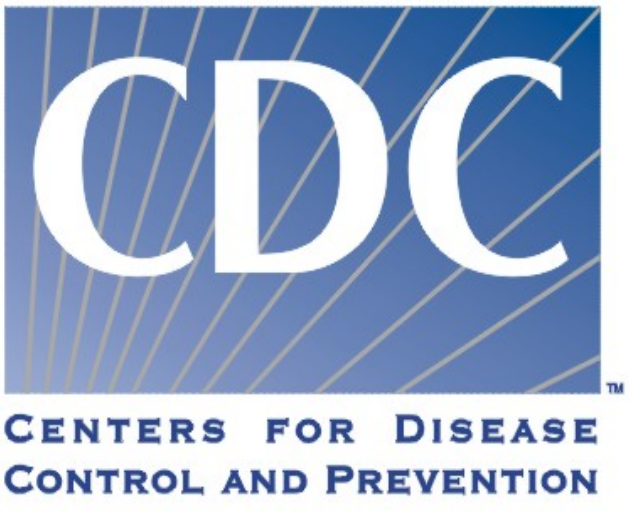
# DEPARTMENT OF HEALTH AND HUMAN SERVICES
# CENTERS FOR DISEASE CONTROL AND PREVENTION
## National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
## Division of Tuberculosis Elimination


# Advisory Council for the Elimination of Tuberculosis
## November 2-3, 2010
## Atlanta, Georgia

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## Record of the Proceedings

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# ATTACHMENT 1

## List of Participants

(*Note:* The Designated Federal Official conducted a roll call of the ACET voting members and the non-voting *ex-officio* members on both November 2 and 3, 2010 and confirmed the presence of quorum on both days of the meeting.)

**ACET Members**
Dr. Michael Fleenor, Chair
Dr. Christine Hahn
Mr. Shannon Jones III
Mr. Joseph Kinney
Dr. Ana Lopez-de Fede [via conference call]
Dr. Masahiro Narita
Dr. Barbara Seaworth

**ACET Designated Federal Official**
Dr. Hazel Dean, NCHHSTP Deputy Director

**ACET *Ex-Officio* Members**
Dr. Naomi Aronson (Department of Defense)
Dr. William Baine (Agency for Healthcare Research and Quality)
Mr. Warren Hewitt (Substance Abuse and Mental Health Administration)
Dr. John Redd (Indian Health Service)
Dr. Gary Roselle (Department of Veteran Affairs)
Dr. Diana Schneider (Department of Homeland Security)
Dr. Theresa Watkins-Bryant (Health Resources and Services Administration)

**ACET Liaison Members**
Dr. Robert Benjamin (National Association of County and City Health Officials)
Ms. Kimberly Field (National Tuberculosis Controllers Association)
Ms. Belinda Haerum (Alternate, Association of State and Territorial Health Officials)
Ms. Jennifer Maurer (RESULTS Educational Fund)
Dr. Edward Nardell (International Union Against Tuberculosis and Lung Disease)
Dr. Lee Reichman (American College of Chest Physicians)
Mr. Dan Reyna (Alternate, U.S.-Mexico Border Health Commission, U.S. Section)
Ms. Rachel Stricof (Association of Professionals of Infection Control and Epidemiology, Inc.)
Dr. Litjen Tan (American Medical Association)
Dr. Maria Teresa Zorrilla (U.S.-Mexico Border Health Commission, Mexico Section)

**CDC Representatives**
Dr. Kenneth Castro, DTBE Director
Ms. Lori Armstrong
Dr. Sapna Bamrah
Ms. Eileen Bell
Dr. Terence Chorba
Mr. Terry Comans
Ms. Ann Cronin
Ms. Kendra Cuffe
Ms. Beverly DeVoe
Ms. Mollie Dowling
Ms. Judy Gibson
Dr. Kathleen McDavid Harrison
Mr. Andy Heetderks
Dr. Michael Iademarco
Dr. John Jereb
Dr. Dolly Katz
Dr. Awal Khan
Ms. Ann Lanner
Mr. Yecai Liu
Dr. Philip LoBue
Dr. Sundari Mase
Dr. Beverly Metchock
Dr. Patrick Moonan
Dr. Thomas Navin
Ms. Bonnie Plikaytis
Ms. Lauren Polansky
Dr. Drew Posey
Dr. Krista Powell
Ms. Lee Ann Ramsey
Ms. Cheri Rice

Mr. Joseph Scavotto
Ms. Margie Scott-Cseh
Ms. Anne Shuttleworth
Mr. Phillip Talboy
Ms. Melisa Thombley
Mr. Sean Toney
Ms. Silvia Trigoso
Dr. Elsa Villarino
Dr. Jessie Wing

**Guest Presenters and**
**Members of the Public**

Dr. Jennifer Flood (California Department of Health Services)
Dr. Masae Kawamura (San Francisco Department of Public Health)
Dr. Jon Krohmer (Department of Homeland Security)
Dr. David Lakey (Texas Department of State Health Services)
Ms. Eileen Napolitano (Stop TB USA)
Mr. Eddie Olivarez (Hidalgo County Health Department) [via conference call]
Ms. Carol Pozsik (National Tuberculosis Controllers Association)
Mr. John Seggerson (Stop TB USA)
Dr. Charles Wallace (Texas Department of State Health Services)
Ms. Kelly Wroblewski (Association of Public Health Laboratories)

# ATTACHMENT 2

## Glossary of Acronyms

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|---|---|
| ACET | Advisory Council for the Elimination of Tuberculosis |
| ADS | Associate Director for Science |
| AMK | Amikacin |
| ASTHO | Association of State and Territorial Health Officials |
| BHC | (U.S.-Mexico) Border Health Commission |
| CAP | Capreomycin |
| CBP | U.S. Customs and Border Patrol |
| CRH VMD | Cho Ray Hospital Visa Medical Department |
| DGMQ | Division of Global Migration and Quarantine |
| DHS | Department of Homeland Security |
| DOT | Directly Observed Therapy |
| DST | Drug Susceptibility Testing |
| DSTDP | Division of STD Prevention |
| EMB | Ethambutol |
| ERO | (ICE) Enforcement and Removal Operations |
| FBP | Foreign-Born Persons |
| FDA | Food and Drug Administration |
| FLDs | First-Line Drugs |
| FOA | Funding Opportunity Announcement |
| FQ | Fluoroquinolones |
| GLC | Green Light Committee |
| HCP | Healthcare Personnel |
| HHS | Department of Health and Human Services |
| HRSA | Health Resources and Services Administration |
| ICE | U.S. Immigration and Customs Enforcement |
| IGRAs | Interferon Gamma Release Assays |
| IND | Investigational New Drug |
| INH | Isoniazid |
| IOM | Institute of Medicine & International Organization for Migration |
| IRB | Institutional Review Board |
| KAN | Kanamycin |
| LTBI | Latent TB Infection |
| *M.tb* | *Mycobacterium Tuberculosis* |
| MDDR | Molecular Detection of Drug Resistance (Service) |
| MDR-TB | Multidrug-Resistant TB |
| MSM | Men Who Have Sex With Men |
| NACCHO | National Association of County and City Health Officials |
| NCET | National Coalition for the Elimination of Tuberculosis |
| NCHHSTP | National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention |
| NEDSS | National Electronic Disease Surveillance System |
| NHANES | National Health and Nutrition Examination Survey |
| NTCA | National Tuberculosis Controllers Association |

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|---|---|
| NTP | National TB Program |
| NTSS | National TB Surveillance System |
| OHA | (DHS) Office of Health Affairs |
| OHE | (NCHHSTP) Office of Health Equity |
| PCR | Polymerase Chain Reaction |
| PCSI | Program Collaboration and Service Integration |
| PHLs | Public Health Laboratories |
| PPACA | Patent Protection and Affordable Care Act |
| PZA | Pyrazinamide |
| QFT | QuantiFERON |
| RDDR | Rapid Detection of Drug Resistance (Service) |
| RLT | (DTBE) Reference Laboratory Team |
| RMP | Rifampin |
| RTMCCs | Regional Training and Medical Consultation Center |
| SAMHSA | Substance Abuse and Mental Health Services Administration |
| SDH | Social Determinants of Health |
| SLDs | Second-Line Drugs |
| TATB | “Ten (States) Against Tuberculosis” |
| TB GIMS | Tuberculosis Genotyping Information Management System |
| TBTC | TB Trials Consortium |
| TBTIs | TB Technical Instructions |
| TCID | Texas Center for Infectious Diseases |
| TST | Tuberculin Skin Test |
| USAID | U.S. Agency for International Development |
| USBP | U.S.-Born Persons |
| USPSTF | U.S. Preventive Services Task Force |
| WHO | World Health Organization |
| XDR-TB | Extensively Drug-Resistant TB |

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## ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
## November 2-3, 2010
## Atlanta, Georgia

# Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHHSTP) Division of Tuberculosis Elimination (DTBE) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on November 2-3, 2010 in Building 8 of CDC's Corporate Square Campus, Conference Room A/B/C in Atlanta, Georgia.

### Opening Session

Dr. Hazel Dean, Deputy Director of NCHHSTP and Designated Federal Official of ACET, called the meeting to order at 8:34 a.m. on November 2, 2010. She welcomed the attendees to the proceedings and conducted a roll call of the ACET members and the non-voting *ex-officio* members to establish a quorum for day 1 of the meeting.

After confirming the presence of a quorum, Dr. Dean announced that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. 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 noted the following changes to ACET's membership. Ms. Belinda Haerum is serving as the alternate liaison to the Association of State and Territorial Health Officials (ASTHO) on behalf of Dr. José Montero. Dr. Robert Benjamin replaced Dr. Robert Kim-Farley as the liaison to the National Association of County and City Health Officials (NACCHO).

Ms. Jennifer Maurer is a new liaison to RESULTS Educational Fund. Ms. Maria Teresa Zorrilla replaced Secretary Clemente Villalpando as the liaison to the Mexico Section of the U.S.-Mexico Border Health Commission. Dr. Diana Schneider has resumed her previous role as the *ex-officio* to the Department of Homeland Security (DHS).

Dr. Dean welcomed three guest speakers who would make presentations during the ACET meeting on various TB-related issues. Dr. Jon Krohmer is the Senior Medical Officer of the DHS Office of Health Affairs. Dr. David Lakey is the Commissioner of Health in the Texas Department of State Health Services. Dr. Jennifer Flood is a former ACET member and the Chief of Surveillance and Epidemiology in the Tuberculosis Control Branch of the California Department of Health Services.

Dr. Dean also welcomed other guests who were in attendance. Dr. Charles Wallace is a former ACET member and the TB Program Director of the Texas Department of State Health Services. Ms. Kelly Wroblewski is a Program Manager for the Association of Public Health Laboratories (APHL). Ms. Eileen Napolitano the Chair-elect of Stop TB USA.

Dr. Dean announced that the 180-day extension of terms would end on December 31, 2010 for the following ACET members: Drs. Michael Fleenor (Chair), Ana Lopez-de Fede and Masahiro Narita, Mr. Joseph Kinney and Ms. Sirlura Taylor. CDC has submitted nomination packages for the new ACET members to the White House Liaison.

At the conclusion of her announcements, Dr. Dean opened the floor for introductions. The list of participants is appended to the minutes as Attachment 1.

## NCHHSTP Director's Report

**Hazel Dean, ScD, MPH**
Deputy Director, NCHHSTP
Centers for Disease Control and Prevention

Dr. Dean covered the following areas in the update on behalf of Dr. Kevin Fenton, Director of NCHHSTP. At the agency level, the CDC Center for Global Health named its leadership: Dr. Kevin DeCock (Director), Dr. Patricia Simone (Principal Deputy Director), Mr. Donald Shriber (Deputy Director for Policy and Communication), Mr. Nick Farrell (Acting Deputy Director for Management and Overseas Operations), Dr. Deborah Birx (Division of Global HIV/AIDS Director), Dr. Scott Dowell (Division of Global Disease Detection and Emergency Response Director), Dr. Mark Eberhard (Division of Parasitic Diseases and Malaria Director), and Mr. Bassam Jarrar (Division of Public Health Systems and Workforce Development Acting Director).

At the National Center level, Dr. Frederick Bloom is the Acting Associate Director for Science (ADS) in NCHHSTP due to Dr. Terence Chorba's new position as Chief of the DTBE Field Services and Evaluation Branch. Dr. Bloom is the Deputy ADS in the Division of STD Prevention (DSTDP). Dr. Charlotte Kent is the Acting Director of DSTDP. NCHHSTP plans to complete its recruitment efforts by the end of 2010 to fill the two positions of the DSTDP Director and NCHHSTP ADS.

NCHHSTP made Program Collaboration and Service Integration (PCSI) awards in September 2010 to six state and local health departments under the funding opportunity announcement

(FOA), “Addressing Syndemics through PCSI.” The health department grantees are New York City, North Carolina, Philadelphia, San Francisco, Texas and Washington, DC. The PCSI awards will total $6.2 million over a three-year funding cycle for the grantees to combine and streamline health services for HIV/AIDS, STDs, viral hepatitis and TB.

The NCHHSTP Social Determinants of Health (SDH) White Paper, *Establishing a Holistic Framework to Reduce Inequities in HIV, Viral Hepatitis, STDs and Tuberculosis in the United States*, was published in October 2010. The white paper outlines NCHHSTP’s strategic vision for reducing health disparities and promoting health equity related to HIV/AIDS, STDs, viral hepatitis and TB by incorporating an SDH approach. The purpose of the white paper is to advance a holistic approach to the design of NCHHSTP’s public health programs to advance the health of communities and increase their opportunities for healthy living.

The white paper was distributed to ACET for review and also is available to the public at www.cdc.gov/socialdeterminants. Dr. Dean thanked ACET for providing extensive and helpful input on the draft white paper. ACET’s comments were incorporated into the final published version.

CDC is operating under a continuing resolution through December 3, 2010 with funding at FY2010 levels.

