on the strengths and weaknesses of the proposed project and whether the direction of the project is appropriate. At this point, DTBE senior leadership has not approved the project and a principal investigator has not been identified.

Several ACET members were challenged by providing guidance in response to Dr. Colbert's request for input on the flagship project to prevent future TB cases. The ACET members noted that the organizational structure to conduct the project has not been articulated and the overall process for DTBE to select and fund any of the flagship projects has not been clearly defined. Other ACET members expressed concern about the potential for the project to duplicate efforts because LTBI might be a major research focus in the new cycle of TBESC.

Some ACET members were divided on whether the five-year timeline of the project was appropriate or too lengthy. On the one hand, some ACET members believed the timeline should be shortened. For example, Phase 1 of the project (infrastructure building) could be accelerated if the Workgroup analyzed evaluation plans submitted by TB control programs to CDC in the last five-year cycle of the cooperative agreement. The Workgroup could compile and distribute these data to the funded project sites because many of the 67 evaluation plans submitted by grantees described strategies to address adherence to LTBI treatment.

On the other hand, some ACET members believed the timeline should be maintained. LTBI has a lengthy incubation period of two to three years before conversion to TB disease. Moreover, time would be needed to develop and sustain partnerships with TB controllers and other organizations that have established strong relationships with hard-to-reach groups at high risk for LTBI, such as homeless persons and substance abusers.

Some ACET members questioned the true value and need of the project because most of the research issues the project proposes to address are already known. For example, the vast majority of TB controllers have extensive knowledge of their high-risk groups, reasons for non-adherence to LTBI treatment, effective strategies to increase adherence, and staffing that would be needed to track and treat homeless persons and other high-risk groups. However, none of this knowledge could be applied to actual practice without funding streams to prioritize LTBI in TB control programs. The ACET members hoped the project would help to generate serious investments in increasing adherence to LTBI treatment to prevent future TB cases.

The ACET members made a number of specific comments and suggestions in response to Dr. Colbert's request for input on the proposed project.

- The Workgroup should explore creative strategies to engage the community in some of the activities proposed for the project. For example, public health departments could allocate funding for lay community workers to administer the three-month INH/rifapentine (RFP) regimen to LTBI patients through DOT.
- The Workgroup should not design prescriptive tools for states to use in improving LTBI treatment completion rates. Instead, broad templates should be developed for states to use in creating tools to address specific LTBI needs at the local level. DTBE should then compile and disseminate the most effective and successful state-specific tools as best practices in LTBI.
- DTBE should select and fund the project sites based on states that have no existing infrastructure or have made minimal progress in addressing LTBI (*i.e.*, Arkansas and Mississippi).
- The Workgroup should review case records maintained by public health departments to collect solid data on reasons patients do not complete LTBI treatment. This information could be gathered from case management notes taken by public health managers.
- The Workgroup should review experiences from the HRSA “Disease Collaboratives.” The self-management component of this initiative has been extremely successful in empowering patients who are homeless, migrant farmworkers or substance abusers to take personal responsibility in improving their diabetes outcomes. Lessons learned from HRSA’s project could be extremely valuable to CDC’s proposed LTBI project because both initiatives target the same populations.

Dr. Castro confirmed that the Workgroup and DTBE would thoroughly consider all of the concerns, comments and suggestions ACET raised during the discussion. He made several remarks for the Workgroup to consider in refining the project. The shorter four-month RIF regimen should be included in Phase 3. This regimen would be effective for persons who are intolerant to INH or those who have been exposed to persons with INH-resistant TB. A recent meta-analysis found the four-month RIF regimen to be safe and well tolerated.

Dr. Castro agreed with ACET that opportunities exist to shorten the five-year timeline of the project. For example, TBTC Study 26 is comparing a weekly regimen of RFP/INH for three months versus a daily regimen of INH for nine months for LTBI treatment. The Workgroup has proposed initiating Phase 3 of the project in 2013, but DTBE expects to produce reliable results from Study 26 on the efficacy and safety of the shorter RFP/INH regimen in late 2010 or early 2011.

**Rapid Detection of Drug-Resistant TB in High-Risk Persons.** Dr. Peter Cegielski, of DTBE, reported that DTBE initiated a strategic planning process in 2008 to develop broad-based and collaborative projects to address the top priorities for TB elimination, including mitigating the impact of MDR-/XDR-TB. DTBE convened a series of retreats in which senior staff identified, discussed and reached consensus on LTBI and drug-resistant TB serving as the two major topics for the flagship projects. Workgroups were established to develop proposals for the two flagship projects.

The Drug-Resistant TB Workgroup was established in June 2009 with representatives from the DTBE Office of the Director and each branch, DTBE field staff and NTCA. The Workgroup

reviewed an inventory of current DTBE projects related to drug-resistant TB; solicited creative and innovative ideas on potential projects; and iteratively discussed and consolidated the ideas into two specific proposals focusing on rapid TB diagnosis domestically and internationally. During this process, the Workgroup maintained communications with DTBE leadership and senior staff through interim progress reports, consultations and requests for guidance. The workgroup continues to hold weekly meetings.

The domestic component of the proposed project would focus on the rapid diagnosis of drug-resistant TB in persons at high risk and would be designed to achieve two major objectives. A National Rapid Diagnostics Service (NRDS) would be implemented and its costs, benefits and limitations would be evaluated based on ACET's previous resolution and recommendations by an expert panel. Rapid point-of-care (POC) testing would be implemented and assessed for persons being evaluated for TB who would enter the United States.

The NRDS would be based on the concept of developing regional referral laboratories. A competitive process would be implemented to select two U.S. public health laboratories from cooperative agreement grantees that currently provide molecular and conventional DST. The two pilot laboratories would be funded to expand capacity to offer ~1,500 molecular and ~150 phenotypic DSTs per year.

Molecular tests would be performed for mutations associated with INH and RIF resistance using in-house methods. Phenotypic tests would include a full panel of first- and second-line drugs when mutations are detected. Isolates would be sent to the CDC laboratory for archiving and DNA sequencing if needed.

The NDRS would test ~3,000 patients per year in the first phase of a phased approach to even broader testing. Local care providers would identify patients in accordance with defined criteria, request rapid testing, and provide information required for proper evaluation. TB controllers would approve rapid testing. Specimens would be sent to state public health laboratories for microscopy, culture, NAAT and conventional DST.

NAAT-positive sediments of specimens would be sent to regional referral laboratories for molecular testing. Referral laboratories would report results within two working days. The detection of INH- or RIF-resistant associated mutations would initiate reflex testing with a full panel of phenotypic DST to ensure prompt availability of first- and second-line DST results.

A rigorous evaluation would be performed to assess certain laboratory aspects in providing the NDRS: operating costs of and impact on laboratories; feasibility and start-up costs of expanding laboratory capacity; practices for integrating assays into the laboratory workflow; information management and communication with providers and programs; recommendations for expanding NDRS and incorporating new technologies in the future; test performance in terms of turnaround times and comparisons with both phenotypic and sequencing results; the effectiveness of criteria for selecting patients; and the suitability of testing and reporting algorithms.

A rigorous evaluation also would be performed to assess certain clinical and programmatic aspects to determine the costs and impact of NDRS on patient care, facilities, TB programs and healthcare providers. To perform this evaluation, laboratory results would be linked through

state case numbers with RVCT data to determine the breadth of experience in conducting rapid testing. A competitive process would be implemented to select three state or big city TB control programs from current cooperative agreement grantees to collect more in-depth data from a prospective cohort. The Workgroup has proposed several potential targets for the evaluation:

- Selection of patients for rapid testing.
- Strategies to apply results in treatment decisions.
- The time to initiation of appropriate treatment.
- Adherence to treatment.
- Time to culture conversion.
- Frequency of acquired drug resistance.
- Treatment outcomes.
- Quality of life.
- Communications between providers and patients on rapid test results and treatment.
- Efficiency of the process for accessing the NDRS.
- Education and communication needs for providers, programs and patients.
- The impact of the NDRS on infection control practices and policies.
- The costs and impact of discordant tests.
- The impact of the NDRS on case management procedures and policies.
- The impact of the NDRS on contact investigations.
- The costs and effects of the NDRS on TB control programs.