## DTBE Director’s Report

**Kenneth Castro, MD**
Director, DTBE
Centers for Disease Control and Prevention

Dr. Castro covered the following areas in his update. DTBE regrettably announced that its dear colleague and friend, Susan Bacheller, passed away the previous week. Ms. Bacheller dedicated >15 years of service to the U.S. Agency for International Development (USAID) and the global public health community. The participants joined Dr. Castro in a moment of silence to pay tribute to Ms. Bacheller.

DTBE and its federal partners investigated several TB outbreaks from February-October 2010 that involved various populations and settings, including federal prisons, a jail, homeless shelters, hospitals and rural communities.

TB prevention and control cooperative agreements, including support for Regional Training and Medical Consultation Centers (RTMCCs) and laboratory activities, accounted for the vast majority of the DTBE FY2010 budget of ~$147 million. The remainder of the FY2010 budget was allocated to staff salaries, direct assistance and project support, the TB Trials Consortium (TBTC), TB Epidemiologic Studies Consortium, the TB trial in Botswana, and external partnerships.

DTBE had nearly $6 million in unobligated funds at the end of FY2010. This unusual trend was due to changes in the management of funds in HHS-CDC contracts, severable versus non-severable contracts, and changes in funding abilities. DTBE leadership decided to make strategic one-time investments to address priority needs in three areas of concentration.

Area 1 focuses on "strengthening and protecting programs." DTBE awarded ~$100,000 to facilitate the transition from the TB Information Management System to the National Electronic Disease Surveillance System (NEDSS) in ten program areas, assist in the migration to NEDSS and provide real-time reporting.

DTBE is improving contact investigations by collaborating with RTMCCs to provide updated training, using National Tuberculosis Indicators Project data to identify weaknesses in contact investigations, and incorporating an evaluation component. DTBE enhanced capacity for outbreak response and management of multidrug-resistant TB (MDR-TB) in three states and provided resources to support further development of the Electronic Disease Notification System to enable the submission of timely information to state TB programs. CDC's confidentiality agreements with states prohibit DTBE from releasing the names of states with TB outbreaks.

Area 2 focuses on "increasing access to new diagnostics" to protect and strengthen local infrastructures. DTBE is increasing access to molecular diagnostics to all 64 laboratories in the country under cooperative agreements with APHL and selected programs. DTBE will allocate funding in 2011 to increase access to interferon gamma release assays (IGRAs).

Area 3 focuses on "improving the knowledge of the burden of disease in the United States." A TB component will be incorporated into the National Health and Nutrition Examination Survey (NHANES). A survey will be administered to determine the national prevalence of latent TB infection (LTBI). A study will be conducted to bridge the QuantiFERON (QFT)-in tube test and tuberculin skin test (TST).

DTBE has been partnering with the NCHHSTP Office of the Director since April 2010 internally and collaborating with the George Washington University Health Policy Department externally after the Patient Protection and Affordable Care Act (PPACA) was enacted in March 2010. DTBE submitted two TB proposals for funding under five-year Community Transformation Grants.

The first proposal focused on homeless persons because recent investigations by DTBE and health departments showed that this population accounts for 78% of TB outbreaks. The second proposal focused on incarcerated populations to ensure continuity of TB care after these persons are released. DTBE is coordinating with the CDC Policy Office to use the PPACA Prevention and Wellness Fund to conduct prevention activities through health care.

DTBE submitted a TB screening and treatment topic to the U.S. Preventive Services Task Force (USPSTF) for a review of the evidence. TB was only mentioned with a reference to the DTBE website in the last USPSTF review in 1996. If USPSTF gives the TB screening and treatment topic an "A" or "B" recommendation based on its review of the evidence, first-dollar coverage

under PPACA for TB screening and treatment would apply and consumers would not be required to pay a co-payment for TB screening.

DTBE's special PPACA-TB consultation in October 2010 with ~30 national representatives served as NCHHSTP's first consultation on PPACA with external partners. The consultation included exceptional presentations and rich discussions on TB control in a changing health environment under PPACA. DTBE categorized recommendations from the consultation in five major areas.

The partnership between CDC and the Health Resources and Services Administration (HRSA) should be strengthened. Existing partnerships between HRSA-funded Community Health Centers and TB programs should serve as a model. To respond to this recommendation, DTBE is currently collaborating with the National Tuberculosis Controllers Association (NTCA) to solicit examples of model partnerships and has submitted a TB Leads proposal to develop PPACA-TB activities.

An infectious disease package should be developed for primary healthcare centers to use for screening. To respond to this recommendation, DTBE is taking an integrated approach to model infectious diseases, influenza, TB, STDs, HIV and hepatitis and also will take advantage of the offer by the Infectious Diseases Society of America National Global Public Heath Committee to address concerns of perceived threats to TB program subject-matter expertise.

TB services should be provided to undocumented persons because this population is not covered under PPACA. To respond to this recommendation, DTBE has asked George Washington University to explore potential solutions for safety nets. Meaningful use electronic health records standards should be used for surveillance and evaluation data. DTBE plans to release a white paper based on findings from the consultation.

The DTBE Aberration Detection Workgroup met in September 2010 and issued several priority recommendations to advance TB genotyping: prepare best practices for aberration detection; develop a toolbox of cluster investigation resources; draft a formal research agenda for aberration detection; enhance the Tuberculosis Genotyping Information Management System (TB GIMS) to collate risk factor data that might predict the growth of clusters and facilitate earlier action by health departments; and incorporate tools into TB GIMS to manage cluster investigations. The workgroup will hold periodic conference calls and convene face-to-face meetings in the future to respond to these recommendations.

NTCA conducted an evaluation of TB GIMS users in consultation with DTBE. The evaluation showed that 71% of users were satisfied with TB GIMS and 77% of users utilized TB GIMS to assess genotype clusters. DTBE is currently pursuing opportunities to expand TB GIMS training activities with videos, live webinars and self-study modules. DTBE has redesigned TB GIMS to send automatic alerts when a cluster grows to a critical threshold or a user-designated cluster increases in size to interrupt the chain of TB transmission.

The DTBE International Research and Program Branch is conducting a study to translate research to practice. In the scientific research component, DTBE is conducting a TB/HIV study

in Cambodia, Thailand and Vietnam to identify a new approach to more accurately diagnose TB in persons living with HIV/AIDS by incorporating and validating algorithms.

In the national and international policy change component, Cambodia will change its national policy and the World Health Organization (WHO) will change international guidelines based on findings of the study. In the evaluation component, effectiveness studies will be conducted in the program settings of Cambodia, Thailand and Vietnam. In the validation and incorporation component, secondary studies will be conducted to validate findings in other regions and include new and different uses of diagnostic advances.

In response to Mr. Jones' question, Dr. Castro confirmed that DTBE would provide an overview during a future ACET meeting on the role of the National HIV/AIDS Strategy in TB elimination and the role of TB in HIV prevention.

The ACET members made three key suggestions in response to Dr. Castro's report for DTBE to consider in improving its TB elimination activities.

- The NHANES bridging study on the QFT-in tube test and TST should be linked to findings on vitamin D. This approach might help to better understand disparities in QuantiFERON and TST results, particularly in minority populations.
- DTBE should encourage TB program managers to identify their states by name when a TB outbreak occurs. This approach would help to facilitate advocacy and raise public awareness of the continued problem of TB.
- DTBE should review its existing recommendations on TB control in healthcare facilities due to the recent outbreaks in hospitals. An overview should be placed on a future ACET agenda of the outcomes of DTBE's recent outbreak investigations in hospitals.

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

**Drew Posey, MD, MPH**
Team Leader, Medical Assessment and Policy
Immigrant, Refugee and Migrant Health Branch, DGMQ
Centers for Disease Control and Prevention

Dr. Posey covered the following areas in his update. DGMQ's implementation of directly observed therapy (DOT) and culture in the screening algorithm for U.S.-bound immigrants and refugees in 30 countries represents 60% of immigrants and the majority of refugees. DGMQ's implementation of the TB Technical Instructions (TBTIs) was expanded to Ghana, India and Nigeria in October 2010 and will include seven additional countries in FY2011: Bangladesh, Guatemala, Indonesia, Malaysia, Peru, South Korea and Thailand.

The ACET/NTCA evaluation of the implementation of the TBTIs in Guangzhou, China will be conducted in the summer of 2011. Regional training courses will be offered to panel physician programs in Lima, Peru in August 2011 and Bangkok, Thailand in March 2011.

DGMQ is collecting data from panel physician programs in the largest source countries for immigrants and refugees to determine TB and MDR-TB rates based on FY2009 arrivals. These data include TB rates per 100,000 and MDR-TB rates in the source countries based on U.S. and WHO screening. DGMQ will use these data to monitor the effectiveness of overseas TB screening programs.

India is the fourth largest source country of immigrants to the United States and accounted for 25,324 arrivals in FY2009. DGMQ enhanced strong collaborations with its intergovernmental partners in Australia and Canada to establish panel sites In India in 2008. These partnerships led to creating a TB Laboratory Network in India in October 2010, conducting site visits and providing training.

DGMQ represented the United States in the 7th Intergovernmental Immigration and Refugee Health Workgroup meeting that was held in October 2010. Australia, Canada, New Zealand and the United Kingdom also were represented. During the meeting, the workgroup identified three major priorities related to TB: alignment of panel physician programs among the partner countries, interoperability through information technology, and common standards for refugee health.

DGMQ is linking immigration screening to in-country programs. The Ciudad Juarez, Mexico panel site reflects collaboration between two private physicians, includes an onsite laboratory, and uses liquid and solid media to perform first-line drug susceptibility testing (DST). In addition to Ciudad Juarez, Tijuana and Veracruz also provide DOT. DGMQ is continuing its involvement in U.S.-Mexico binational TB activities. For example, the role of Project Juntos is to treat binational TB cases in the El Paso-Ciudad Juarez region and send sputum specimens to the panel site for culture and DST.

## Overview of the Vietnam TB Screening and Treatment Program Evaluation

**Jennifer Flood, MD, MPH**
Chief, Surveillance and Epidemiology
Tuberculosis Control Branch
California Department of Health Services

Dr. Flood presented an overview of the evaluation of the Vietnam TB Screening and Treatment Program for U.S.-bound immigrants and refugees. The purpose of the evaluation was to assess implementation of the revised TBTIs, identify model practices for other immigrant screening programs, and provide recommendations to CDC for improving the 2007 TBTIs.

The methodology and design of the evaluation included observations of all aspects of the Vietnam TB Screening and Treatment Program; structured interviews with patients and staff; a review of medical records of 62 children and adults and 47 chest radiographs; and interviews with partners and stakeholders, including the Consulate in Ho Chi Minh City and the National TB Program (NTP) in Hanoi.

The TB rate in Vietnam of ~189/100,000 is extremely high. Vietnam is one of 22 countries with the highest burden of TB globally. TB/HIV co-infection increased from <1% in 1994 to ~5% in 2006. NTP recently started providing short-course TB treatment and MDR-TB therapy. The Vietnam Immigrant Screening Program began implementing a revised protocol in February 2008.

The Cho Ray Hospital Visa Medical Department (CRH VMD) performs most U.S. immigrant screening and provides all TB treatment for immigrants and refugees. The International Organization for Migration (IOM) screens immigrants bound for Canada, Australia and New Zealand as well as refugees and some immigrants bound for the United States. The CRH Laboratory performs smear, culture and first-line DST and the PNT Laboratory performs second-line DST.

The evaluation panel found Vietnam's TB case detection practices to be impressive and conducted in an efficient process despite the high volume. Vietnam consistently adhered to the TBTIs and has implemented an effective referral process from panel physicians to specialists. Dr. Flood highlighted the evaluation panel's major findings on the Vietnam TB Screening and Treatment Program.

In terms of screening, of 21,609 persons in Vietnam who applied for permanent residence in Canada, Australia, New Zealand or the United States in 2009, 202 were culture-positive representing a TB rate of ~900/100,000. Of the 202 persons identified with TB, 61% were pan-susceptible, 4% had mono-resistance to isoniazid (INH), 14 had mono-resistance to other drugs, 15% had non-MDR-TB poly-drug resistance, and 5.3% had MDR-TB. In 2009, 129 of 180 (or 72%) of TB cases on treatment were smear-negative/culture-positive. These cases would not have been detected under the previous TBTIs.

In terms of treatment outcomes, treatment regimens and duration were consistently modified based on DST. Sputum conversion was documented in ~95% of patients within 90 days of the start of therapy. In 2008, 90% of TB cases treated were cured, 0.8% died, 3.7% defaulted, 4.1% did not register for treatment, and 1.2% were still on treatment.

In terms of case detection, the review of chest x-rays for 47 patients found that the quality of the technique used and interpretation of the radiographs was outstanding. Concordance between an external reviewer and a staff radiology or physician was high. TST placement and reading procedures were determined to be excellent. However, vials of purified protein derivative solution were not available for a long period of time and resulted in a backup in screening.

Sputum collection was found to be optimal in terms of volume, quality and processing, but gastric aspirates were not performed. No active TB cases in pediatric populations have been identified to date. Laboratory performance was determined to be excellent overall based on performance indicators. However, delays were observed in reporting results of valid first-line DST for confirmatory testing. Notification of second-line DST results from the PNT Laboratory exceeded 6-8 weeks in multiple cases.

In terms of clinical management, a single clinician provides cares to a large volume of patients and gives outstanding attention to clinical detail. However, the evaluation panel was concerned

that the clinician has no backup and limited access to expert consultation for MDR-TB and other complicated cases. The evaluation panel provided the clinician with technical assistance in accessing the RTMCC to obtain medical consultation. The requirement of patients to pay $4,400 to begin an MDR-TB regimen led to treatment delays and refusals. The removal of HIV as an inadmissible condition resulted in no HIV testing of TB cases in 2010.

In terms of linkages and capacity building, exchanges between the panel site and NTP are in the early stages of development. TB cases are not reported from the panel site to NTP. NTP does not recognize the CRH Laboratory and clinical program. MDR-TB treatment recently began in both NTP and the screening program.

The evaluation panel made four key recommendations to CRH and IOM. Pediatric case detection should be enhanced and further monitored. Laboratory reporting should be improved. Staffing should be augmented to ensure access to expert clinical consultation. Exchanges should be expanded among IOM, CRH, NTP and VMD.

The evaluation panel made four key recommendations to CDC. Recommendations should be clarified to ensure HIV testing of TB suspects and cases. Joint efforts should be made with IOM, CRH and VMD to alleviate patient cost barriers to MDR-TB treatment. Linkages between NTP and the panel screening program should be encouraged. Screening protocols should be harmonized across destination countries.

Dr. Flood concluded that the 2007 TBTIs have made a significant impact on domestic TB control. In California, for example, TB cases among B-notification arrivals total ~6,000 each year. With the previous TBTIs, 3%-7% of B-notification arrivals to California were diagnosed with active TB within six months of arrival. After implementation of the 2007 TBTIs, this rate decreased to <1% among B-notification arrivals to California from Mexico, the Philippines and Vietnam.

## Overview of the Impact of Global Migration on TB in the United States

**Yecai Liu, MS**
Mathematical Statistician, DGMQ
Centers for Disease Control and Prevention

Mr. Liu presented data that DGMQ is using to estimate the impact of global migration on TB in the United States. Foreign-born persons (FBP) accounted for 59% of the 11,540 TB cases in the United States in 2009. The TB rate was 19 cases/100,000 population among FBP and 2 cases/100,000 population in U.S.-born persons (USBP) in 2009. Data collected from the National TB Surveillance System (NTSS) from 2001-2008 and the 2007 and 2008 Cain, *et al.* studies showed that FBP within one year after U.S. arrival accounted for 19% of foreign-born TB cases, 31% of foreign-born MDR-TB cases, and had a TB rate of 110-121 cases per /100,000 population.

The DHS Office of Immigration Statistics data show the number of FBP who entered the United States in 2009 included 538,000 immigrants and refugees, 163 million non-immigrant visitors and an unknown number of unauthorized visitors. Of 163 million non-immigrant visitors, 36 million had an arrival-departure card (or an I-94 form) and 127 million from Canada and Mexico did not have an I-94 form. Of 36 million visitors with an I-94 form, 3.4 million were long-term visitors (e.g., students and exchange visitors, temporary workers and diplomats) and 32.5 million were short-term visitors (e.g., tourists and business travelers).

Overseas TB screening is required for U.S.-bound immigrants and refugees and is a relatively high-yielded intervention. Each year, ~500,000 immigrants and refugees are screened overseas. Overseas TB screening is not required for millions of non-immigrant visitors who arrive in the United States annually, but many of these FBP are from countries with a high TB incidence and can remain in the United States for multiple years.

The objectives of DGMQ's data analysis were to estimate the incidence of TB among newly arrived FBP and the potential yield of screening for TB in these populations. The study populations included immigrants and refugees, and non-immigrant visitors with an I-94 form. The long-term visitors (e.g., students, exchange visitors, temporary workers and diplomats) had a U.S. visa for an initial stay $\geq$6 months. Short-term visitors (e.g., business travelers and tourists) had a U.S. visa for an initial stay <6 months. Immigrants and refugees obtained a U.S. visa for permanent resident overseas.

Data sources that DGMQ used in the analysis included 2001-2008 admission data by country of citizenship and year of arrival. CDC data were used to determine the number of admissions for refugees. DHS data were used to determine the number of admissions for non-immigrant visitors who required an I-94 form and immigrants. WHO data included annual estimates of country-specific TB incidence rates, and the 2004 and 2008 country-specific MDR-TB proportions among new TB cases.

"High-incidence" countries (e.g., India, the Philippines and Vietnam) were defined as those with the 2008 WHO-estimated TB incidence rate of $\geq$100 cases per 100,000 population per year. "Medium-incidence" countries (e.g., China, Japan and Korea) were defined as those with the 2008 WHO-estimated TB incidence rate of 20-99 cases per 100,000 population per year. "Low-incidence" countries (e.g., Canada, Mexico and the United Kingdom) were defined as those with the 2008 WHO-estimated TB incidence rate of 0-19 cases per 100,000 population per year.

DGMQ made a number of assumptions in estimating the number of TB incident cases among FBP. Due to the large decrease in the foreign-born TB rate by year of arrival, the data analysis was restricted to the first year after arrival in the United States. FBP within one year after arrival in the United States were defined as "newly arrived."

To estimate the number of TB incident cases among newly arrived FBP, country-specific incidence rates and the time of stay within one year after arrival in the United States were needed. FBP arriving in a specific year were assumed to have WHO-estimated incidence rates for their country of citizenship in that year. Immigrants and refugees were assumed to have remained in the United States for at least one year after arrival. DHS means were used to determine the length of stay for non-immigrant with an I-94 form (e.g., 180 days for students,

exchange visitors and temporary workers; 79 days for diplomats; and 22 days for short-term visitors). However, the DHS means were calculated by including the time of stay >1 year. DGMQ developed a method to adjust the DHS means with an assumption that the mean length of stay was 1.5 years for FBP who stayed >1 year.

Person-years for newly arrived FBP were stratified by country of citizenship and year of arrival. For long- and short-term visitors, person years were calculated as the number of admissions multiplied by the adjusted DHS-estimated mean length of stay. Person-years for immigrants and refugees were equal to the admissions since they were assumed to stay for at least 1 year in the United States after arrival.

Stratified by country of citizenship and year of arrival, the number of TB incident cases was equal to the number of person-years multiplied by WHO-estimated country-specific TB incident rate. Stratified by country of citizenship, the number of MDR-TB incident cases was equal to TB incident cases in 2001-2004 multiplied by WHO-estimated country-specific MDR-TB rate in 2004 plus TB incident cases in 2005-2008 multiplied by WHO-estimated country-specific MDR-TB rate in 2008.

DGMQ acknowledges several limitations of the data analysis. FBP may have a low TB incidence rate due to better socioeconomic status. WHO-estimated country specific MDR-TB rates were limited to the years of 2004 and 2008 in new TB cases. The DHS-estimated means of length of stay were based on departing data in 2003 and were not country-specific. The burden of TB could not be estimated for unauthorized visitors and commuters from Canada and Mexico without an I-94 form.

Mr. Liu highlighted the estimates of DGMQ's data analysis. Of ~259 million FBP admitted to the United States in 2001-2008, 9.5% were long-term visitors, 89% were short-term visitors, and 1.5% were immigrants/refugees. Of the 16,025 estimated TB incident cases among FBP admitted to the United States in 2001-2008, long-term visitors accounted for 40%, short-term visitors accounted for 30%, and immigrants/refugees accounted for 30%. Of the 441 estimated MDR-TB cases among FBP admitted to the United States in 2001-2008, long-term visitors accounted for 41%, short-term visitors accounted for 26%, and immigrants/refugees accounted for 33%.

NTSS data showed that in 2001-2008, FBP within 1 year in the United States after arrival accounted for 12,099 TB cases and 249 MDR-TB cases. DGMQ's likely over-estimated both the number of TB cases and the number of MDR-TB cases among newly arrived foreign-born persons during the same period. DGMQ's overestimation most likely was due to the small likelihood of short-term visitors seeking care in the United States since they only stayed in the United States for a short period.

The top 54 newly arrived foreign-born populations with the largest estimated TB incident rate were immigrants and refugees from high-incidence countries (236 cases/100,000 admissions), long-term visitors from high-incidence countries (83 cases/100,000 admissions), immigrants and refugees from medium-incidence countries (69 cases/100,000 admissions), long-term visitors from medium-incidence countries (23 cases/100,000 admissions), and immigrants and refugees from low-incidence countries (17 cases/100,000 admissions).

Mr. Liu presented some more results on long-term visitors. Of ~25 million newly arrived long-term visitors to the United States in 2001-2008, 37% were students or exchange visitors, 54% were temporary workers, 9% were diplomats, 61% were male, and 80% were 15-44 years of age. Only 19% of long-term visitors were from high-incidence countries, but they accounted for 62% of the 6,354 estimated TB incident cases and 63% of the 182 estimated MDR-TB cases among newly arrived long-term visitors. Approximately 30% of long-term visitors were from India, Korea, China, the Philippines and Mexico, but they accounted for 49% of estimated TB cases in newly arrived long-term visitors.

Overall, the data analysis showed that newly arrived long-term visitors substantially contribute to the burden of foreign-born TB in the United States. The potential yield of screening in long-term visitors from high-incidence countries was likely larger than the yield of screening in any foreign-born population with the exception of immigrants/refugees from high-incidence countries. DGMQ recommends conducting additional studies to evaluate overseas TB screening in long-term visitors from high-incidence countries.

Note: Mr. Liu's presentation was based on the preliminary results of the DGMQ's study. Mr. Liu and his colleagues continue to work on the analysis for improving the estimation.

Dr. Fleenor confirmed that during the business session on the following day, ACET would discuss DGMQ's request for input in three areas: (1) implementation of the 2007 TBTIs to build linkages with in-country TB programs; (2) recommendations on the evaluation of the Vietnam TB Screening and Treatment Program; and (3) DGMQ's data analysis to estimate the impact of global migration on TB in the United States.

## Update by the NCHHSTP Office of Health Equity

**Kathleen McDavid Harrison, PhD, MPH, FACE**
Associate Director for Health Equity, NCHHSTP
Centers for Disease Control and Prevention

Dr. McDavid Harrison provided an update on NCHHSTP's health equity activities. NCHHSTP's strategic focus on health equity was driven by persistent observations of unequal health outcomes in terms of race, gender, socioeconomic status, sexual orientation and housing status. The mission of the Office of Health Equity (OHE) is to improve the health of populations disproportionately affected by HIV, viral hepatitis, STDs, TB and other related diseases and conditions with ultimate goal of eliminating health disparities and inequities.

Health equity is one of six goals in the NCHHSTP 2010-2015 Strategic Map. NCHHSTP established three objectives to achieve this goal: (1) advance science in identifying and eliminating disparities; (2) mobilize partners to promote health equity and social determinants of health; and (3) identify and address key social determinants of health for programs.

HHS and CDC have defined several health equity terms. "Health disparity" is a particular type of health difference that is closely linked with social or economic disadvantage. "Heath inequity" is a difference or disparity in health outcomes that is systematic, unfair and avoidable. "Health equity" is attainment of the highest level of health for all persons. Achieving health equity requires valuing all persons equally with focused and ongoing societal efforts to address avoidable inequalities, historical and contemporary injustices, and the elimination of health and healthcare disparities.

"Individual-level risk factors" are characteristics of individuals that may explain health status or behavior (e.g., age, sex or marital status). "Social determinants of health" (SDH) are complex, integrated and overlapping social structures and economic systems that are responsible for most health inequities. SDH is shaped by the distribution of money, power and resources at global, national and local levels that are themselves influenced by policy choices. SDH does not focus on individual factors that cause health disparities, but serves as the "causes of the causes" of health disparities and inequities.

Dr. McDavid Harrison highlighted OHE's major health equity accomplishments in 2010. A *Public Health Reports* Supplement, *Social Determinants of Health in the Prevention and Control of HIV/AIDS, Viral Hepatitis, Sexually Transmitted Infections and Tuberculosis*, was electronically published in June 2010. A call for papers on data systems and SDH was released in a *Public Health Reports* Supplement for publication in 2012. Health equity and SDH language were developed for inclusion in NCHHSTP FOAs. The 2009 SDH Activities Report was created for each NCHHSTP division and SDH category.

The Health Equity Symposium, "Establishing a Holistic Framework to Reduce Inequities in HIV, Viral Hepatitis, STDs and Tuberculosis in the United States," was held in October 2010. The purpose of the symposium was to release the SDH white paper and celebrate the sixth year of the Health Equity Scientific Lecture Series. Keynote speakers made presentations on science, policy, communications and health equity from a state perspective.

The SDH white paper that was released in October 2010 outlines NCHHSTP's commitments to this effort. Guidance on SDH definitions, measures, indictors and data sources for NCHHSTP staff will be prepared and disseminated. A strategic communication plan will be created to support action by partners and program staff. SDH and health equity will be addressed in all of NCHHSTP's FOAs in the future.

Structural, social and other determinants will be included in existing prevention program portfolio. Materials will be developed with definitions, a clear rationale and examples of SDH activities for ongoing training of partners and NCHHSTP staff. The number and type of partners who can engage in SDH policy development will be strengthened, diversified and augmented. Many of the activities in the SDH white paper are aligned with the goal in the National HIV/AIDS Strategy to end health disparities.

The white paper also describes activities for NCHHSTP partners to consider. Partners should serve as champions and identify senior leaders in their organizations to also become champions in addressing SDH. Conversations should be initiated about the social and structural drivers of NCHHSTP's epidemics and strategies to address these drivers.

SDH measures should be incorporated into surveillance systems. SDH should be addressed in organizational FOAs and prevention program portfolios. SDH and health equity messages should be included in communication materials. Other partners should be educated in SDH. The existing base of partners who are currently engaged in SDH and health equity activities should be diversified.

OHE plans to conduct a number of activities in 2011 to further advance its health equity portfolio. Health equity and SDH language will be incorporated into all NCHHSTP FOAs. All funded projects with an SDH component will be rigorously monitored and evaluated by category. An SDH guidance document will be developed for NCHHSTP surveillance systems to monitor SDH-related variables. A communication science plan will be developed with a partnership engagement plan. Prevention portfolios will be expanded to include structural, social and other determinants. The 2010 SDH Activities Report will be published.

The number and types of partners internal and external to CDC will be diversified and augmented. SDH and health equity materials and tools will be developed and distributed to NCHHSTP staff and partners, including training slide sets, a glossary of terms, and a frequently asked questions document. The SDH website will be enhanced. Workgroup and leadership activities will continue to be coordinated across NCHHSTP, including the Health Equity, Corrections, and Men Who Have Sex With Men Workgroups.

Overall, SDH are the "causes of the causes" of poor health outcomes and inequities. NCHHSTP is committed to incorporating an SDH approach to change social, economic, political or environmental factors determining risk and vulnerability for disease and premature death. Efforts to addressing SDH are well underway in NCHHSTP and will continue to be an important part of NCHHSTP's plans for a balanced approach to addressing inequities in HIV, viral hepatitis, STD and TB prevention.