The Workgroup has proposed the following timeline to implement and evaluate the NRDS in the domestic component of the project. Planning and preparation activities would begin in 2009 and would be completed in 2010. The NRDS would be initiated in 2010. Patients would be enrolled for 2010 with one-year follow-up of patients to determine treatment outcomes, with follow-up to be completed in 2012. Results would be analyzed and reported in 2012. The NRDS would be revised and expanded in 2013.

The international component of the proposed project would focus on rapid POC testing for TB and simultaneously for drug-resistant TB in persons entering the United States. The epidemiological context of the international component of the project is based on the tremendous burden of drug-resistant TB cases in the United States from China, India, Mexico, the Philippines and Vietnam.

The programmatic context of the international component of the project is based on U.S.-Mexico binational programs that are uniquely positioned to implement and evaluate rapid testing for drug-resistant TB. TB diagnosis is solely based on microscopy in much of Mexico through the binational projects. Through the existing binational project, specimens are transported to U.S. public health laboratories for culture and DST. TB patients who cross the border are treated in the United States, but are not counted in U.S. surveillance systems. TB screening of immigrant and refugee visa applicants would present another prime opportunity to provide rapid POC testing for drug-resistant TB.

The international component of the proposed project would be designed to achieve two major objectives. Rapid POC molecular testing would be implemented at the time of initial evaluation

for TB among persons who are likely to enter the United States (*i.e.*, U.S.-Mexico binational TB control projects and applicants for immigrant or refugee visas). The feasibility, performance and cost would be evaluated to determine the impact of the project on timeliness and continuity of appropriate treatment, acquired drug resistance, patient outcomes, and U.S. and Mexico TB programs.

The Workgroup has proposed the following timeline for the five-year international component of the project. Sites would be identified, a common research protocol would be developed, and local laboratories and personnel would be prepared in year 1 (2010). Rapid testing would be implemented in the first and second sites in years 2 and 3, respectively. Patients would be enrolled for 1 year and followed for an additional year to determine process and outcome indicators and data would be collected to inform the evaluation in years 4-5. The results would be reported and analyzed and the project would be revised and expanded through a feedback mechanism in year 5.

Dr. Cegielski requested input from ACET on both the domestic and international components of the flagship project on rapid detection of drug-resistant TB for high-risk persons. He noted that ACET's feedback would be extremely useful to the Workgroup in refining the proposed project for a formal presentation to DTBE leadership and developing and releasing a funding opportunity announcement.

ACET commended the Workgroup on designing an exciting concept for the proposed project on rapid detection of drug-resistant TB in high-risk persons. The ACET members made two key suggestions for the Workgroup to consider in enhancing the project.

First, the Workgroup should shorten the five-year timeline of the drug-resistant TB project. For example, the proposed laboratory methods could be reduced by at least five days on average if NAAT was performed on raw specimens rather than on NAAT-positive sediments of specimens.

Second, the Workgroup should review data from a rapid TB testing study that was recently conducted in California and would soon be submitted to a journal for publication. The study showed that rapid methods resulted in a 40-day reduction in the amount of time to start patients on effective TB therapy compared to conventional DST. Lessons learned and challenges in the California study could be extremely beneficial to the evaluation of the CDC project in terms of analyzing different outcomes.

ACET also raised the question whether specimens positive for *M. tuberculosis* but negative for drug resistance by molecular methods need further testing (at all) by conventional phenotypic methods, potentially eliminating the need for phenotypic DST in a large fraction of cases. Dr. Cegielski responded this strategy would have implications for nationwide universal surveillance for drug resistance that would have to be taken into consideration because the current case reporting format does not capture drug resistance based on molecular testing.

With no further discussion or business brought before ACET, Dr. Fleenor recessed the meeting at 5:42 p.m. on October 27, 2009.

## Overview of Health Reform

Dr. Dean reconvened the ACET meeting at 8:30 a.m. on October 28, 2009 and yielded the floor to the first presenters.

Mr. Donald Shriber is the Acting Associate Director for Policy and Mr. Michael Craig is a Public Health Analyst in the CDC Washington, DC Office. They provided an overview of health reform and its potential implications for CDC. Health reform is intended to address two major programs in the American healthcare system. The first problem is that 47 million Americans lack health insurance and millions more are under-insured and exposed to huge medical bills. Potential solutions to this problem include reforming and restructuring the health insurance market through exchanges and regulation; requiring employers to provide and individuals to have health insurance; and offering subsidies to help low-income families purchase health insurance.

The second problem is rapidly growing healthcare costs, even for insured persons, with no real improvement in health status. Obesity and other conditions threaten to further increase healthcare costs. Potential solutions to this problem include making Medicare and Medicaid more efficient; generating an evidence base to demonstrate effective strategies and expose wasteful spending; and “bending the curve” over the long term by creating incentives for efficient and high-quality care.

Two committees have jurisdiction for health reform in the Senate. The Health, Education, Labor and Pensions Committee (HELP) and the Finance Committee passed bills in July and October 2009, respectively. However, leadership must resolve the liberal bill by the HELP Committee and the moderate bill by the Finance Committee. Three committees have jurisdiction for health reform in the House. The Ways and Means, Energy and Commerce, and Education and Labor Committees jointly developed one “Tri-Committee” bill. All three committees passed their bills in July 2009, but differences still need to be reconciled before bringing the bill to the floor.

The next steps in the health reform process are for leadership in each chamber to craft and bring a bill to the floor and structure a debate through the amendment process. The House and Senate would debate and vote on the bills. The Conference Committee would negotiate differences that are expected to be substantial. Significant political obstacles remain, but most observers still expect some sort of health reform bill to pass by the end of 2009.

Several controversial topics are associated with health reform. The Exchange is a regulated market through which individuals and small businesses could purchase coverage from private companies. The Exchange would allow for pooling of many smaller groups and “apples-to-apples” comparisons. Debates still remain regarding state, regional and national structures of the Exchange, the level of regulatory power for the Exchange, and the extent to which insurance companies could vary premiums in the Exchange.

Tax credit subsidies would be offered to low-income persons who purchase insurance on the Exchange. Debates still remain on the amounts of these subsidies. The public option is a “Medicare-like” government run plan that would compete with private insurance companies on

the Exchange. Individuals could choose to purchase insurance from the public option or private insurance. Multiple variations of the public option have been proposed. The Senate Finance Committee has proposed taxing “Cadillac Plans,” particularly expensive insurance plans.

Health reform potentially would impact CDC in several areas. CDC might gain new grants and funding of \$2-\$10 billion each year. CDC might be given new high-priority authority to oversee calorie labels at chain restaurants, the collection of better health data, a “health in all policies” program, and mandatory reporting of healthcare-associated infections. Stronger public health institutions are expected to be built within and across the federal government. Major reforms (*i.e.*, vaccines recommended by ACIP and cancer screening or other services recommended by the U.S. Preventive Services Task Force (USPSTF)) would give more individuals access to preventive services.

The Senate and House bills include major and stable funding sources for prevention activities. The Senate HELP Committee bill proposes \$30 billion over five years and \$10 billion per year after 2014, but this bill has not identified specific allocations. The House Tri-Committee bill proposes \$15.2 billion over five years with the following allocations to CDC: \$150 million to conduct Task Force activities, \$1.75 billion to enhance CDC’s internal infrastructure, \$5.4 billion to strengthen external infrastructures of states, \$1 billion to implement prevention research grants, and \$7 billion to implement community intervention grants. The final health reform bill is not expected to fund prevention activities at quite these levels, but a significant investment as much as \$2 billion per year is likely.

The House bill proposes allocations of funds for new and exciting approaches that would be mandatory rather than just authorized. Truly transformative grants would facilitate a shift from disease-specific funding to holistic state and local support. Both the Senate and House invest hundreds of millions of dollars in broadening the public health workforce through an expansion of the Epidemic Intelligence Service Program, the development of new programs for loan repayment, and a new Public Health Service Corps.