At the National Center level, ACET thanked NCHHSTP for providing each member with an opportunity to submit comments on the important SDH white paper. ACET was particularly pleased that health equity and SDH language would be incorporated into all NCHHSTP FOAs in the future. At the division level, ACET commended DTBE on providing extensive technical assistance to address TB disparities. For example, Dr. John Redd, the *ex-officio* member for the Indian Health Service, announced that DTBE recently provided a great deal of surveillance and epidemiologic support to address TB disparities in Native American populations.

The vast majority of ACET members were frustrated that NCHHSTP's health equity activities continue to be developed at the federal level without expansion and implementation to state, local and community levels to achieve a true impact on health equity in the field. ACET members also were discouraged that TB continues to be excluded from the HHS list of disparities.

ACET made three key suggestions for NCHHSTP to consider in refining its health equity portfolio in 2011.

- NCHHSTP should engage HHS and community leadership with experience in health equity to obtain input on making progress in implementing an actual and proactive health equity strategy.
- NCHHSTP should link its health equity portfolio to the National Partnership for Action to end Health Disparities that the HHS Office of Minority Health will release in the near future.
- NCHHSTP should explore the opportunity of naming and placing an Associate Director for Health Equity in both DTBE and the Division of Viral Hepatitis for center-wide impact.

## Update on Stop TB USA Activities

**Eileen Napolitano, BA**
Deputy Director, New Jersey Medical School Global Tuberculosis Institute
Chair-elect, Stop TB USA

Ms. Napolitano provided an update on activities conducted by Stop TB USA. TB project grants were awarded from 1961-1972. The TB project grants program was authorized in August 1981 and funded in FY1982 with supplemental funding of $1 million. The constant decline in TB rates leveled in 1984 and TB rates began to rise in 1985. ACET defined "TB elimination" as a case rate of <1/1 million in 1989. The TB case rate at that time was 9.3/100,000.

The American Lung Association, American Thoracic Society and CDC held a meeting in June 1991 to discuss challenges to TB control and TB resurgence. The key challenges identified during the meeting included the failure to sustain domestic TB control, the failure to maintain an active TB research effort, and the persistent misperception among the public and policymakers that TB is only a minor problem and found only in minorities and poor populations. The concept of the National Coalition for the Elimination of Tuberculosis (NCET) was proposed at that time.

NCET was organized in January 1992 with an initial grant from the Robert Wood Johnson Foundation. The 58 founding members represented public health, health care, professional medical organizations and Congressional health committees concerned with the care of individuals with TB or its control. NCET was reorganized in November 2002 with new goals aimed at implementing the Institute of Medicine Report (IOM) recommendations, new bylaws and a governance structure.

NCET's initial successes are highlighted as follows. A venue was created for the development of public-private partnerships. Support was provided for staff, travel and meetings, including the TB Research Scholar Program that led to the development of the North American Region meeting. New leaders within the TB community were established. The meeting of like minds for the first time resulted in benefits from synergy. Non-traditional partners for advocacy were introduced.

The Comprehensive TB Elimination Act and Stop TB Now Act were developed to address the IOM recommendations for domestic TB elimination and global TB control activities. The *Federal Funding Gap* Report was developed to highlight funding issues in support of annual domestic

appropriations for TB control. Partner organizations provided Congressional testimony on the report each year. Advocacy training resources were developed, including workshops and *TB Elimination: An Advocate's Guide*.

In August 2007, NCET leadership, advocacy partners and CDC unanimously agreed to transition NCET to Stop TB USA. The NCET goals, bylaws and governance structure would be retained. Advocacy and communications tools, including Stop TB Wire and "*TB No Longer a Problem*," would be continued. A website would be created at www.stoptbusa.org. An updated TB Elimination Plan as required by the Comprehensive TB Elimination Act would be developed and presented to ACET for endorsement. A Writing Committee and Launch & Advocacy Committee were established for this effort.

Stop TB USA released *A Call for Action on the Tuberculosis Elimination Plan for the United States* in March 2010. The major purposes of A Call to Action are to update the IOM plan and recommendations for eliminating TB, provide a foundation for making specific action plans to implement the IOM recommendations, and engage stakeholders in the effort to eliminate TB in the United States. The stakeholders include policymakers at all levels of government, the public health sector, medical practitioners, professional societies, community-based organizations and voluntary organizations. ACET formally endorsed A Call to Action during a previous meeting.

Key challenges for Stop TB USA at this time are mobilizing new partners and ensuring an environment in which all partners collaborate to achieve the goal of TB elimination; leveraging direct and indirect resources for Stop TB USA to undertake its mission; and continuing to address three major issues to reach TB elimination: the changing face of TB care and control in the United States, the impact of global TB care and control on U.S. efforts, and new tools.

Stop TB USA convened a retreat in September 2010 to review its mission and bylaws and NCET's ongoing activities. The interactions and contributions of the membership would be enhanced and the organizational structure would be updated to achieve this goal. The retreat also provided a forum to develop a work plan for the *Tuberculosis Elimination Plan for the United States*, including the identification of critical issues related to TB care, control and elimination.

The 21 participants at the retreat represented national, state and local TB programs, key advocacy partners and a patient representative. Two workgroups were formed to address the two goals. Workgroup A focused on the mission, structure and function of Stop TB USA by assessing resources and reviewing ongoing activities. Workgroup B focused on the TB Elimination Plan by proposing marketing and implementation strategies. The workgroups reported their recommendations to the full group for discussion.

Ms. Napolitano highlighted the key discussion points raised during the retreat. Stop TB USA should be adequately and appropriately resourced with a full-time paid Executive Director, funding for partnership activities and the ability to accept donations. Transparency and a solid structure should be established by defining the benefits and expectations of members, developing clear mechanisms for involvement, creating a membership roster, forming a Membership Workgroup and Communications Workgroup, and reorganizing the membership categories with the addition of a patients/families category.

The patient voice should be a key component to help identify and drive priorities and activities, engage communities at risk, and build trust and gain access. A Patient's Forum should be established to raise awareness among persons with TB, provide a mechanism for patients to discuss problems or challenges and exchange information, and create and support opportunities for patients to advocate for TB care and treatment.

A priority activity of the TB Elimination Plan is to prevent TB in high-risk populations. TB rates in many areas have remained stable in part due to problems in accessing high-risk communities. The public health infrastructure remains under assault, but capacity to screen, diagnose and treat TB should be maintained. A collaborative approach should be established with HRSA-funded Community Health Centers to focus on TB prevention in high-risk populations through outreach to the community in partnership with patient members. Funding for several pilot projects should be leveraged to demonstrate successful approaches.

A five-year plan is being developed to guide the future efforts of Stop TB USA. The bylaws will be revised to provide for a Coordinating Board and establish a more active and visible Board. A Patient's Forum and workgroups will be developed to fully engage TB patients, partner organizations and members in Stop TB USA's activities. The Stop TB USA Secretariat will be formalized to further mobilize resources to create a 501(c)(3) organizational structure.

ACET urged Stop TB USA to create a 501(c)(3) organizational structure as quickly as possible because this mechanism would increase capacity to leverage resources from private-sector organizations. ACET also advised Stop TB USA to engage non-traditional groups as members to identify new champions. For example, the Homeless Clinicians Network and Migrant Clinicians Network conduct advocacy initiatives for their respective populations of homeless persons and migrants.

## Update by the BCG Workgroup

**Elsa Villarino, MD, MPH**
Team Leader, Tuberculosis Trials Consortium, DTBE
Centers for Disease Control and Prevention

Dr. Villarino covered the following areas in her update. During the June 2010 meeting, Dr. Castro advised the workgroup to distribute the "TB Prevention and Control Measures for U.S. Healthcare Workers and Volunteers Serving in High Risk Setting for Exposure to *Mycobacterium tuberculosis*" Guidelines to various end-users for external review and comment. Since that time, DTBE circulated the document to 22 reviewers with expertise in infection control, BCG and vaccine availability. Dr. Villarino listed the names and affiliations of the members of the expert review panel.

The deadline for the expert review panel to provide DTBE with input is November 29, 2010, but Dr. Villarino has been reviewing some of the comments submitted to date. Some reviewers strongly disagreed with the document's sole focus on the risk for acquiring MDR-TB. The

reviewers noted that a risk for acquiring TB also exists in high-incidence countries with inappropriate infection control precautions.

The comments submitted to date also show disagreement among the reviewers regarding the timing of performing the repeat IGRA after healthcare personnel (HCP) and volunteers return to the United States and the adequacy of monitoring with IGRAs due to the potential of being unable to distinguish between an exposure-induced or vaccination-induced reaction. The reviewers advised DTBE to change the term "healthcare workers" in the title of the document to "healthcare personnel" to be consistent with documents developed by other CDC federal advisory bodies.

Dr. Villarino's next steps would be to collate comments submitted by individual members of the expert review panel, identify additional expert reviewers, and present the revised document during the next ACET meeting.

Several ACET members expressed concern about Dr. Villarino's next steps because ACET unanimously endorsed the document during the June 2010 meeting and recommended its publication and full implementation. The ACET members pointed out that further delaying the release of the document to incorporate comments by the expert review panel would be detrimental to U.S. HCP and volunteers who serve in high-risk settings and need clear guidance on TB prevention and control measures.

Dr. Fleenor confirmed that during the business session on the following day, ACET would revisit its existing resolution for publication and full implementation of the document and explore strategies to capture comments by the expert review panel without further delaying the release of the document.

## Update on the Foreign-Born Guidelines

**Dolly Katz, PhD, MPH**
Surveillance, Epidemiology and Outbreak Investigations Branch, DTBE
Centers for Disease Control and Prevention

Dr. Katz reported that the final draft of the updated *Guidelines for Prevention and Control of TB in Foreign-Born Persons in the United States* was distributed to ACET in the meeting packets for review and endorsement. CDC's decision to update its previous foreign-born guidelines was based on several factors.

The gap in TB case rates between USBP and FBP in the United States increasingly widened from 1993-2009. Sub-Saharan Africa, East Asia/Pacific, South America, Central America and Mexico have TB rates ranging from 69.4-389.2/100,000 among FBP <2 years in the United States and 14.6-51.9 among FBP ≥2 years in the United States. These rates are dramatically higher than the U.S. TB rate of 2.5/100,000. The risk for TB disease is high among nearly all FBP regardless of their duration of residence. Individual physicians need simple guidance. Health departments and other institutions have limited resources for screening.

A 40-member advisory group was convened to develop the revised guidelines and was specifically charged with approving the draft outcome and general concepts. Workgroups were formed to write and submit specific sections to a 10-member consensus panel that was charged with reaching agreement on identifying populations to screen, performing screening with IGRA or TST, and determining persons to treat following a diagnosis of LTBI.

Dr. Katz highlighted the major recommendations in the revised guidelines. Every U.S. resident born in a TB-endemic country should be screened for TB and tested for LTBI at least once as part of routine health maintenance. Australia, Canada, New Zealand and Western European countries are "non-TB-endemic countries." The groups recommended for LTBI treatment include FBP with residence in the United States $\leq$2 years, FBP $\leq$35 years of age, and FBP with standard risk factors for progression of disease (e.g., diabetes, HIV, certain types of cancer and recent contacts of a TB case).

IGRAs are preferred over TST for most FBP due to higher specificity in persons vaccinated with BCG. Children <5 years of age are the exception to the recommendation due to the lack of data on screening in this population. Specific guidance is provided to health departments for follow-up and evaluation of immigrants entering the United States with B-notifications under both the 2007 and 1991 TBTIs. The guidelines were expanded to include recommendations for institutions and businesses that interact with FBP (e.g., academic institutions with access to foreign-born students).

Specific guidance is directed to the federal government. Oversight of civil surgeons should be transferred to CDC to ensure that panel physicians and civil surgeons are given the same guidance. Long-term non-immigrant residents should be required to have TB evaluations. TB screening should be added to the Healthcare Effectiveness Data and Information Set as a performance measure. Global TB control strategies should be funded. Specific guidance is directed to state governments. Regulations for TB risk screening and follow-up testing and treatment should be promulgated in colleges and universities.

The final steps on the updated guidelines are to obtain ACET approval and initiate the CDC clearance process with reviews by both DTBE and DGMQ. Dr. Katz concluded her update by thanking the members of both the advisory group and consensus panel for their contributions over four years to develop, revise and refine the updated guidelines.

**Masae Kawamura, MD**
Director, Tuberculosis Control Section, San Francisco Department of Public Health
Assistant Professor of Medicine, University of California-San Francisco
Co-Principal Investigator, Francis J. Curry National Tuberculosis Center

Dr. Kawamura is a former member and Chair of ACET. She reported that the overarching purpose of the guidelines is to respond to the 2000 IOM recommendations on screening and prevention of TB among FBP and provide new guidance not included in other documents. She asked ACET to specifically provide input to the workgroup in response to five questions.

1. Are the guidelines effective in addressing the reservoir of TB among FBP in the United States?

2. Does ACET have consensus on the major recommendations?
3. Are the roles and responsibilities clear?
4. Does the document have appropriate emphasis on the important recommendations and entities or individuals who will implement the guidance?
5. Do the guidelines have any major gaps?

ACET's comments and suggestions in response to Dr. Kawamura's request for input on the five questions are outlined below.

- ***Question 3:*** The "Cultural Competence" section is vague and does not give private practice providers clear guidance on specific actions to take to deliver culturally competent health care to patients.
- ***Question 4:*** The important recommendations and other key messages should be highlighted to ensure the guidance is not diluted by extraneous information. For example, the case studies in Appendix C will not be useful to private practice providers.
- More emphasis should be placed on H1 visas and student visas with stronger language recommending the use of the 2007 TBTIs for overseas screening prior to U.S. arrival.
- ***Question 5:*** Guidance should be provided on the role of re-infection. Data show that TB rates decline in FBP of both younger and older ages after arrival to the United States.
- New language should be added on INH resistance because the drug is recommended for preventive therapy.
- Measurable outcomes or indicators should be added to the guidelines to help TB programs focus their TB prevention and control efforts in FBP.
- Additional language should be included to discuss adverse effects associated with LTBI treatment.
- A new website link should be added to country guides developed by the Southeastern National Tuberculosis Center as an additional educational resource.
- CDC should develop succinct and concise implementation guides for the various target audiences after the guidelines are published. The implementation guide should provide primary care physicians with referrals for TB treatment. Dr. Litjen Tan is the ACET liaison to the American Medical Association. He offered to assist CDC in developing an implementation guide for primary care physicians.

Dr. Fleenor confirmed that ACET would have further discussion on the guidelines during the business session on the following day before taking formal action.

## Update on the Dissemination Plan for the Law Menu

**Melisa Thombley, JD, MPH**
Office of the Director, DTBE
Centers for Disease Control and Prevention

Ms. Thombley described CDC's dissemination plan for the "Menu of Suggested Provisions for State Tuberculosis Prevention and Control Laws." ACET initially asked CDC to develop a

model TB control act. State and local TB programs also asked CDC to compile examples of existing laws that are effective in their jurisdictions.

CDC adopted a "menu" approach to offer multiple alternative provisions and provide the most flexibility for state, local, tribal and territorial TB programs, their legal counsel and other partners. The Menu provisions include existing, new and modified versions of state statutes and regulations. Non-U.S. TB programs are a secondary target audience of the Menu.

CDC distributed a "Dear Colleague" letter along with a copy of the Menu to CDC staff, ACET numerous professional societies and external partners. An announcement was published in the *Morbidity and Mortality Weekly Report*. The Menu was posted on the websites of DTBE, the CDC Public Health Law Program, NTCA, ASTHO and NACCHO.

CDC and NACCHO will jointly broadcast a webinar in December 2010 or January 2011 featuring a discussion on the Menu and the "Evaluation of Local Health Jurisdictions' Public Health Practices Regarding Isolation of Persons with Infectious Tuberculosis" Report. Abstracts on the Menu were submitted to relevant conferences. Ms. Thombley asked ACET to provide input on additional approaches to further disseminate the Menu.

ACET commended Ms. Thombley for her leadership in convening partners and stakeholders to develop the Menu. ACET noted that the Menu would be an extremely valuable resource for TB programs across the nation. Several ACET members found the dissemination plan for the Menu to be comprehensive and inclusive of diverse partners and organizations at multiple levels. Dr. Redd advised CDC to notify the National Indian Health Board about the availability of the Menu for broader dissemination to tribal health departments.

## Overview of the DTBE Homeless Initiative

**Sapna Bamrah, MD**
Outbreak Investigations Team, DTBE
Centers for Disease Control and Prevention

Dr. Bamrah presented an overview of DTBE's new initiative to address TB in the homeless population. Estimates show that 1% of the U.S. population experiences homelessness each year. Of the homeless population, 65% are minorities, 23% are families, 26% have serious mental illness with 5%-7% requiring institutionalization, and 30%-65% have substance abuse problems, most frequently with alcohol.

TB was recognized as a disease disproportionately affecting persons in unhealthy living conditions as early in 1815. An editorial was published in the *Journal of the American Medical Association* in 1914 citing TB as a "disease of malnutrition, bad housing and low wages." The editorial further noted that cheap lodgings frequented by homeless persons were "veritable breeding places" for TB. Since 1993, 4%-6% of U.S. TB cases occurred among persons who were homeless during the year prior to diagnosis.

ACET published recommendations in 1992 addressing TB in homeless populations. ACET's guidance called for more robust TB case finding and treatment completion; LTBI screening and treatment of HIV infection or other medical conditions that increase the risk for TB; an examination and potentially re-treatment of inadequately treated recent TB disease and infection; and improved contact investigations, including screening at shelters.

DTBE's investigations showed that homeless populations accounted for 28 of 32 (or 72%) of domestic TB outbreaks from 2002-2010. These outbreaks involved vulnerable populations with HIV infection, substance abuse, mental illness or other comorbidities in crowded congregate settings. The investigations further demonstrated the limited utility of traditional name-based contact investigations and the challenges associated with timely diagnosis and treatment of TB disease and LTBI.

DTBE has been conducting analyses to determine the ability of homelessness to serve as a predictor of genotype cluster growth. DTBE examined 65 TB genotype clusters that grew from 0 cases in 2005 to at least 3 cases by the end of 2007. In 2008, 36 of the 65 genotype clusters continued to grow. The analyses showed that 95% of clusters continued to grow if at least one of the first three affected persons was homeless.

The risk factors most associated with growth for 65 clusters at the time of the third case was homelessness (92.3%), substance abuse (78.3%), low-education neighborhood (76.7), Asian (31.3%), female (28.6%), and U.S.-born Asian (0%). The rate of all clusters that grew was 55.4%.

DTBE convened its internal subject-matter experts to develop a homeless initiative logic model with an outcomes-based approach to eliminate TB in this population. The "Healthy People" component would focus on TB control by finding and curing TB and finding and treating recent infection. The "Healthy Communities" component would focus on TB prevention by targeting testing, treating homeless populations for TB and LTBI, and preventing transmission in sites used by homeless persons.

DTBE's activities to date on the new homeless initiative include meeting with leadership of the National Health Care for the Homeless Council in June 2010; initiating discussions during the June 2010 NTCA meeting with TB control experts who have experience in addressing TB in homeless populations; convening a CDC-wide homeless symposium in August 2010; and continuing to hold DTBE internal meetings in June-September 2010 to propose strategies to further advance the logic model.

DTBE's experience with the recent contact investigations and discussions with TB/homeless experts has led to the identification of six focus areas to refine the homeless initiative. DTBE has proposed initial projects for two of the six focus areas.

To "define the problem," DTBE will evaluate NTSS data, review strategies TB programs are currently utilizing to address TB in homeless populations, identify new or revitalize existing interventions, test interventions based on current economics and structures of TB control programs, and update the 1992 ACET guidelines for implementation in the field. DTBE

submitted a TB Leads proposal to determine the feasibility of conducting a study to examine the effects of Housing First programs on uptake of TB screening and completion of treatment.

To "examine current approaches," DTBE will administer a best practices survey to TB control programs, Health Care for the Homeless providers, clients and shelters. DTBE will use the survey results to compile existing models, successes and lessons learned in addressing TB in homeless populations and also to determine whether TB is considered a priority in homeless populations.

DTBE is current discussing key issues for the remaining focus areas DTBE of the homeless initiative. To "identify innovative interventions," TBTC Study 26 results will be used to inform the use of a three-month INH/rifampin (RMP) regimen to determine the most appropriate strategy for LTBI treatment in homeless populations. Genotyping data will continue to be used and additional rate-of-growth studies will be conducted to determine clusters that might require more rapid intervention.

To "test interventions," DTBE will decide whether interim guidelines should be developed since the last recommendations on TB in homeless populations were published in 1992. To "establish new guidelines," DTBE will determine whether the recommendations should be expanded with more guidance on LTBI testing and treatment. To "implement new guidelines," DTBE will decide whether U.S. and non-U.S. government partners should be engaged in this effort.

ACET advised DTBE to use its membership to initiate discussions with key partners (e.g., HRSA, the Substance Abuse and Mental Health Services Administration (SAMHSA), Department of Veterans Affairs, and community-based social service agencies) to strengthen outreach to homeless populations.

These collaborations will be particularly important to access homeless persons with TB who do not utilize shelters and address important co-morbidities, such as mental illness and substance abuse.

## Panel Presentation: TB Issues Along the U.S.-Mexico Border

A panel of DTBE leadership and invited guest speakers presented a series of overviews on ongoing efforts to address TB issues along the U.S.-Mexico Border. The presentations are summarized below.

**Kenneth Castro, MD**
Director, DTBE
Centers for Disease Control and Prevention

Dr. Castro announced that the U.S.-Mexico Summit was held in June 2010 with representation by the Mexico NTP, local health departments along the border, DGMQ and the U.S.-Mexico Border Health Commission. Key recommendations from the summit are highlighted below.

A unified effort should be developed to assure binational TB cases complete therapy regardless of whether the diagnosis was made in the United States or Mexico. Program and financial management should be enhanced by developing a joint financial TB control vision for increased effectiveness and political will. A "TB Care Network" (*i.e.*, a national referral capacity building mechanism) should be established to broaden the focus to include more than uncured TB cases.

TB project management should be strengthened. Data sharing should be improved by creating a mutual electronic medical record system between the United States and Mexico. TB care and control guidelines should be harmonized in both countries with consistent reports and guidance on capacity, education, social outreach, immigration and travel issues. A resource inventory should be designed to house shared experiences in binational TB programs and worldwide resources.

Adherence to TB treatment should be improved by the increasing the proportion of documented and undocumented patients on DOT to reduce the risk for relapse and development of drug resistance. Protection of human rights should be assured. Collaborations with the U.S. Immigration and Customs Enforcement (ICE) and U.S. Customs and Border Protection (CBP) should be enhanced to identify persons with TB detained in ICE facilities. Laboratory capacity should be strengthened for DST and rapid testing.

A process should be developed to improve the storage and transport of TB specimens across the U.S.-Mexico Border. Communications should be enhanced by establishing contacts with agencies that play key roles in TB control and prevention in the four U.S. states and six Mexico states along the border. CDC and the Mexico NTP should develop a memorandum of understanding to achieve this goal. Key stakeholders should be identified to design a framework to evaluate U.S.-Mexico TB projects that have been sponsored and funded to date.

**Dan Reyna, MSS, MPA**
General Manager, U.S. Section
U.S.-Mexico Border Health Commission

Mr. Reyna described three key milestones in U.S.-Mexico Border TB prevention and control activities over the past 15 years. In June 1985, health officers in the ten U.S.-Mexico Border states proposed the development of a binational initiative during the U.S.-Mexico Border Health Association meeting. In 1997, U.S. and Mexico health secretaries in the ten states signed the joint "Ten Against Tuberculosis" (TATB) statement of collaboration. In November 2002, TATB was officially designated as the U.S.-Mexico Border Health Commission's (BHC) technical advisory group on TB.

BHC's recent accomplishments are highlighted as follows. The U.S. TB Legal Issues Forum was held in October 2007 with representation by HHS, CDC, the four U.S. Border states and other groups. Steps were initiated in April 2008 on a cross-border pilot project to facilitate the transport of TB specimens across the U.S.-Mexico Border.

TB was identified as one of six priorities during BHC's strategic planning process in 2008. The Transnational Workgroup published the Border TB White Paper in June 2009 with a

recommendation to address cross-border TB legal issues. Funds were provided to support a new binational TB pilot project in the New Mexico-Chihuahua Region.

From February-August 2010, BHC held the Mexico TB Legal Issues Forum, identified "Border TB Models of Excellence," released the Mexico report on border TB, convened an initial meeting of the TB Consortium, and held the U.S.-Mexico TB Legal Issues Forum.

The primary goal of the TB Consortium is to enhance the integration of binational and border-wide efforts on mutual binational TB issues among the ten border states, federal partners, and other public and private partners. To achieve this goal, the TB Consortium ensures that border states have a voice in binational issues and generate products for policymakers, including local city councils, state governors and Congressional staff. The TB Consortium partners include the U.S. and Mexico Sections of BHC; federal, border state and local TB program representatives; and non-governmental organizations.

The TB Consortium and TB Legal Issues Forum agreed to address six key questions and develop concrete action plans to accomplish short-, mid- and long-term goals,

1. What strategies can be implemented to improve the availability and effectiveness of DOT in border states?
2. What steps should be taken to improve laboratory access, capacity and quality?
3. What steps should be taken to evaluate the completeness of reporting?
4. What steps should be taken to address continuity of care for active TB cases that are deported to Mexico or other countries?
5. What strategies must be implemented to address the diagnosis and treatment of drug-resistant TB, particularly MDR-TB?
6. Are infection control measures available at all key levels in the health system?

The TB Consortium identified six priority activities to address its portion of the six key questions. Binational laboratory capacity should be expanded. Binational DOT strategies should be expanded. Intrastate and binational reporting of TB cases should be improved. Coordination with DHS should be enhanced to better address TB deportation cases. Coordination on cross-border transportation of specimens should be improved. Binational TB training and education should be coordinated.

The TB Legal Forum identified five priority activities to address its portion of the six key questions. The proposed binational guidelines for mutual assistance that have been in development since 2004 should be approved to support state-to-state coordination. Procedures for exchange of patient information should be clarified.

Procedures for isolation and quarantine of TB cases in Mexico should be clarified. CDC's "Menu of Suggested Provisions for State Tuberculosis Prevention and Control Laws" should be used as a model to develop and publish binational legal guidelines. A framework should be established for communication, education and training of cross-border legal issues.

Mr. Reyna concluded that at this time, BHC is asking ACET to take action in the following areas to make further progress in TB prevention and control along the U.S.-Mexico Border. U.S.

interagency efforts among HHS, DHS and USAID should be encouraged to address border TB issues. Approval of the *Guidelines for U.S.-Mexico Coordination on Epidemiologic Events of Mutual Interest* should be encouraged. The development of similar binational standards of care for TB diagnosis and treatment should be promoted. Additional funding to areas of need and an assessment of technical, training and laboratory TB capacity should be supported on both the U.S. and Mexico sides of the border.

**Terence Chorba, MD, DSc**
Chief, Field Services and Evaluation Branch, DTBE
Centers for Disease Control and Prevention

Dr. Chorba described several ongoing binational TB initiatives along the U.S.-Mexico Border. In 1993, the four U.S. states and six Mexico states had a population of ~9 million persons covering 1,952 miles along the border. The annual border crossings were ~50 million at that time. The TB rate was 14.2/100,000 for the four U.S. Border states compared to the rate of 9.7/100,000 for the general U.S. population.

In 2008, the four U.S. states and six Mexico states had a population of ~17 million persons covering 1,952 miles along the border. The annual border crossings were ~100 million at that time. The TB rate was 6.4/100,000 for the four U.S. Border states compared to the rate of 4.2/100,000 for the general U.S. population.