CDC’s new authority under health reform might would include requiring all chain restaurants to place calorie information on their menus; developing a mandatory system to track healthcare-associated infections that would be administered by CDC; assessing health impacts of federal building projects; and taking steps to coordinate and improve data collection and surveillance by creating “Key National Health Indicators.” These provisions could be more comprehensive.

Both the Senate and House authorize and fund activities conducted by USPSTF and the Community Preventive Services Task Force. The Senate and House also have called for the creation of a National Prevention Strategy. The Task Force activities and National Prevention Strategy could affirm the importance of certain prevention priorities.

Reforms have been proposed for Medicare and Medicaid payments to increase reimbursement for primary care. Private insurers, Medicare and Medicaid would cover preventive services, including vaccines recommended by ACIP and services recommended by USPSTF, without cost-sharing. With these reforms, vaccines and preventive screening would become available to nearly every American at no charge.

ACET thanked Mr. Craig and Mr. Shriber for attending the meeting to provide an informative overview of health reform. Several members raised the possibility of ACET developing and passing a formal resolution to encourage free TB preventive services and treatment of active TB disease in health reform. The TB language could be included with reforms for vaccines and preventive screening that would be offered at no charge in health reform.

A number of ACET members asked Mr. Craig and Mr. Shriber to keep ACET informed of the timeline for the health reform bill. This approach would provide ACET with an opportunity to identify external partners and allies who could advocate to Congress for the inclusion of TB issues in health reform legislation.

Some ACET members raised the possibility of forming a new workgroup to specifically address the implementation of health reform issues, particularly since CDC most likely would be given new funding and public health authority.

Dr. Fleenor confirmed that ACET would revisit the topic of health reform during the business session for the members to propose resolutions for consideration, discussion and possible adoption. Dr. Castro added that ACET and DTBE would maintain open lines of communication with Mr. Craig and Mr. Shriber in the CDC Washington, DC Office to ensure any resolutions formally adopted by ACET would be appropriately worded from a policy perspective.

### **Update on the TBTC Recompetition**

Dr. Andrew Vernon, of DTBE, covered the following areas in his update. TBTC conducts programmatically relevant clinical research concerning the diagnosis and treatment of TB disease and LTBI. TBTC was established in 1993 and initially included sites in North America only. TBTC was reorganized in 1998 as a formal consortium and grew to include 28 study sites in North America, South America, Europe and sub-Saharan Africa.

TBTC's formal bylaws define a committee structure that relies on protocol teams and workgroups with an extensive system for communication, quality assurance and attention to human subjects protection. The bylaws further define the organization of TBTC and support its democratic and participatory governance. AIDS Clinical Trials Groups (ACTGs) funded by the National Institutes of Health (NIH), particularly the Community Programs for Clinical Research, was used as a model to create TBTC and its formal bylaws. The TBTC bylaws are revised or supplemented as needed.

The TBTC North American sites are health departments or academic medical centers funded via CDC contracts or a memorandum of understanding (MOU) administered by the Veterans Administration Medical Center. Study sites in Brazil, Uganda, South Africa and Spain are funded via subcontracts that were established by academic medical centers in North America on behalf of and with funding from CDC.

To date, nine major TBTC studies have enrolled 10,844 patients and 12 TBTC sub-studies, primarily focusing on pharmacokinetics, have enrolled 1,421 participants. Study 26 is an evaluation of 12 doses of an INH/RFP regimen once per week for three months and accounted for the enrollment of 8,274 patients. TBTC's new partnerships include projects with ACTG, TB Alliance, the National Institute of Allergy and Infectious Diseases, commercial pharmaceutical manufacturers, MDR-TB partners, and academic institutions (*i.e.*, the Ordway Research Institute and the Tuberculosis Research Unit).

In 2007, an external peer review panel advised CDC to take measures in the next ten-year cycle of TBTC to increase its enrollment capacity and engagement in high-burden countries. Dr. Vernon informed ACET of TBTC's new vision in the 2009-2019 cycle during the October 2008 meeting. Domestic and high-burden sites would be combined. Capacity would be strengthened for TBTC to enroll ~1,000 patients in treatment trials each year.

New international sites would be established with leading external partners and new relationships with CDC field research sites. Complementary animal modeling and microbiology studies would be incorporated. International experts would be formally engaged. DTBE recently launched a large training and coordination activity to address challenges related to TBTC's enhanced capacity.

Dr. Vernon highlighted a number of TBTC's ongoing and future activities to strengthen the 2009-2019 cycle. TBTC currently has ten sites in the United States and ten international sites. TBTC is a productive member of the growing global network of groups that conduct TB clinical trials. TBTC is eager to coordinate and collaborate with other groups, such as the European and Developing Countries Clinical Trials Partnership, in the rapid pursuit of improved therapies for TB infection and disease. DTBE would solicit input from ACET on the new internal and external review process for TBTC that is underway.

To date, 293 patients have been enrolled in Study 29 that would play a major role in the new cycle of TBTC. The study is an evaluation of a rifapentine dose of ~10 mg/kg five times per week. Animal data have shown that this regimen has the potential to substantially shorten TB therapy. Enrollment of all 480 patients in Study 29 is expected to be completed in the spring of 2010.

TBTC and several partners would co-sponsor a collaboration meeting at the International Union Against Tuberculosis and Lung Disease (IUATLD) Conference in Cancun, Mexico in December 2009. The purpose of the collaboration meeting would be for the partners to discuss strategies to enhance collaboration and communications among various trials groups. The partners are confident that rapid progress would be made in the development of new, improved and shorter therapies for treatment of TB disease and LTBI.

ACET commended DTBE on increasing its efforts to engage other domestic and international partners in TBTC. Several members believed that TBTC is one of DTBE's most significant activities and urged DTBE to retain the prominence of this important initiative in the 2009-2019 cycle. Dr. Fleenor confirmed that ACET welcomes the opportunity to provide guidance on the new internal and external review process for TBTC during a future meeting.

## **Update on the Federal TB Task Force (FTBTF)**

Dr. Castro reminded ACET that FTBTF was established in 1991 in response to the resurgence of TB. Since that time, representatives of various federal agencies have used FTBTF as a mechanism to maintain interactions and communications on issues related to TB. The FTBTF membership includes CDC and NIH as co-chairs, DIHS, FDA, HRSA, USAID, NTCA, the Indian Health Service, Office of Global AIDS Coordinator, and Department of Defense.

FTBTF published the *Plan to Combat Extensively Drug-Resistant Tuberculosis* in the *MMWR* in February 2009. During the August 2009 FTBTF meeting, the members identified unmet needs in six priority areas to implement the XDR-TB plan: TB diagnostics, drugs and regimens, epidemiology and surveillance, international program coordination, patient care, provider training, and clinical research and trial infrastructure.

FTBTF formed and charged four workgroups with proposing and developing collaborative interagency demonstration projects with existing resources to advance capacity to respond to MDR-/XDR-TB. The focus areas of the four workgroups are highlighted below:

- Advancing the development, field testing and registration of molecular tests for identification of TB and drug resistance.
- Implementing treatment with quality assured drugs for persons with MDR-/XDR-TB and scaling-up clinical trial capacity by relying on existing CDC and NIH consortia.
- Preventing transmission through infection control with a special emphasis on sites caring for persons living with HIV/AIDS.
- Expanding FDA's existing initiative to develop clinical trial data standards.

During the October 2009 FTBTF conference call, the members agreed to develop a website to rapidly disseminate up-to-date information on its activities. Dr. Castro confirmed that he would provide ACET with the address of the new FTBTF website.

## **Panel Presentation on TB Control in U.S. Affiliated Pacific Islands (USAPIs)**

Dr. Fleenor prefaced the panel presentation by reminding ACET that this topic was placed on the agenda due to the motion ACET unanimously passed during the July 2009 meeting. The ACET members noted that persons from Compact of Free Association states are exempted from TB screening prior to U.S. arrival. However, this policy has placed an additional burden on state and local health departments in the United States.

The panel of keynote speakers presented their perspectives on TB prevention and control efforts that are underway in the USAPIs. The presentations are summarized below.

**CDC Perspective.** Mr. Andy Heetderks is a Program Consultant in DTBE. He reported that the six USAPI jurisdictions include three U.S. flag territories (American Samoa, Commonwealth of Northern Mariana Islands (CNMI) and Guam) and three freely associated states or independent countries (Federated States of Micronesia (FSM), Republic of the Marshall Islands (RMI) and Republic of Palau). The TB case rate is 86.6/100,000 in the USAPI region and 6.7/100,000 for children <5 years of age. Chuuk, FSM reported two simultaneous MDR-TB outbreaks in 2008.

Common public health challenges in the USAPIs include a shortage of healthcare providers; procurement and distribution of testing reagents, supplies and treatment medications; laboratory infrastructure and epidemiological capacity for disease surveillance, reporting and outbreaks; increased health problems that are common to both developed and developing countries (*i.e.*, obesity, diabetes, cancer, leprosy and waterborne diseases); and the submission and administration of grant applications.

The USAPIs are vulnerable due to their small populations, excessive dependence on foreign aid, high transportation and communication costs, little opportunities to create economies of scale, susceptibility to natural disasters, and a limited Congressional voice. DTBE and its partners are taking actions in five major areas to address health disparities in the USAPIs and enhance core TB program and laboratory components.

In terms of “agency collaboration and coordination,” DTBE is partnering with several principal agencies to maximize resources awarded in cooperative agreements for TB prevention and control in the USAPIs. These partners include WHO, the Secretariat of the Pacific Community (SPC), Pacific Island Health Officers Association (PIHOA), CDC Division of Diabetes Translation, Department of Interior, Pacific Chronic Disease Coalition, NIH and Japanese Anti-Tuberculosis Association.

DTBE’s strong network of internal and external partners have generated international synergy in terms of coordinated site visits, program reviews, Epi-Aid investigations, surveillance, funding, technical assistance, training, data reporting, development and delivery of training materials, improved accountability and stronger political will.

In terms of “data recording and reporting data,” DTBE has made efforts to address a number of significant challenges. In 2003, CDC, SPC and WHO had different requirements, forms and time frames for reporting data. Moreover, data were submitted in a fragmented and incomplete manner. Data reporting to all agencies and the use of local data were limited.

New patient and laboratory registries have been developed based on the DOT short course (DOTS) strategy and existing patient registries with CDC enhancements. The registries are now widely utilized in the USAPIs. A Small Business Innovative Research (SBIR) contract was awarded to JBS International to develop the “TBanywhere.net” surveillance system. This fast, interactive and secure web application collects case-level TB surveillance data based on the 2009 revised RVCT, WHO and SPC requirements and transmits data to CDC through PHIN-certified messaging.

TBanywhere.net provides surveillance analysis and reporting in a comprehensive, timely and meaningful manner; integrates TIMS data prior to 2009; and allows for multiple constituents and differential access. The TBanywhere.net online surveillance tool provides a solution for data collection, analysis and reporting with no maintenance. Data are available for local analysis and reporting immediately after being entered into TBanywhere.net. The system can be expanded to integrate additional data elements for diabetes and other conditions and also can be adapted for other countries and diseases.

Overall, TBanywhere.net eliminates the need for maintaining records in paper form and faxing RVCT forms to CDC for data entry; minimizes CDC's difficulties in negotiating corrections and clarifications of data; resolves a challenging information technology environment for installation and maintenance software; meets CDC, SPC and WHO data reporting requirements; and reduces resources needed for data reporting.

In terms of "laboratory services," this component has been greatly enhanced since 2003. All ten laboratories in the USAPI Population Centers now provide local AFB smears and participate in regional reference laboratory shipping for culture and DST. A regional reference laboratory provides diagnostic laboratory services and a California laboratory provides genotyping services of all culture-positive cases.

MDR-TB cases are reported and quantified in the USAPI region. Annual training is offered on staining and reading. Blind-slide rechecking is performed and gaps have been filled between TB laboratories and TB clinics. The enhanced laboratory register includes culture and DST results. The regional reference laboratory contract is scheduled to be recompeted in June 2010. The CDC Division of HIV/AIDS Prevention has expressed an interest in joining this public/private partnership.

In terms of "medical consultation," this component has been improved since 2003. At that time, four different sources provided TB medical consultation to the USAPIs. The San Francisco RTMCC now provides medical consultation on complicated TB cases for the entire USAPI region through e-mailed or faxed requests.

In terms of "regional training and networking," this component has been strengthened since 2002. DTBE and HRSA have an interagency agreement to support training offered by the Pacific Islands TB Controllers Association (PITCA). Agencies, TB programs and laboratories regularly report their accomplishments and challenges. Technical assistance is repeatedly offered onsite with breakout sessions for clinicians, laboratory managers and nurses. Collaborative action plans are developed and announced for the following year. DTBE has implemented the NCHHSTP PCSI Initiative throughout the USAPIs and with other partners, including SPC, WHO, HHS, PIHOA, NIH, diabetes programs and reference laboratories.

DTBE's funding formula for TB prevention and control has been implemented in CNMI and Guam. RMI, FSM and Palau report >10 TB cases per year and receive \$100,000 base funding. American Samoa reports <5 TB cases per year and does not receive \$100,000 base funding. The funding formula does not apply to laboratories. DTBE is exploring the possibility of including USAPIs with "X" number of TB cases in the next formula funding cycle. The ultimate

goal of the TB funding formula is to redistribute all funds to align with data-driven epidemiologic needs by 2013. Of ~\$3.7 million NCHHSTP allocates to the USAPIs for TB prevention and control, DTBE contributes ~\$1.5 million.

DTBE and its partners are continuing to address challenges that are unique to TB prevention and control in the USAPIs. These issues include delivery of second-line TB medications, development and dissemination of patient education materials in Native languages, contact investigations, case management, case reporting, infection control, smear and culture proficiency in laboratories, establishment of a network of local experts, inter-island travel, and strategies to overcome inertia.

DTBE and its partners also are focusing on challenges related to the migration of USAPI residents to the United States. TB outbreaks have been reported in Arkansas and Oklahoma among the Marshallese. Moreover, TB cases in Guam are expected to significantly increase due to contract workers who will be hired to build military facilities. Estimates have shown that the military buildup could result in 140 additional TB cases per year in Guam.

DTBE and its partners have documented several lessons learned during their TB prevention and control activities in the USAPIs. A solid TB control infrastructure, including DOT workers, anti-TB medications and laboratories, must be developed and maintained over time. Strong political will must be obtained and accountability must be transparent in all activities. Patience must be a guiding principle because success will be achieved in small incremental steps over time. For example, the process to procure drugs from GLC could take over one year.

Interventions must be repeated and the PCSI Initiative must be implemented to benefit from synergies. Poor TB control practices are expensive due to the absence of resources for contact investigations and infection control. Opportunities must be leveraged to practice prevention.

DTBE and its partners will take a number of actions to advance TB prevention and control in the USAPIs in the current economic crisis. Existing resources will be maximized. The TB formula will continue to be used to redirect funding to TB programs based on the epidemiology of TB rather than on historic funding. Program accountability and existing collaborations will be enhanced to regionalize services with HIV, diabetes and other disease programs. New collaborations will be identified through public/private partnerships. The contract for the TB regional reference laboratory will continue to be utilized. Pending available resources, regional TB surveillance and data reporting will continue to be supported after the SBIR contract for TBanywhere.net ends.

***Secretariat of the Pacific Community (SPC) Perspective.*** Dr. Janet O'Connor is the head of the SPC TB Section. She reported that SPC is the oldest and largest regional organization in the Pacific with a membership of the United States, France, Australia and New Zealand. The 22 Pacific Island countries provide technical assistance, policy advice, training and research services to its membership through three technical program divisions: Marine, Land and Social Resources. SPC currently conducts activities with 400 staff in three different centers, but this organizational structure will be modified in 2010 with 540 staff in five to six centers.