Despite the dramatic decrease in the TB rate in the four U.S. Border states from 14.2/100,000 in 1993 to 6.4/100,000 in 2008, DTBE continues to be concerned about a number of issues. Some local border counties have much higher TB rates than the overall border rate. An increasing percentage of TB cases are among FBP in the United States. Mexico accounts for 23% of TB cases in the United States among FBP. The incidence of MDR-TB in the United States is greater incidence among Mexican-born populations both in border and non-border states.

DTBE and its partners in Arizona, New Mexico, San Diego and Texas conducted a number of binational TB projects from 1991-2010. The projects included Cure TB, the Chihuahua pilot project, the “Meet and Greet” Program, TB Net, the *Puentas de Esperanza* MDR-TB project, and the Project Concern International media project. Rotary International also conducted border-wide activities in 2008. Continuity of TB care and treatment of binational TB cases were the major focus areas of these projects.

A great deal of progress has been made since 1995 to advance binational TB initiatives along the U.S.-Mexico Border. Discussions are underway to determine the potential to expand direct support DTBE provided from 1995-2008 for public health advisors to serve as the Binational Coordinator in Texas. DTBE and DGMQ formed the CDC TB Border Workgroup in 2008. A Latin American liaison was recently appointed and a summit on binational TB issues was held during the NTCA meeting in June 2010. DTBE funded an evaluation of Cure TB’s continuity of care activities in 2009.

Despite the progress that has been made over the past 15 years, DTBE recognizes the challenges in further advancing binational TB initiatives along the U.S.-Mexico Border. With the

exception of funding by Cure TB in 2010, no additional resources have been devoted to binational TB initiatives along the U.S.-Mexico Border over the past decade. Violence along the U.S.-Mexico Border seriously hinders evaluation of binational TB activities.

The provision of local TB treatment in Mexico will have a significant impact in the United States, particularly since Mexico accounts for 23% of U.S. TB cases among FBP. A number of TB services are overlapping (e.g., specimen transport, surveillance and policy) due to the multitude of participating partners. Delays in the flow of information from TB experts in local border programs to policymakers are considerable.

DTBE collected data from Arizona, New Mexico, Texas, Cure TB, and the *Puentas de Esperanza* MDR-TB project to estimate the cost of addressing unmet needs for cross-border activities. The total cost of ~$2 million was grouped into five broad categories: $888,100 for equipment, $402,000 for personnel, $286,350 for supplies, $50,850 for travel, and $430,800 for other costs.

Specific needs in these broad categories include costs for mileage, digital chest x-rays, courier services, communication devices, incentives and enablers, education and training, and laboratory expenses. However, the state of California recently informed DTBE that ~$4.7 million would be needed to conduct additional activities along the U.S.-Mexico Border.

DTBE will conduct activities in four major areas to further advance binational TB initiatives along the U.S.-Mexico Border. Activities by the U.S.-Mexico TB Workgroup with CDC representation by DTBE and DGMQ will continue to be supported. NTCA's focus on U.S.-Mexico TB issues will continue to be supported. Outcomes from the report of the June 2010 U.S.-Mexico Summit will be supported. Current and expanded investments in fiscal and human resources for TB prevention and control activities and TB laboratory services along the U.S.-Mexico Border will continue to be supported.

**David Lakey, MD**
Commissioner of Health, Texas Department of State Health Services

Dr. Lakey presented data that led to Texas implementing TB activities along the Texas-Mexico Border. Texas accounts for ~13% of all TB cases in the United States and ranks second after California for the national burden of TB cases. The percent of TB cases among FBP continues to rise in Texas along with the incidence of MDR-TB cases and co-morbidities. Despite its high TB burden, Texas has achieved a 15% decline in the number of TB cases since 1998 and a decrease in the TB rate from 9.1/100,000 in 1998 to 6.0/100,000 in 2009.

State data from 1999-2008 showed that TB incidence rates ranged from 12.5-11.6/100,00 along the Texas-Mexico Border and from 7.7-5.6/100,000 in Texas non-border states. State data also showed that FBP accounted for >50% of TB cases in 2000-2009. National data from 2007 showed that the TB rate was 4.4/100,000 in the United States and 6.4/100,000 in Texas. Texas-Mexico Border county rates ranging from 5.4-18.8/100,000 accounted for the higher TB rate in the state of Texas.

Texas has collected a wealth of data to demonstrate that several risk factors increase susceptibility for TB in Texas-Mexico Border counties compared to the remainder of the state. These risk factors include increased legal and illegal migration, higher rates of poverty and unemployment, limited access to primary health care, lower educational attainment, a high rate of uninsured persons, and poor overall health status with higher rates of obesity and diabetes.

Dr. Lakey provided additional details on some of the TB risk factors along the TB-Mexico Border. In terms of migration, the U.S.-Mexico Border is the busiest international border in the world with Texas accounting for ~100 million individual crossings each year. In terms of co-morbidities, HIV rates are lower along the Texas-Mexico Border compared to the remainder the state. The Restrepo, *et al.* study showed that the TB incidence would be reduced by 26% in Texas and 23% in Mexico if diabetes were eliminated and by 5% in Texas and 3% in Mexico if HIV was eliminated. Overall, the study documented that diabetes is a greater risk factor for TB than HIV in Texas-Mexico Border counties.

Texas has identified five major challenges to effective TB treatment along the border: MDR-TB, continuity of care, violence, cross-border transport of laboratory and medical supplies, and social factors (e.g., migratory populations and language barriers). Texas is implementing a number of activities in an effort to address these problems.

In terms of drug-resistant TB, Texas reported 134 cases in 2009. Of these cases, 17 were resistant to both INH and RMP, six were resistant to RMP, 75 were resistant to INH, and 36 were resistant to other anti-TB drugs. The Texas-Mexico border counties accounted for 41% of the MDR-TB cases that Texas reported in 2009. These cases were resistant to four drugs on average. Of 17 MDR-TB cases Texas reported in 2009, five are receiving inpatient treatment at the Texas Center for Infectious Disease (TCID).

Texas invested ~$30 million to build TCID as a 75-bed, negative pressure isolation hospital in San Antonio to assure continuity of care to TB patients in the state. TCID is the largest new construction in the United States in the last 50 years for inpatient care and treatment of TB. TCID provides patient care, scientific investigation, and therapeutic and educational services that support public health needs. The construction of TCID was completed in September 2010.

In terms of cross-border TB care to outpatients, Cure TB is a U.S.-Mexico binational TB referral program that has facilitated continuity of care of TB patients migrating between the United States and Mexico since 1997. The Texas Sister City Binational Initiative pairs six U.S. and Mexico cities to coordinate care of TB patients.

Violence is a major concern in providing care to persons with TB along the Texas Border. Violence among Mexican drug cartels has killed >29,000 individuals since December 2006, including ~200 Americans. Over the past year, security spending has increased by 33% along the U.S.-Mexico Border. The Texas Health and Human Services Commission restricted its employees to travel to Mexico in February 2010.

Despite this concern, infectious disease control efforts are improving along the U.S.-Mexico Border. Binational communications and telecommunications have improved. Enhancements have been made in the exchange of epidemiological information across borders and laboratory

cooperation. Opportunities are being explored for additional collaboration and expanded partnerships. Efforts are underway to sustain these improvements over time.

Activities are being conducted to eliminate barriers to TB. Safety protocols have been created to facilitate oversight and support at Sister City sites. TB training courses in Spanish are being offered to Mexican physicians and nurses. Laboratory capacity is being built in Mexico. Material support is being expanded with additional vehicles, laboratory equipment, supplies and training. Different standards of care for TB diagnosis are being harmonized. Binational TB patient identification cards have been distributed to ensure continuity of care when persons travel across the border.

The success of TB control along the U.S.-Mexico Border will depend on essential partners, including local and regional public health departments, state programs, CDC, DHS, international partners, BHC, academia and the private sector.

**Jon Krohmer, MD**
Senior Medical Officer & Liaison, U.S. Immigration and Customs Enforcement
Department of Homeland Security Office of Health Affairs

**Diana Schneider, DrPH, MA, CDR U.S. Public Health Service**
Chief, Epidemiology, ICE Health Service Corps
Enforcement and Removal Operations
U.S. Immigration and Customs Enforcement

Drs. Krohmer and Schneider described DHS's transnational collaborations. The mission of the Office of Health Affairs (OHA) is to provide medical, health and scientific expertise in support of the DHS mission to prepare for, respond to, and recover from all threats. OHA provides department-level support and oversight to DHS and other agencies on health issues. OHA closely collaborates with its federal partners to coordinate the "Do Not Board" and "Lookout" Lists to address public health issues among legal and non-legal migrants who enter the United States.

The mission of ICE Enforcement and Removal Operations (ERO) is to promote public safety and national security by ensuring the departure of all removable aliens from the United States through fair and effective enforcement of the nation's immigration laws. ICE-ERO operational settings include servicing processing centers, staging facilities, contract detention facilities, juvenile and family residential centers, and intergovernmental service agreements for facilities dedicated for ICE and non-dedicated local jails.

ICE recently realigned its organizational structure. The ICE Health Service Corps (formerly the Division of Immigration Health Services) was relocated to ERO Headquarters. The realignment is designed to improve coordination and communication, enhance integration of medical and enforcement policies and directives, and strengthen the review and update of alerts and hold processes.

The new ICE detainee locator allows persons to search for detainees $\geq$18 years of age who have been in custody during the past 60 days. Searches can be performed by alien number

and country of birth or first/last names and country of birth with date of birth as an optional entry. Users are provided with a telephone number for the corresponding field office if the detainee was released from ICE custody. The detainee locator is available on the ICE website.

ICE's major challenges are advance notification of TB cases from other facilities, patients who are still contagious at the completion of their criminal sentence, identification of patients with ICE detainers, clinical clearance versus a medical hold until a continuity of care plan is created, enrollment in the transnational referral program, communications and collaborations, "meet and greet" of TB patients at the port of entry, and non-adherence to TB treatment and reentry to the United States.

Patients with MDR-TB, other medically complex conditions or concomitant mental health conditions who have a Final Order of Removal must be deported, but their country of nationality may not have sufficient capacity to appropriately manage the case. A stay of removal may be considered, but the TB patient may be released from custody. The local jurisdiction would be responsible for TB treatment and case management of the patient if released. However, the patient may not have relationships in the community where detained.

ICE managed a complex case in March 2009 in which a male 40 years of age from Djibouti arrived at an international airport with second-line anti-TB drugs. CBP detained the traveler and consulted with DGMQ. The traveler was hospitalized, found to be resistant to six anti-TB drugs, and was subsequently processed into ICE custody in October 2009 at a county jail.

The detainee was ordered to be removed, but the state health department did not seek a stay of removal. ICE, CDC and the state collaborated to procure and ship drugs to a physician in Djibouti. WHO will provide guidance to the treating physician. The removal of the detainee from the United States to Djibouti was coordinated with agency representatives in November 2010.

Overall, ICE's mission supports removal based on U.S. immigration laws and its realignment fosters improved coordination of medical and enforcement functions. Different detention settings experience various challenges. Close collaboration between law enforcement entities is critical. MDR-TB and medically complex patients require extensive collaboration and commitment of resources. These public health issues are both binational and transnational.

The ACET members, CDC staff, and public health colleagues in Mexico and Texas who joined the meeting by conference call had an extensive discussion on various TB issues along the U.S.-Mexico Border. The following suggestions were proposed to enhance TB prevention and control along the U.S.-Mexico Border.

- Discussions should be held at the national level in both the United States and Mexico and state departments to resolve policy and legal complications in two areas. First, undocumented parents of U.S.-born children with TB can be deported. Second, Border Patrol has detained public health employees at checkpoints in Texas for illegally transporting undocumented TB patients to state hospitals for treatment.
- The White House Office of National Drug Control Policy convenes a binational conference every two years with representation by the research, public health, law

enforcement and trafficking communities to discuss common issues and problems across these disciplines. The TB community should attend the conference to present issues along the U.S.-Mexico Border. Mr. Warren Hewitt is the ACET *ex-officio* member for SAMHSA. He offered to provide DTBE with contact information and additional details on the next binational conference.

- Case management conferences are held for physicians in the United States and Mexico to share lessons learned and experiences in managing complex MDR-TB cases. Because the conferences have been extremely useful and helpful to physicians, opportunities should be explored to expand and formalize this effort. For example, a formal memorandum of understanding could be developed between CDC and Mexico for RTMCCs to convene the case management conferences.
- The overarching goal of TB projects along the U.S.-Mexico Border should be to build capacity, particularly to treat and manage highly complex cases. Infectious disease physicians in Mexico have excellent capacity to support this goal.

With no further discussion or business brought before ACET, Dr. Fleenor recessed the meeting at 5:02 p.m. on November 2, 2010.

## Update on the CDC Molecular Detection of Drug Resistance (MDDR) Service

Dr. Dean reconvened the ACET meeting at 8:48 a.m. on November 3, 2010 and conducted a roll call of the ACET voting members and the non-voting *ex-officio* members to establish a quorum for day 2 of the meeting. After confirming the presence of a quorum, she reminded the ACET members of their responsibility to identify potential conflicts of interest and recuse themselves from participating in discussions or voting on issues in which they have a real or perceived conflict. Dr. Dean yielded the floor to the first presenter.

**Beverly Metchock, DrPH, D(ABMM)**
Team Lead, Reference Laboratory, DTBE
Centers for Disease Control and Prevention

Dr. Metchock presented an update on the first year of CDC's MDDR Service. DST of *Mycobacterium tuberculosis* (*M.tb*) complex should be conducted in accordance with current recommendations. The initial isolate should be tested against primary or first-line drugs (FLDs) (e.g., INH, RMP, pyrazinamide (PZA) and ethambutol (EMB)). Isolates that are resistant to RMP or any two FLDs should be tested against second-line drugs (SLDs) (e.g., amikacin (AMK), fluoroquinolones (FQ), kanamycin (KAN) and capreomycin (CAP)).

Current practices for FLDs are summarized as follows. Broth-based methods are routine and widely available in the United States. Results for these methods generally are available within 28 days of the laboratory receiving specimens, but some laboratories lack confidence or are reluctant to report drug resistance prior to confirmation. Molecular assays for INH and RMP are available in a few jurisdictions and are directly performed on clinical specimens or culture isolates. Results for these assays are available within 1-2 days.