At this time, the six sections of the SPC Public Health Department include HIV/STDs, Healthy Pacific Lifestyles, Adolescent Health and Development, the Global Fund, surveillance and TB. In 2010, the SPC Public Health Department will be reorganized with four sections: health protection, health promotion, health information systems, and grant management quality assurance and performance.

The SPC TB Section is based on the six overarching objectives of the 2006-2010 WHO regional strategy: pursue high-quality expansion of the DOTS strategy; address MDR-TB, TB/HIV co-infection and other challenges; contribute to strengthening health systems; engage all care providers; empower individuals and communities affected by TB; and enable and promote operational research. SPC expanded its collaborations with CDC and WHO to include other jurisdictions in addressing TB control and prevention and shift toward health equity in delivering TB services in the USAPIs.

In the USAPIs, the Micronesia sub-region accounts for a high TB rate of >80/100,000; the Melanesia sub-region accounts for a medium TB rate of 40-80/100,000; and the Polynesia sub-region accounts for a low TB rate of 0-40/100,000. Ethnic, cultural and linguistic variations make a significant contribution to the differences in TB case rates among the three USAPI sub-regions.

SPC developed and targeted specific strategies to address the high, medium and low TB rates in the Micronesia, Melanesia and Polynesia sub-regions, respectively. These strategies included enhanced case finding/case holding, the establishment of systems with standardized approaches and guidelines, improved treatment success rates, monitoring and evaluation, surveillance, stronger NTP capacity, community outreach and education, and targeted screening with INH prophylaxis. SPC's close collaborations with CDC and WHO have resulted in tremendous progress in implementing the DOTS strategy in the USAPIs since 1998.

Round 7 of the Global Fund will benefit 11 USAPI countries, including FSM, RMI and Palau. The majority of this funding will be targeted to human resources to build capacity in the following areas: DOT to ensure completion of TB treatment; community outreach activities, especially to vulnerable populations; active case finding, particularly in households with sputum smear-positive persons; TB/HIV co-infection; second-line drugs for MDR-TB; and the development of standardized guidelines for surveillance, monitoring, evaluation and training. To support these activities, the Global Fund will allocate \$1.3 million to RMI, \$986,500 to FSM and \$430,400 to Palau.

SPC has taken other actions to improve TB prevention and control in the USAPIs. A database and listserve were developed to track TB patients who cross borders within the USAPI countries. A partnership was established to strengthen molecular epidemiology capacity. SPC will continue to collaborate with CDC in launching the TB/diabetes study in the USAPIs in 2010.

SPC and its partners have achieved several successes to date in improving TB prevention and control in the USAPIs. The DOTS framework is well established with 100% coverage. The TB treatment success rate is >85% and the TB case detection rate is >70%. NTPs are functional for the most part and are well integrated within national health systems.

SPC recognizes the need to address a number of challenges to further strengthen TB prevention and control in the USAPIs. National health systems are inadequate at this time to support and sustain high-quality TB services due to insufficient political commitment; poor surveillance due to a lack of standard or harmonized approaches to data management; recurring TB drug shortages due to poor national procurement systems; and unreliable laboratory results due to high turnaround, shortage of personnel and lack of monitoring and evaluation.

Access to second-line drugs through GLC for MDR-TB is limited in the USAPIs. For example, RMI has spent >\$200,000 to procure only 66% of the drugs required for the entire MDR-TB treatment regimen. Moreover, FSM still needs drugs for the MDR-TB outbreak that occurred in 2008. The development of a framework to treat MDR-TB in the USAPIs is slow. CDC's priorities in the USAPIs in terms of financial assistance and in-country technical assistance are unclear.

A standardized testing protocol for TB/HIV co-infection has not been created. Implementation of collaborative activities between TB and HIV programs in the USAPIs continues to be weak. Surveillance is problematic due to the inadequate quality of TB data submitted, poor timeliness of data reporting, and a weak and fragmented national TB information system.

SPC's minimal TB funding is limited to supporting USAPI countries outside of the Global Fund (*i.e.*, Guam, CNMI and American Samoa). Laboratory results of TB screening tests in the USAPIs are not readily available to SPC. Monitoring and evaluation of TB prevention and control efforts are difficult due to the geographical isolation of FSM, RMI and Kiribati.

The impact of two upcoming developments on TB prevention and control efforts in the USAPIs is unknown: the new organizational structure of the SPC Public Health Department and the relocation of U.S. Marines to Guam. Implementation of the Global Fund must be accelerated for SPC to conduct phase 2 activities in June 2010. SPC is concerned that these barriers might result in missing its 2010 targets (*i.e.*, a 50% reduction in TB prevalence and mortality based on the 2000 baseline) by a narrow margin.

SPC has proposed several approaches to address these challenges and continue to improve TB prevention and control in the USAPIs. A CDC/SPC MOU is being developed at this time, but a letter of agreement also should be created to clearly define both joint and individual activities and resources in specific areas for both agencies. CDC/SPC joint work plans should be aligned with and complementary to national strategies and priorities of the USAPIs.

Surveillance and monitoring systems should be developed to harmonize and link data among SPC, CDC and WHO. A USAPI repository should be established to improve access to second-line drugs through GLC. SPC, CDC and WHO should continue plans for joint missions, training and DOTS implementation in the USAPIs.

***Commonwealth of the Northern Mariana Islands (CNMI) Perspective.*** Dr. Richard Brostrom is the Public Health Medical Director of the CNMI Department of Public Health. He reported that

the incidence of TB in the USAPIs has a significant impact on TB prevention and control in the United States. At this time, >10,000 USAPI residents have migrated to Arkansas, Oklahoma and other parts of the country to work.

Dr. Brostrom summarized recent efforts to respond to an MDR-TB outbreak in Chuuk. In 2007, a CDC Epi-Aid Team investigated a significant outbreak of 24 MDR-TB cases in Chuuk involving four deaths and 240 household contacts. At this time, 160 contacts have been screened and efforts are underway to administer prophylaxis to the remaining 80 contacts. The Chuuk government assured political commitment and began to assemble an action plan. CDC and the U.S. Department of the Interior leveraged funding from Congress to complete the Epi-Aid investigation.

Several problems remained after the CDC Epi-Aid Team departed Chuuk in July 2008. The MDR-TB cases are not isolated and MDR-TB transmission is still ongoing. No cases have been treated because second-line drugs are not available and a TB isolation or treatment facility has not been constructed. Moreover, the evaluation of TB contacts is incomplete.

A number of actions were taken at the local level to address these problems, such as hiring and training 19 new DOT workers and a DOT coordinator and purchasing three four-wheel drive vehicles and gas to administer DOT in the field. Despite these efforts to build local capacity, the TB case rate doubled in Chuuk from January 2008-April 2009. Additional actions were taken to decrease the TB case rate in Chuuk as a result of these surprising findings.

An air handling and infection control facility was constructed with a negative flow design, ultraviolet light, hepa-filtration and strict isolation measures until patients were smear-negative. Droplet precautions and N-95 respirators also were required in the new isolation ward. Second-line medications were procured to treat MDR-TB; medical supplies were obtained; MDR-TB patients were admitted; inpatient treatment was initiated; medical complications were monitored; and community commitment was secured for food services and ongoing education for school-age children.

Preliminary outcomes and next steps for the 95 MDR-TB cases that received daily prophylaxis by DOPT are summarized as follows. Prior to the arrival of the CDC Epi-Aid Team in Chuuk, the number of MDR-TB cases was five, four persons died and the fatality rate was 80%. After the arrival of the CDC Epi-Aid Team in Chuuk, the number of MDR-TB cases was 19, one individual died and the fatality rate was 7%. The significant decline in the Chuuk fatality rate now exceeds that in the United States.

In May 2009, the first MDR-TB cohort in Chuuk was discharged after completing nine months of treatment in isolation. The MDR-TB patients began two years of oral therapy in October 2009 in a closely structured monitoring program. The Public Health Outpatient Center would be remodeled in November 2009 with improved air handling measures. Effective administration of DOT would be assured for 19 MDR-TB cases in the community. In January 2010, prophylaxis of the 95 MDR-TB cases would be completed and standard contact investigations would be initiated for all smear-positive cases.

Dr. Brostrom summarized recent efforts to respond to MDR-TB outbreaks in Guam and RMI. A Chuuk resident 19 years of age failed standard TB therapy and was given medical treatment in an isolation unit of a Guam hospital in September 2009. The patient was identified as having MDR-TB, but appropriate second-line drugs were not available in Guam. The mother of the patient was smear-negative with an abnormal CXR that indicated MDR-TB. At this time, ~20 close contacts of the patient are being investigated.

A new MDR-TB case in RMI in February 2009 was lost to follow-up in September 2008. The patient was isolated in a Majuro hospital for nine months, but no second-line drugs were available for the first five months of treatment. The Epi-Aid investigation identified a nurse with pleural effusion who spent a significant amount of time caring for the patient. Of 23 contacts identified for treatment in the first week, none have started treated to date. Liquid levofloxacin has been delivered from Chuuk for close contacts who have been identified in Hawaii and Seattle.

In the past four years, six MDR-TB cases have been detected on the island of Ebeye. Of these six cases, three were lost to follow-up, one patient died, none were completely treated and all had diabetes. Contact investigations have not been conducted for any of the six cases. Estimates show that 100 contacts of the six cases are in California and Hawaii, but significant program upgrades are needed. At this time, >30 MDR-TB cases with 250 contacts in the USAPIs are undergoing treatment or will need treatment in the future.

Dr. Brostrom proposed a number of recommendations that should be considered to improve responses to MDR-TB outbreaks in Chuuk, Guam and RMI. CDC should increase its presence in the field in providing expert clinical and programmatic technical assistance to the USAPIs. The USAPIs account for 33% of the MDR-TB cases in the United States at this time.

CDC, SPC and WHO should share responsibility in providing support to create a stockpile of second-line TB drugs in the USAPIs. The six- to eight-month delay in procuring drugs to treat MDR-TB cases has dire consequences. PITCA regional meetings should continue to be supported to build technical expertise at the local level. An ACET member should be designated to serve as a liaison to PITCA. CDC, SPC and WHO should share responsibility in adjusting the TB funding formula to increase funds to the most vulnerable areas in the USAPIs. Dr. Brostrom described the impact of TB/diabetes co-infection in the USAPIs. An assessment conducted by WHO showed an extraordinarily high rate of diabetes of ~40% in American Samoa and FSM. Data collected in 2008 showed that ~75%-80% of adult Pacific Islanders with TB have diabetes. Diabetic patients with TB are more likely to have lower lobe disease, cavitary disease and a higher burden of disease at diagnosis. These patients also are more likely to remain smear-positive at eight weeks of treatment and have a three to five times higher risk of death during treatment. Relapse rates in these patients are unknown at this time due to the lack of solid data and small populations.

The CNMI Department of Public Health developed four standards for TB/diabetes care in the USAPIs based on the best available data in the literature. Diabetes should be diagnosed in TB patients. TB regimens should be adjusted for patients with diabetes. DOT workers should be trained to educate patients on lifestyle changes to self-manage their diabetes during TB treatment. Steps should be taken to prevent TB in patients with diabetes.

To further improve the care of TB/diabetes patients, the CNMI Department of Public Health is drafting standards for the entire USAPI region; investigating the relationship between diabetes and TB in Kiribati; collaborating in the development of IUATLD standards; and participating in the December 2009 webinar on TB/diabetes that will be hosted by the San Francisco RTMCC. The CNMI Department of Public Health also has recommended the development of peer-reviewed TB control guidelines for persons with diabetes.

Dr. Brostrom described efforts that will be undertaken in Guam to screen contract workers for TB. A large number of active TB cases is expected to be detected during mandatory screening of 15,000 Filipino construction workers who will be hired to build military base housing in Guam. The following proposal has been developed for TB screening in Guam. Primary screening should be conducted in the Philippines. Best practices in TB screening from the St. Louis Extension Clinic, particularly the addition of culture, should be applied.

Primary screening should be aggressively conducted by CXR in a single visit to find TB early. The initial examination should be performed within two weeks of the contract worker arriving in Guam. IGRAs are not available in the USAPIs. Consideration should be given to adding an HIV test during the first examination. Prior TB screening experience has shown that the activation of LTBI among imported labor occurs >5 years of arrival.

Private sector clinicians in Guam should perform annual screening and refer cases, but the TB program in the Guam health department should manage referrals and cases. Additional resources should be allocated to the Guam TB program because TB cases during the construction phase of the military buildup in Guam are expected to double.

***U.S. Department of the Interior (DOI) Perspective.*** Ms. Roylinne Wada is the Special Advisor on Health to the Assistant Secretary for Insular Affairs. She reported that the Office of Insular Affairs (OIA) conducts a number of significant activities in the USAPIs on behalf of the DOI Secretary. OIA directs, guides and coordinates federal policy in territories; manages grants and directs financial assistance to the territories; administers and oversees U.S. assistance to FSM, RMI and Palau as delegated by the DOI Secretary and authorized by law; and administers Compact impact grants. Of OIA's entire budget, ~98% is passed to the insular areas in the form of grants or direct assistance.

OIA's assistance to the USAPIs covers a broad range of areas: operations, maintenance and covenant grants to build and construct government facilities; general technical assistance to resolve problems and launch pilot projects; Brown Tree Snake control and coral reef initiatives; insular management controls for audits as well as financial and personnel management; administration and performance oversight of the Compacts of Free Association grant program; provision of funds to other federal departments to support services to the Compact countries; administration of funds for the use and operating rights of the military base in Kwajalein; support for residents to redevelop and relocate to the island of Enewetak; and Compact impact assessments and provision of grant aid.

OIA's assistance to the USAPIs specifically related to health care and systems development includes constructing hospitals, health centers and other health facilities; improving power, potable water, wastewater and solid waste treatment facilities; purchasing medical equipment; directly financing health departments; serving as the focal point for the Interagency Group for Insular Affairs and the Interagency Coordinated Assets for Insular Health Response; coordinating pharmaceutical and other support; developing health information and accounting systems; and conducting strategic planning activities.

A public law was passed in 2004 that split the combined FSM/RMI Compact of Free Association into two separate agreements until 2023. The United States defends FSM and RMI as U.S. territories. The U.S. defense arrangements will continue until at least 2066. Financial and other selected provisions were renegotiated to promote economic advancement and budgetary self-reliance. Over a 20-year period of the amended Compacts, \$2.1 billion will be allocated to FSM and \$1.5 million will be allocated to RMI.

Healthcare, including primary, secondary and tertiary care, is one of the top priorities in the amended Compacts to improve the capacity of health departments to operate efficiently and self-sufficiently over time. At the end of the 20-year period of the amended Compacts, a trust fund will replace annual assistance. At this time, allocations of the amended Compacts funding include 35% for education, 27% for infrastructure and 22% for health.

A number of important provisions will be continued in the amended Compacts. Compact citizens are considered as "non-immigrants" and are exempted from meeting U.S. passport, visa and labor certifications when entering the United States. The migration of Compact citizens has increased by 86% since 2003 with Guam accounting for 56% of migrants. At this time, 33,000 migrants are estimated to be living in Guam, CNMI, Hawaii and American Samoa.

As authorized by law, OIA provides grant assistance to Guam, CNMI, Hawaii and American Samoa to mitigate the financial impact of Compact citizens who migrate. OIA will allocate \$17 million to Guam in FY2010. With the exception of Hawaii, no other U.S. states is included in the mitigation strategy. The grants are designed to meet the anticipated needs of the growing influx of migrants (*i.e.*, health insurance coverage, hospital financing, improved education and health status) and address problems that drive citizens to migrate from FSM and RMI. OIA acknowledges that healthier and more educated citizens are likely to be net contributors to their new communities.