Current practices for SLDs are summarized as follows. Very few laboratories have technical expertise or capacity in SLD. SLD testing often is performed in a piecemeal fashion through referral algorithms. The turnaround time is slow with the direct agar proportion method (e.g., sputum sediment) requiring ~21 days to perform and the indirect agar proportion method requiring ~28 days to perform after isolation of *M.tb* from culture. Some laboratories have verified and validated methods for broth-based testing of SLDs, but these methods typically include only a few drugs rather than the entire panel.

The CDC *M.tb* DST Performance Evaluation Program assessed the capacity of U.S. laboratories to detect extremely-drug resistant TB (XDR-TB) in May 2010. Of 96 U.S. laboratories that participated in the evaluation, 30 tested at least one SLD, excluding streptomycin; 19 tested KAN or AMK, CAP and FQ; and eight tested KAN, AMK, CAP and FQ. SLD testing often is not performed as a comprehensive panel.

The DTBE Reference Laboratory Team (RLT) serves as the reference laboratory for public health laboratories (PHLs). For PHLs that only test FLDs, RLT confirms drugs resistance and tests additional drugs. For PHLs that test both FLDs and SLDs, RLT confirms drug resistance and may test different drugs. RLT also helps with validation and troubleshooting of problems within PHLs. RLT's current protocol is to use the agar proportion method for FLDs and SLDs, the MGIT 960 system for PZA susceptibility testing, and the MDDR Service.

During the March 2009 meeting, ACET endorsed DTBE's plans to offer the MDDR Service beginning in September 2009. MDDR is a clinical service that is offered to domestic TB control programs and physicians and is compliant with the Clinical Laboratory Improvement Amendments. The MDDR Service provides rapid confirmation of RMP resistance and MDR-TB. Laboratory testing data on SLD resistance are available in cases of RMP resistance or MDR-TB.

New technologies may fill the role of the MDDR Service in the future, but the demand for the service exists at this time. DTBE uses traditional DNA Sanger sequencing as the platform for the MDDR Service. DTBE made a conservative estimate that its anticipated workload with the MDDR Service would be 1-2 isolates per week. The MDDR Service tests the following drugs and genes: RIF and INH for MDR-TB and FQ, AMK, KAN and CAP for XDR-TB. DTBE added EMB and PZA to the panel in October 2010.

In the testing algorithm, PHLs obtain permission to submit isolates to DTBE for MDDR testing. DTBE performs a molecular analysis and conventional DST, develops an interim report with the molecular results, and completes the final report with molecular and conventional DST results. Requests for the MDDR Service were two per week from September 2009-February 2010, but the demand increased to four per week from March 2010 to the present.

From September 2009-August 2010, DTBE received 158 isolates from 145 patients in 32 states and Puerto Rico. Of the 158 isolates submitted, 87 were broth medium, 66 were solid medium and five were sputum sediments. PHLs complete a requisition form to inform DTBE of the indicators for MDDR testing (e.g., high-risk country, known MDR-TB or RMP resistance, previous treatment, mixed or non-viable results, suspect MDR-TB or RMP resistance, >1 indication or other indicators).

Turnaround times from the date the request was approved until DTBE received the isolates ranged from 1-11 days (or a mean of 3.2 days) in the first six months of the MDDR Service and from 1-29 days (or a mean of 3.7 days) in the second six months. DTBE attributed the delay in the turnaround times during the second six months to shipping problems from the PHLs.

Turnaround times from the date DTBE received the isolates until reports were issued ranged from 1-5 days (or a mean of 2 days) for MDDR testing and from 2-97 days (or a mean of 38 days) for DST. DTBE is attempting to improve the turnaround times for MDDR testing from 67%-~80% within two days and for DST from 67%-80% within 35 days.

DTBE reviewed antibiogram data to distinguish between requests for MDDR and conventional testing. The PHLs requested MDDR testing for 45 MDR-TB patients (or 31%) and conventional testing for 11 MDR-TB patients (or 5.2%). The PHLs requested MDDR testing for 23 (or 15.9%) non-viable, no-growth or contaminated specimens and conventional testing for 16 (or 7.6%) of these same types of specimens. DTBE attributed this finding to problem isolates being submitted for MDDR.

From January-June 2010, turnaround times from the date of specimen collection until DTBE received the isolates ranged from 2-202 days (or a mean of 41 days) for MDDR testing and from 19-266 days (or a mean of 84 days) for conventional testing. DTBE's comparison of MDDR and conventional DST for INH and RMP showed agreement of 97% for INH and 95.5% for RMP between the two methods. The data analysis also showed that 32 states requested MDDR testing and 22 states requested conventional testing.

Overall, a two-day turnaround time is required for MDDR testing after DTBE receives the isolate for DNA and polymerase chain reaction (PCR) sequencing. The agar proportion method is used for sub-culture and DST of isolates with a 38-day turnaround time.

DTBE is incorporating the MDDR Service into its research and development. For the "research" component, DTBE determines new mechanisms of resistance and applies these results to refine DST. For the "development" component, DTBE is continuing to correlate molecular (*i.e.*, genotypic) and DST (*i.e.*, phenotypic) results. In the future, DTBE will add new drugs and alleles to the MDDR Service and progress to the implementation of the Rapid Detection of Drug Resistance (RDDR) Service.

DTBE presented its plans for the RDDR Service to ACET during the March 2010 meeting. The new service will expand MDDR tersting to directly include RDDR testing from INH and RMP clinical specimens. The RDDR Service will utilize the pyrosequencing platform and will have greater sensitivity than the standard Sanger sequencing used in the MDDR Service. The RDDR analysis will be automated. The verification process for the RDDR Service is underway.

DTBE is considering a number of issues for RDDR testing. All mechanisms of resistance are not known. The lack of a mutation is not equivalent to susceptibility. DST is considered as the "gold standard," but this method is imperfect. All mutations are not associated with drug resistance. DTBE is uncertain whether clinicians will trust detection of drug resistance results or wait for conventional DST results. DTBE recognizes the need to build educational partnerships with laboratories, TB programs and clinicians to address this uncertainty.

DTBE has developed a plan to advance its detection of drug resistance services. The current MDDR Service includes full-panel PCR and DNA sequencing of isolates for 9 loci. The second generation of the MDDR Service will include full-panel PCR and DNA sequencing of both isolates and specimens for >9 loci.

The third generation of the MDDR Service will include first screening of RMP and INH and full-panel PCR and DNA sequencing on an as-needed basis. The RDDR Service will include pyrosequencing for 3 loci of nucleic acid amplification positive primary specimens. When the RDDR Service detects INH or RMP resistance, these results will be used to inform the MDDR Service in terms of confirmation and SLD testing.

Overall, DTBE implemented the MDDR Service according to schedule and determined that the selection of patients for MDDR was appropriate. The MDDR Service provides useful information for treatment guidance ~36 days earlier than the agar proportion method for DST. However, logistical issues related to the shipping of isolates and laboratory staffing may limit turnaround times for both the MDDR Service and the agar proportion method for DST. Dr. Metchock concluded that DTBE welcomes ACET's input on its proposed strategic directions to advance the MDDR Service.

ACET commended DTBE for successfully implementing the MDDR Service in the first year and noted that the MDDR Service has been extremely responsive to the needs of TB programs and laboratories across the country in a rapid fashion. ACET members who have utilized the MDDR Service were impressed with the quality of service in meeting the clinical needs of TB programs and laboratories.

ACET made three key suggestions in response to Dr. Metchock's request for feedback on DTBE's proposed strategic directions to advance the MDDR Service.

- DTBE should engage the RTMCCs to develop and issue standardized guidance to build trust among clinicians in the MDDR results. Most notably, the MDDR Service should be linked to clinical consultation, particularly for physicians who have no knowledge of the next steps after submitting their isolates to DTBE.
- DTBE should ensure that the MDDR Service is available for TB programs to use in conjunction with patients identified on the "Do Not Board" List.
- DTBE should collect clinical and outcomes data from states that request the MDDR Service. These data will be extremely important in establishing a cohort of TB patients that have received new techniques from the MDDR Service and identifying any modifications in treatment decisions. The possibility of using the MDDR Service to collect clinical outcome data on potential MDR-TB patients should be linked to DTBE's future plans to enhance MDR-/XDR-TB surveillance.

Dr. Fleenor confirmed that during the business session, ACET would determine whether formal action on the MDDR Service is needed at this time.

## Overview of Challenges in Obtaining Second-Line Drugs in the United States

**Jennifer Flood, MD, MPH**
Chief, Surveillance and Epidemiology
Tuberculosis Control Branch
California Department of Health Services

Dr. Flood described obstacles TB patients in the United States encounter during treatment if SLDs are difficult to obtain. At the domestic level, ACET recommended two essential components of all U.S. TB prevention and control programs: ensure TB patients receive appropriate treatment until cured and treat patients without consideration of their ability to pay. At the international level, the overarching standard for TB control programs is to assure an uninterrupted supply of solid quality anti-TB drugs.

WHO further identified three key components of an effective drug supply and management system at the global level. First, an uninterrupted and sustained supply of quality assured anti-TB drugs is fundamental to TB control. Second, a reliable procurement and distribution system of all essential anti-TB drugs to all relevant health facilities should be available.

Third, anti-TB drugs should be available free of charge to all TB patients. Many TB patients are poor and cannot afford treatment. Moreover, TB treatment has benefits that extend beyond individuals to society as a whole. For example, the cure of TB patients will prevent transmission to other persons.

The ability to assure an adequate TB drug supply continues to be a problem in the United States at the present time because TB patients and programs at state and local levels still experience difficulties in accessing MDR-TB drugs. Issues contributing to this problem include drug shortages, increased costs of TB drugs to build a strong MDR-TB regimen, multi-step processes over several weeks to procure essential drugs, and "out-of-reach" drugs for uninsured or uncovered MDR-TB patients due to cost. Dr. Flood highlighted a number of key questions that must be answered to address these issues.

Question 1: What factors impede the MDR-TB drug supply to patients in the United States? The Food and Drug Administration's (FDA) inspection of overseas drug companies often is delayed by several months. Materials to make TB drugs typically are in short supply. The Institutional Review Board (IRB) process for non-FDA-approved drugs is lengthy. High costs place certain TB drugs beyond the reach of patients.

Question 2: Which drugs have a tenuous supply? Materials to produce AMK have been in short supply due to the lengthy time required for the FDA overseas inspection process. The change in the company that previously produced CAP has resulted in a huge increase of the drug. Drug shortages and increased costs also are associated with cycloserine. Manufacturing has been halted on clofazamine and restricted to use for patients with Hansen's disease. This change now requires IRB approval and the FDA investigational new drug (IND) process for each patient.

Question 3: What is the cost of an MDR-TB treatment regimen? The total MDR-TB drug costs would be $64,352 for a 340 B clinic and $101,553 for a common hospital. The total costs for specific drugs would be $49,770 for linezolid (or $39 per dose), $23,975 for CAP (or $137 per dose), $15,721 for levofloxacin (or $4.80 per dose), $9,876 for cycloserine (or $12.50 per dose), and $2,212 for PZA (or $1.40 per dose). The total cost of a less expensive regimen without CAP or linezolid would be $27,490 (e.g., $15,721 for levofloxacin, $6,952 for ethionamoide, $2,212 for PZA, $2,048 for EMB, and $630 for AMK).

Question 4: What TB patients and programs cannot afford TB treatment? TB patients who cannot afford TB treatment fall into three major categories: employed MDR-TB patients who have a large co-pay or limit; students, temporary workers and undocumented persons; and indigent persons who are not Medicaid-eligible. For TB programs, drug costs typically are larger than their budget.

Question 5: What populations are affected by an interrupted supply of MDR-TB drugs? TB patients, providers and programs have the greatest impact of an interrupted supply of MDR-TB drugs. TB patients could worsen in their disease or acquire further drug resistance. TB could spread throughout the community if providers are unable to treat and manage their cases. TB programs could lose their credibility and capacity to meet core functions. The response to outbreaks could fail if TB is not controlled due to drug shortages or an abundance of disease.

Dr. Flood described recent cases in California to emphasize the impact of an interrupted supply of MDR-TB drugs. At the patient level, a female 26 years of age with a work visa from a European country had a high incidence of MDR-/XDR-TB. The patient was diagnosed with smear-negative/culture-positive cavitary MDR-TB two weeks prior to travel from the country of origin to the United States and was given a ten-day supply of medications by the Green Light Committee (GLC). The physician advised the patient not to worry because “TB medications are free everywhere in the world.”

The patient was found to be smear-positive on arrival to the United States. Second-line DST results were not initially known. The patient had health insurance from her employer, but payment for treatment was disallowed due to the preexisting condition of MDR-TB. The patient was prescribed an initial regimen, but the cost of CAP to the TB program was $140.00 per dose.

The patient was on MDR-TB drugs without an injectable agent >10 days. The receiving jurisdiction treats and manages ~10 TB cases per year and was unable to afford the TB drug regimen, physician, nurse care, DOT and isolation for the subject case. Delivery of GLC medications from the originating country was subsequently arranged through diplomatic channels.

At the local level, one California county reports ~6-10 MDR-TB cases per year in which all patients need an injectable agent. Due to the cost of CAP, the county changed its regimen and pharmacy contract to AMK. The TB controller became concerned when AMK had a protracted shortage.

A special case in California with clofazamine has implications for new drugs. The indications for clofazamine are for persons who are intolerant to other SLDs and also have XDR-TB (*i.e.*, a

third-line option). The timeframe between California's recommendation of clofazamine and for the TB patient to actually receive the drug generally has been 8-10 weeks. Clofazamine has not been available through the traditional pharmaceutical distribution system since 2004, but the drug can be used for Hansen's disease and special circumstances for MDR-TB treatment. WHO, the United States and Novartis have engaged in a joint effort to develop an international compassionate care program for the use of clofazamine.