A public law codified the 1994 Palau Compact of Free Association. In Palau, funding is allocated up front rather than annually and infrastructure development is emphasized. Federal grants and most other services will continue under the Palau Compact. DOI and DOS are currently reviewing this Compact.

DOI recognizes that funding is not sufficient in any of the three Compacts to support health care maximally in the USAPIs. Issues related to communicable disease control and recent MDR-TB outbreaks have required DOI to play a more active role in designing and implementing support strategies. For example, DOI redirected ~\$1.9 million in Compact funds to assist the Epi-Aid investigation and response to the MDR-TB outbreak in Chuuk.

Ms. Wada proposed several options that should be considered in addressing the problem of insufficient Compact funds and improving TB prevention and control in the USAPIs. Matching funds parallel to the DOI grants should be required to support DOT workers and ensure an adequate supply of TB drugs. Standards should be developed to assure uniformity and sustainable performance in TB control programs over time. A process should be created to allow the USAPI region to have an initial three- to four-month supply of second-line drugs. This strategy would eliminate the need to deplete the TB drug stockpile in Chuuk.

Grant support should be adjusted to increase resources to jurisdictions with a higher TB burden. Technical resources with expertise in TB should be deployed to the field on a full-time basis or conduct site visits to the USAPI region on a more regular basis. This strategy would help local programs in the USAPIs to build capacity and increase confidence.

At the conclusion of the panel presentation, Dr. Brostrom reviewed nine key recommendations that would play a critical role in improving local healthcare systems and controlling the spread of TB to neighboring islands in the USAPIs with technical assistance and direct funding.

1. Adjust the TB funding formula to increase funds to the most vulnerable areas in the USAPIs.
2. Increase CDC's presence in the field in providing expert clinical and programmatic technical assistance to the USAPIs.
3. Provide support to plan for and create a stockpile of second-line TB drugs.
4. Continue to support PITCA regional meetings to further build technical expertise at the local level among clinicians, nurses and laboratory managers.
5. Support the development of peer-reviewed TB control guidelines for persons with diabetes.
6. Continue to support the regional reference laboratory.
7. Continue to support regional surveillance efforts through TBanywhere.net.
8. Engage the USAPIs in operational research, where appropriate, for TB research and the compilation of best practices.
9. Continue to enhance multi-agency activities to eliminate discordant recommendations among agencies.

ACET and CDC thanked the USAPI representatives for traveling a long distance to attend the meeting and provide comprehensive presentations on the unique challenges associated with TB prevention and control in the USAPIs.

Dr. Fleenor announced that time would not permit ACET to draft, discuss and adopt a formal resolution in response to the nine recommendations proposed by Dr. Brostrom. However, he confirmed that TB prevention and control in the USAPIs would be placed on the next agenda for ACET's further discussion and formal action.

Dr. Castro outlined CDC's initial responses to the nine USAPI recommendations.

1. CDC and NTCA developed the current TB funding formula to reflect TB morbidity, MDR-TB and other complex situations. Most notably, five U.S. states (not the USAPIs) account for ~40%-50% of national TB morbidity. CDC would have virtually no ability to adjust the current TB funding formula unless modifications were proposed with NCTA's full support and endorsement.
2. CDC is planning to place a public health advisor in Guam. The medical officer in Hawaii would continue to oversee TB control efforts in Hawaii, but agreement has been reached to expand responsibilities of this position to include oversight of regional approaches.
3. CDC is prohibited from using Congressionally-appropriated funds to purchase drugs.
4. CDC would continue to support PITCA regional meetings.
5. CDC welcomes the opportunity to support the development of peer-reviewed TB control guidelines for persons with diabetes, but the evidence base for this guidance is unknown. For example, no data have been collected to date to show that TB rates would decrease by achieving better glycosylated hemoglobin status in the USAPI population. DTBE and the Division of Diabetes Translation would need to identify and narrowly focus specific operational research questions to better understand the relationship between high diabetes rates and excess TB burden in the USAPIs.
6. CDC would continue to support the regional reference laboratory, but increased funding could not be guaranteed at this time.
7. CDC would continue to support regional surveillance efforts, but a survey should be administered in the USAPIs to determine actual TB morbidity that is anticipated.
8. CDC would extensively engage the USAPIs in operational research and the compilation of best practices.
9. CDC would continue to enhance activities with other agencies to implement standards throughout the USAPI region.

Several ACET members made preliminary suggestions in response to the recommendations proposed by the USAPI representatives.

- CDC should completely remove the USAPIs from the current TB funding formula. CDC, NTCA and the USAPIs should jointly develop a new "USAPI-specific" TB funding formula. The current formula addresses the needs of U.S. states with high TB morbidity, but does not account for the unique challenges associated with TB prevention and control in the USAPIs. A USAPI-specific formula might lead to more equity in distributing and matching TB dollars among the islands.
- CDC should consider establishing an exchange program in which TB controllers and other experts in the United States would be deployed to the USAPIs to enhance existing capacity. Lessons learned from the USAPIs also could greatly improve TB prevention and control practices in the United States.
- CDC should prioritize the development of a TB/diabetes research agenda at this time. Many TB controllers in the United States are reporting diabetes as a cause of delayed or inaccurate diagnoses of TB.
- CDC and its federal partners should enhance collaborations and communications with states, particularly those with large populations of migrants from the USAPIs. For example, states were not notified about the need to locate contacts of TB patients who migrated from the USAPIs.

- DOI should explore the possibility of partnering with the Centers for Medicare and Medicaid to provide Medicaid to Compact citizens with TB who migrate to the United States. Medicaid funds would decrease the financial burden on state and local health departments in providing TB care to Compact citizens who are in the United States.

## ACET Business Session

Dr. Fleenor opened the business session and called for ACET's formal action on the following issues.

**ISSUE 1:** A motion was properly placed on the floor and seconded by Mr. Kinney and Mr. Jones, respectively, for ACET to approve the previous meeting minutes. ACET **unanimously approved** the July 14-15, 2009 Draft Meeting Minutes with no further discussion or changes.

**ISSUE 2:** A motion was properly placed on the floor and seconded by Dr. Bakhtawar and Ms. Taylor, respectively, for ACET to accept the recommendations of the program review of the Nepal TB screening and treatment program. ACET **unanimously accepted** the Nepal program review recommendations with no further discussion.

**ISSUE 3:** A motion was properly placed on the floor and seconded by Dr. Fleenor and Mr. Kinney, respectively, for CDC and HHS to extend an invitation for RESULTS to serve as a new ACET liaison member. ACET **unanimously approved** the motion for RESULTS to serve as a new liaison member with no further discussion.

**ISSUE 4:** A motion was properly placed on the floor and seconded by Drs. Fleenor and Narita, respectively, for Dr. Thomas Frieden, Director of CDC, to address ACET during the first meeting in 2010. ACET **unanimously approved** the motion for CDC to invite Dr. Frieden to attend the next ACET meeting with no further discussion.

**ISSUE 5:** A motion was properly placed on the floor and seconded by Dr. Fleenor and Ms. Taylor, respectively, for HHS Secretary Kathleen Sebelius or her designee to address ACET in person or via video conferencing or a conference call as early as possible in 2010. If Secretary Sebelius' schedule would not permit her in-person attendance or participation in a meeting via video conferencing or conference call, ACET requested that a small group of members, led by Dr. Fleenor, meet with Secretary Sebelius or her designee in Washington, DC.

ACET **unanimously approved** the motion for CDC to invite Secretary Sebelius to address ACET. ACET agreed that key topics should be identified in advance to make the most efficient and productive use of Secretary Sebelius' time. Dr. Fleenor instructed the ACET members to submit potential discussion items to him via e-mail.