TB drug shortages have been a longstanding issue. The International Union Against Tuberculosis and Lung Disease documented the problem in a 1994 publication and multiple agencies, programs and individual TB patients have made efforts in the field to reach a resolution. However, responses have been on a case-by-case to date and the timeframe from detecting a shortage to actually distributing drugs to TB patients is extremely lengthy.

Dr. Flood proposed a process to obtain clofazamine for the treatment of TB cases in the United States. After patients completed a simple form, providers would complete the entire application package through the hospital IRB and submit the individual IND to FDA for TB patients who require clofazamine. The application package would include completed forms downloaded from the FDA website, the physician's curriculum vitae, the patient's current laboratory results (e.g., complete blood count, chemistry and sensitivity data), a signed informed consent document, and an IRB approval letter adhering to the Clofazimine Treatment Protocol.

The provider would send the application package to FDA after receiving IRB approval. After FDA approval, clofazamine would be provided to the patient through Hansen's Division/Novartis at no charge. The turnaround time typically is 10-14 days from FDA receiving the faxed application package to the provider receiving clofazimine.

Question 6: What are potential proactive solutions for a continuous drug supply in the United States in 2011 and beyond? A stockpile should be created for TB drugs similar to the anti-botulism toxin stockpile. CDC should closely collaborate with FDA and its other federal partners to establish a simple mechanism for accessing TB drugs, particularly drugs that should be available for compassionate use of XDR-TB cases. A new policy should be passed in which all TB patients would be eligible for and able to access TB drugs with no payment restrictions.

A centralized IRB mechanism should be developed for compassionate use of new or old TB drugs. NTCA's proposal to partner with HRSA to fund MDR-TB drugs should be supported. GLC was established in 2000 to enable access to affordable, high-quality and second-line anti-TB drugs for MDR-TB treatment. This mechanism should be more widely used in the United States.

ACET thanked Dr. Flood for making an extremely important and compelling presentation. The ACET members were concerned with the problems in obtaining SLDs in the United States to treat MDR-/XDR-TB patients. ACET proposed a number of suggestions to address this issue.

- Two of the proposed solutions will not be feasible to assure a continuous supply of MDR-TB drugs in the United States. First, the short expiration dates of drugs, such as AMK and CAP, will not allow for the creation of an MDR-TB drug stockpile. Second,

GLC traditionally has served as a barrier to the scale-up of MDR-TB drugs globally. This mechanism is expected to be dissolved in the near future.

- CDC established an IND protocol with FDA for diphtheria anti-toxin. This mechanism recently allowed the Idaho Department of Health and Welfare to receive the drug directly from the manufacturer in Brazil in one day. The possibility of using CDC's IND with FDA to rapidly obtain MDR-TB drugs in the United States should be considered as an alternative to a stockpile.
- ACET should pass a formal resolution for DTBE to publish Dr. Flood's presentation on challenges in obtaining SLDs in the United States as an expert opinion from the TB community.
- DTBE should use the challenges in obtaining SLDs in the United States as an opportunity to strongly emphasize the need to eliminate co-pays and deductibles for TB drugs under PPACA. DTBE should inform USPSTF that proper treatment of TB is a preventive measure against drug resistance and transmission.
- DTBE should collaborate with NTCA to administer a survey to determine the extent to which states other than California are encountering problems in obtaining SLDs to treat MDR-TB cases. NTCA also should administer a survey to systematically document drug shortages states have encountered over the past two years as well as the cost of drugs to TB programs.
- DTBE should approach leadership in the HRSA 340B Drug Pricing Program to determine whether the program could be expanded to include TB drugs.
- DTBE should launch an educational and training campaign to ensure primary care providers, particularly safety net providers, are aware of available resources for TB drugs in their local communities.
- ACET should write a letter to Dr. Donald Berwick, Administrator of the Centers for Medicaid and Medicare Services (CMS). CMS's new Innovation Center recently began operations with a budget of $10 billion over the next ten years to foster new innovations in patient care, coordinated care models and community health. Because the Innovation Center is testing new payment models, ACET's letter to Dr. Berwick could raise the possibility of using the serious problem with the shortage of SLDs to treat MDR-/XDR-TB patients in the United States as a demonstration project.
- ACET should establish a new workgroup to propose innovative solutions and develop a comprehensive strategy to address the challenges in obtaining SLDs in the United States for the treatment of MDR-/XDR-TB cases. One of the charges of the new workgroup should be identify strategies to streamline the FDA process to rapidly provide TB drugs to patients.

Dr. Castro proposed additional solutions to address the challenges in obtaining SLDs in the United States. DTBE and NTCA should have discussions with manufacturers to conduct a rigorous inventory of the current supply, existing capacity and anticipated shortages of SLDs in the future.

The Treatment Action Group and other parts of the external TB community could play a pivotal role in publicizing the challenges in obtaining SLDs in the United States and emphasizing that a drug shortage for persons with MDR-/XDR-TB is unacceptable in this country. The CDC Drug

Service utilized its central IND in the past to provide streptomycin due to shortages of the drug. This mechanism should be considered as an additional alternative to an MDR-TB stockpile.

## ACET Business Session

Dr. Dean conducted a roll call of the ACET voting members and the non-voting *ex-officio* members and confirmed the presence of a quorum for voting purposes. Dr. Fleenor opened the business session and called for ACET's formal action on the following topics.

***TOPIC 1:*** A motion was properly placed on the floor and seconded by Mr. Joseph Kinney and Dr. Barbara Seaworth, respectively, for ACET to approve the previous meeting minutes. ACET **unanimously approved** the June 29-30, 2010 Draft Meeting Minutes with no changes or further discussion.

***TOPIC 2:*** A motion was properly placed on the floor and seconded by Drs. Barbara Seaworth and Masahiro Narita, respectively, for "DTBE to collect outcome data for all patients whose specimens are submitted to the MDDR Service." **ACET unanimously approved the motion.**

***TOPIC 3:*** A motion was properly placed on the floor and seconded by Drs. Christine Hahn and Barbara Seaworth, respectively, for "DTBE to seek the direct support of USAID for new TB-related initiatives in Mexico in partnership with the U.S.-Mexico Border Health Commission." **ACET unanimously approved the motion.**

***TOPIC 4:*** The following motion was properly placed on the floor and seconded by Dr. Masahiro Narita and Mr. Shannon Jones, respectively: "Whereas, universal genotyping has improved understanding of TB transmission dynamics among the homeless, be it resolved that ACET recommends that DTBE update the guidelines on TB prevention and control among the homeless." **ACET unanimously approved the motion.**

***TOPIC 5:*** The following motion was properly placed on the floor and seconded by Drs. Masahiro Narita and Ana Lopez-de Fede, respectively: "ACET recommends that all persons entering the United States on long-term work or study visas (*i.e.*, more than six months) be required to undergo screening for TB and treatment if indicated utilizing the existing TB Technical Instructions prior to arrival in the United States." **ACET unanimously approved the motion.**

***TOPIC 6:*** The following motion was properly placed on the floor and seconded by Mr. Joseph Kinney and Dr. Christine Hahn, respectively: "ACET recommends that DTBE perform more detailed and descriptive epidemiology of the incidence of TB within major racial/ethnic groups as a routine component of surveillance. ACET recommends that DTBE commission or perform studies to enable estimation of the attributable risks of established acquired and genetic risk factors within major racial/ethnic groups. ACET recommends that DTBE commission or perform studies to enable estimation of the attributable risks of vitamin D deficiency within major racial/ethnic groups. ACET recommends that DTBE institute routine surveillance of presentation with cavitary disease with major racial/ethnic groups as an indicator of presumed treatment delay." **ACET approved the motion with a majority vote of 4 in favor and 2 opposed.**

***TOPIC 7:*** The following motion was properly placed on the floor and seconded by Mr. Shannon Jones and Dr. Christine Hahn, respectively: "ACET recommends a routine report at future meetings and an update on the health equity implementation and evaluation plans as put forth by the NCHHSTP Office of Health Equity. This report should include efforts currently underway by the African American Workgroup and other minority health initiatives and activities, including the U.S.-Mexico Border Health Commission and those efforts that came forth from the Social Determinants of Health initiatives by NCHHSTP. Timelines and expected completion dates should be part of the report." **ACET unanimously approved the motion.**

***TOPIC 8:*** The following motion was properly placed on the floor and seconded by Drs. Barbara Seaworth and Ana Lopez-de Fede, respectively: "ACET recommends that a workgroup be constituted to include NTCA, CDC, and other relevant agencies and organizations not later than January 2011 to compile data on the national availability and cost of second line MDR-TB drugs, and make recommendations on appropriate funding mechanisms for treatment of MDR-TB, and additionally that CDC partner with the Food and Drug Administration to provide a rapid and seamless method to obtain needed second- and third-line drugs." **ACET unanimously approved the motion.**

***TOPIC 9:*** Dr. Fleenor reminded ACET that the following motion was tabled during the June 2010 meeting for formal action during the current meeting: "ACET recommends that states and local jurisdictions, acting in accordance with local regulations and statutes, provide county-level *Mycobacterium tuberculosis* genotype data in the TB GIMS database, for access by designated public health officials for the purpose of facilitating and improving tuberculosis control." Dr. Susan Dorman made the motion during the previous meeting, but was unable to attend the current meeting. **ACET agreed to again table the motion until the March 2011 meeting for further discussion with Dr. Dorman.**

***TOPIC 10:*** Dr. Fleenor pointed out that the delay at the federal level in appointing the new Chair and replacing the five outgoing members has impaired ACET's ability to continue to provide timely and expert advice to the Director of CDC and Secretary of HHS in a seamless manner. To address this issue, a motion was properly placed on the floor and seconded by Dr. Fleenor and Mr. Kinney, respectively, for Dr. Fleenor to write a letter to the HHS Secretary on ACET's behalf requesting the appointment of the new Chair and five outgoing members by the end of 2010. **ACET unanimously approved the motion.**

***TOPIC 11:*** Dr. Fleenor returned the discussion to the draft Foreign-Born Guidelines for ACET to provide additional comments or suggestions.

- Page 5: The overview contains a strong statement that TB among FBP is due to reactivation rather than recent transmission. Dr. Edward Nardell is the liaison to the International Union Against Tuberculosis and Lung Disease. He offered to provide Dr. Katz with supporting evidence to demonstrate that recent transmission indeed plays a role in TB among FBP.
- Pages 5-11: The subsections in the overview should be prioritized based on their importance. For example, "federal requirements for screening of foreign-born persons" and "transnational TB control issues" should be moved to an appendix at the end of the document. This approach would allow providers to focus on the two most important

subsections in the overview at the outset: "prevention of TB in foreign-born persons as part of an overall elimination strategy" and "need for new guidelines for treatment and prevention of TB in foreign-born persons." Other ACET members did not agree with this suggestion because all of the subsections in the overview would be helpful to private practitioners, particularly the guidance for providers to consult with state or local health departments on the TB history of their foreign-born patients.

- Page 10: The five bullets describing the "major changes from previous guidelines" should be placed in a box or table to emphasize these points.
- Page 11: The third sentence in the first paragraph of the "standard of care" subsection should be changed to: "Persons born in countries where TB rates are similar to or lower than U.S. rates do not require routine screening."
- Page 11: New language should be added to the end of the first paragraph in the "standard of care" subsection: "Foreign-born persons account for the majority of TB cases in Australia, Canada and all Western European countries. Providers should be mindful of these rates when assessing populations from low-risk countries."
- Page 23: A new subsection on refugees should be added to the "recommendations and guidelines" section for special populations.
- Page 23: New subsections should be added to specify the "roles and responsibilities" of federal agencies and state health departments in TB prevention and treatment among FBP.
- Page 51: New bullets should be added to Box 5. New bullet 5: "These findings are less likely to represent, but do not exclude active TB disease and are dependent on the expertise of the radiologist." New bullet 6: "A negative chest x-ray does not include active TB disease in HIV-infected persons or asymptomatic persons."
- Page 52: A review should be conducted to identify specific tables that can be combined to streamline this section.
- Page 55: The two "Table 7's" should be renumbered.

ACET agreed to embed written editorial, grammatical or formatting changes into the draft and submit these changes to Dr. Katz at ddk4@cdc.gov no later than November 30, 2010. The final draft with ACET's verbal and written comments would be discussed during the March 2011 meeting for formal adoption.

***TOPIC 12:*** Dr. Fleenor led ACET in a review of future agenda items. (*Editor's Note:* The updates and overviews would be presented by NCHHSTP or DTBE unless otherwise indicated.)

- Overview by DGMQ of guidelines for TB screening and management of refugees.
- Update on lessons learned, successes and effective strategies related to DOT.
- Overview of the role of TB in the National HIV/AIDS Strategy.
- Presentation with recent surveillance data on the current prevalence of TB in the United States by specific categories (e.g., race/ethnicity, gender, urban communities and other geographic locations, and other risk factors).
- Overviews by the Department of Defense: (1) guidelines that influenced the new military requirement for LTBI treatment before formal enlistment into the U.S. Armed Services and (2) TB rates among military personnel who return to the United States from overseas assignments.

- Overview of ACET's activities to fulfill its mission, purpose and commitment of focusing on TB "elimination" versus "prevention and control."
- Overview by NTCA on its January 2011 advocacy training course to TB controllers and patients.
- Update by Stop TB USA on its activities.
- Overview by the Indian Health Service on its recent review of surveillance data to assess the incidence of TB in Native American populations.
- Update on the FDA classification system to evaluate and approve new diagnostics for TB.

## Public Comment Session

Mr. John Seggerson is the Executive Director of Stop TB USA. He has been attending ACET meetings for nearly 25 years as a CDC employee previously and as the Executive Director of Stop TB USA currently. His 25-year involvement with ACET with numerous chairs placed him in a unique position to commend Dr. Fleenor on his extraordinary efforts on improving the focus and direction of ACET. The participants joined Mr. Seggerson in applauding Dr. Fleenor's outstanding leadership of ACET during his tenure as the Chair.

## Closing Session

The next three ACET meetings would be held on March 1-2, 2011; June 7-8, 2011; and October 4-5, 2001. With no further discussion or business brought before ACET, Dr. Fleenor adjourned the meeting at 2:30 p.m. on November 3, 2010.

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

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Date

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