**ISSUE 6:** A motion was properly placed on the floor and seconded by Dr. Bakhtawar and Ms. Taylor, respectively, for CDC to expedite the reprint of the corrected TB Infection Control

Guidelines in the *MMWR*. ACET **unanimously approved** the motion for CDC to immediately publish the corrected guidelines in the *MMWR* with no further discussion.

**ISSUE 7:** A motion was properly placed on the floor and seconded by Drs. Bakhtawar and Narita, respectively, for CDC to maintain the categorical status of TB as program integration is further explored in the PCSI Initiative. **The motion was withdrawn**, but would be revisited (if necessary) based on two outcomes. Dr. Bakhtawar would review and submit comments to Drs. Dean and Fleenor on the PCSI white paper by the end of the next week. Dr. Fleenor would raise these issues during the NCHHSTP BSC Workgroup meeting in November 2009 to discuss the Strategic Plan.

**ISSUE 8:** The following motion was properly placed on the floor and seconded by Mr. Jones and Ms. Taylor, respectively:

WHEREAS, previous efforts to develop a strategy to reduce TB among African Americans have met with less acceptable results;

WHEREAS, if current trends go unabated over the course of the next ten years, African Americans will continue to bear a disproportionate share of the domestic TB burden;

WHEREAS, the development of a systematic effort to address TB in the African American community is complicated by multiple, interactive and synergistic health and behavioral health disparities;

THEREFORE, be it resolved that ACET recommends the establishment of a workgroup to be designated as the "African American TB Elimination Strategy Workgroup" and charged with:

- Providing expert consultation to the Director of DTBE or his designees on epidemiology, research, evaluation and treatment efforts to develop and implement a strategy to eliminate TB in the African American community; and
- Providing guidance to ACET in the review and ratification of a strategy to eliminate TB in the African American community.

ACET was divided on whether to approve the motion. On the one hand, some ACET members were in favor of expanding the scope of TB in AAs to more broadly focus on health equity issues in other racial/ethnic groups. Because TB health disparities also are prevalent in Hispanics and Asians, a broader focus on health equity might be more effective in decreasing TB health disparities in all racial/ethnic groups.

On the other hand, some ACET members noted that minimal progress has been made since CDC sponsored the initial "TB in African Americans Summit" in 2003. A broader focus on health equity would not make a significant impact on decreasing the gap of TB disparities in the AA community. The members pointed out that the language of the motion generally reflects the concepts of health equity and social determinants of health.

**ACET passed the motion by a majority vote of 5 in favor and 1 opposed.** ACET proposed next steps to advance activities of the new “African American TB Elimination Strategy Workgroup.” The original AA Workgroup would be reactivated, but Mr. Jones would be unable to continue to serve as chair long-term. During the first conference call, the membership would appoint a new chair and recruit additional ACET members, liaisons and *ex-officios* to serve as needed. DTBE staff would be designated to ensure the workgroup maintained continuity in its activities between ACET meetings.

ACET made two key suggestions for the workgroup to consider in refining its charge. First, DTBE should be advised to implement ACET’s previous recommendations whenever possible in addressing TB in the AA community. Second, DTBE should be urged to design research projects to identify barriers to making further progress in decreasing the gap of TB health disparities in the AA community.

Dr. Dean announced that CDC published an *MMWR* article in 2004 on TB in AAs with data stratified by various demographic factors, including geographic area, gender and age. She confirmed that CDC would distribute the *MMWR* article to ACET.

**ISSUE 9:** The following motion was properly placed on the floor and seconded by Mr. Jones and Dr. Narita, respectively:

WHEREAS, conventional efforts to detect and treat TB have not been successful in reducing the rate of TB among African Americans;

WHEREAS, there is a critical need to coordinate the development of a national strategy to combat TB among African Americans;

THEREFORE, be it resolved that ACET recommends to the Director of DTBE the designation of a fulltime position within DTBE with general responsibility for the coordination of all efforts and sufficient funding to address TB among African Americans as well as specific responsibility to coordinate the development of a comprehensive strategy that embraces systematic outreach, early detection, and treatment of TB among African American populations.

Several ACET members were concerned about approving the motion due to a number of reasons. The current ACET membership does not fully reflect other racial/ethnic groups that are disproportionately affected by TB. Fulltime staff members in DTBE devote their time and responsibility to multiple areas rather than one specific issue. TB is not a significant issue for AAs in all parts of the country.

The scope, diversity and flexibility of the fulltime position within DTBE should be broadened to include responsibility for health equity and social determinants of health across other racial/ethnic groups, particularly Hispanics and Asians. CDC was more successful in addressing and funding HIV, syphilis, hepatitis and TB disparities in the South rather than TB disparities in AAs. These initiatives encompassed large AA populations, but were more effective due to their

broader focus on regions with a disproportionate burden of disease rather than specific groups. **ACET passed the motion with a majority vote of 3 in favor, 1 opposed and 2 abstentions.**

**ISSUE 10:** The following motion was properly placed on the floor and seconded by Dr. Narita and Mr. Jones, respectively:

WHEREAS, access to care for all in the United States (US) is an admirable and desirable health policy goal;

WHEREAS, access to care for the treatment of TB is necessary to achieve health equity and assure the public's health in the US;

WHEREAS, treatment of TB is the most effective way of interrupting transmission in a community;

THEREFORE, ACET recommends that the Secretary of Health and Human Services advise executive and legislative branch health policymakers to assure the following components in any national health plan:

- Unrestricted access to evaluation, diagnosis and treatment of persons with TB disease, latent TB infection or TB exposure.
- Free of cost services and evaluations to patients as noted above. Co-pays and deductibles represent unacceptable obstacles to the protection of the public's health.

**ACET unanimously passed the motion with no further discussion.**

Dr. Fleenor announced that after the adoption of the last resolution, ACET lost its quorum. As a result, any outstanding motions would be introduced during the business session of the next meeting for formal action by ACET. ACET used the remainder of the business session to make suggestions that would improve the operation of future ACET meetings.

Dr. Jane Carter is the liaison member for IUATLD. She raised the possibility of ACET adopting the policy of another federal advisory committee in which voting members are not allowed to book a flight until at least three hours after the meeting is scheduled to adjourn. This approach would ensure that ACET maintains a quorum to complete its business during each meeting.

Dr. Narita pointed out that ACET meetings are heavily weighted with presentations, while less than two hours are set aside for the business session. He noted that agendas should be more balanced between presentations and ACET discussions. For example, day 2 of meetings should be entirely devoted to the business session with no presentations.

Dr. Castro agreed with the comments that the business session is rushed and does not allow ACET to fully deliberate on the proposed motions. He proposed opening the business session immediately after the 10:00 a.m. break if ACET decides to continue to have presentations on day 2 of meetings. He confirmed that he would remind DTBE staff of the critical need to

complete their presentations in the allotted period of time on the published agenda to ensure ACET has an opportunity to provide CDC with guidance and recommendations.

Dr. Dean agreed that the business session is the most important part of ACET meetings. However, voting members leave during this time and ACET is unable to complete its business without a quorum. She supported Dr. Castro's proposal to begin the business session after the 10:00 a.m. break. Alternatively, ACET meetings should be extended until 4:00 p.m.

Dr. Dean reiterated that ACET is chartered to provide expert advice and recommendations to the CDC Director and HHS Secretary on the elimination of TB. Her position was that ACET has not fulfilled its mission over the past few meetings.

### **Public Comment Session**

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

### **Closing Session**

The next ACET meeting was tentatively scheduled for February 2-3 or 9-10, 2010 or March 2-3, 2010. Ms. Margie Scott-Cseh, Committee Management Specialist for ACET, would poll the members by e-mail to determine an exact date for the next meeting.

Drs. Castro and Fleenor thanked the ACET members for their constructive criticism and honest feedback to improve the meetings. They confirmed that ACET's guidance, expertise, passion, enthusiasm, active participation and longstanding commitment to TB elimination have greatly benefited CDC and the broader public health community.

With no further discussion or business brought before ACET, Dr. Fleenor adjourned the meeting at 2:16 p.m. on October 28, 2009.

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