

**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
July 10-11, 2007
Atlanta, Georgia**

Record of the Proceedings

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ATTACHMENT 1

List of Participants

ACET Members

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Dr. Richard Fluck
Mr. Shannon Jones III
Mr. Joseph Kinney
Dr. Ana Lopez-De Fede
Dr. Masahiro Narita
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Ms. Sirlura Taylor

Designated Federal Official

Dr. Kenneth Castro,
Acting Executive Secretary

Ex-Officio and Liaison Members

Dr. William Baine (Agency for Healthcare Research and Quality)
Dr. John Bernardo (National Tuberculosis Controllers Association)
Dr. Amy Bloom (U.S. Agency for International Development)
Dr. Charles Daley
(American Thoracic Society)
Dr. Joseph Goldenson
(National Commission on Correctional Healthcare)
Dr. Margaret Kitt (National Institute for Occupational Safety and Health)
Dr. Michael Leonard (Infectious Disease Society of America)
Dr. Sally Liska (Association of Public Health Laboratories)
Dr. Mamodikoe Makhene
(National Institutes of Health)
Dr. Bonita Mangura (American College of Chest Physicians)
Dr. Edward Nardell
(International Union Against Tuberculosis and Lung Disease)
Dr. Gary Roselle
(Department of Veterans Affairs)

Dr. Diana Schneider (Division of Immigration Health Services)
Ms. Rachel Stricof (Association for Professionals in Infection Control and Epidemiology)
Dr. Litjen Tan (American Medical Association)
Dr. Lornel Tompkins
(National Medical Association)
Dr. Theresa Watkins-Bryant
(Health Resources and Services Administration)
Ms. Claire Wingfield
(Treatment Action Group)

CDC Representatives

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Andrea Barrett (CDC Contractor)
Kris Birkness
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Kevin Cain
Peter Cegielski
Ann Cronin
Hazel Dean
Susan DeLisle
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Judy Gibson
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Denise Koo
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Ann Lanner
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Sandy Price
Margie Scott-Cseh
Thomas Shinnick
Angela Starks
Hillary Strayor
Phillip Talboy
Lisa Thombly
Andrew Vernon
Elsa Villarino
Pei-Chun Wan

Cornelia White
Mitchell Yakrus
Heather Young

**Guest Presenters and
Members of the Public**

David Ashkin
(Florida Department of Health)
Antonino Catanzaro (University of
California-San Diego)
Reynard McDonald (New Jersey Medical
School Global Tuberculosis Institute)
Charles Nolan (Seattle-King County
Department of Public Health)
Carol Pozsik (National Tuberculosis
Controllers Association)
John Seggerson (National Coalition for
the Elimination of Tuberculosis)

ATTACHMENT 2

Acronyms Used In This Report

AAs	— African Americans
ACET	— Advisory Council for the Elimination of Tuberculosis
ACIP	— Advisory Committee on Immunization Practices
AFB	— Acid Fast Bacilli
ATS	— American Thoracic Society
BAL	— Bronchoalveolar Lavage
BSC	— Board of Scientific Counselors
CAPs	— Community-Acquired Pneumonias
CBOs	— Community-Based Organizations
CCID	— Coordinating Center for Infectious Diseases
CDC	— Centers for Disease Control and Prevention
COEs	— Centers of Excellence
CSTE	— Council of State and Territorial Epidemiologists
DEO	— Division of Emergency Operations
DEOC	— Director's Emergency Operations Center
DOD	— Department of Defense
DOS	— Department of State
DOT	— Directly Observed Therapy
DST	— Drug Susceptibility Testing
DTBE	— Division of Tuberculosis Elimination
EPC	— Educational Products Center
FBPs	— Foreign-Born Persons
FBWG	— Foreign Born Workgroup
FTBTF	— Federal TB Task Force
GiMS	— Genotyping Information System
HCW	— Healthcare Worker
HHS	— Department of Health and Human Services
HRSA	— Health Resources and Services Administration
HSV-2	— Herpes Simplex Virus 2
IDSA	— Infectious Disease Society of America
IGRA	— Interferon Gamma Release Assay
IHRs	— International Health Regulations
IMS	— Incident Management System
INH	— Isoniazid
IOM	— International Organization for Migration
LTBI	— Latent TB Infection
MDR-TB	— Multi-Drug Resistant TB
MGIT	— Mycobacteria Growth Indicator Tubes
<i>MMWR</i>	— <i>Morbidity and Mortality Weekly Report</i>
MSM	— Men Who Have Sex With Men
<i>M.tb</i>	— <i>Mycobacterium Tuberculosis</i>
NAAT	— Nucleic Acid Amplification Testing

NCHHSTP	—	National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
NEDSS	—	National Electronic Disease Surveillance System
NIH	—	National Institutes of Health
NTCA	—	National Tuberculosis Controllers Association
NTM	—	Non-Tuberculous Mycobacteria
OEU	—	Outbreak Evaluation Unit
OHRP	—	Office of Human Research Protection
OMB	—	Office of Management and Budget
RAM	—	Program Area Module
PCR	—	Polymerase Chain Reaction
PPD	—	Purified Protein Derivative
OFT	—	QuantiFERON
RIF	—	Rifampin
RTMCCs	—	Regional Training and Medical Consultation Centers
RVCT	—	Reported Verified Case of TB
SARS	—	Severe Acute Respiratory Syndrome
SRMs	—	Streptomycin-Resistant Mutants
TBESC	—	TB Epidemiologic Studies Consortium
TBTC	—	TB Trials Consortium
TIs	—	Technical Instructions
TST	—	Tuberculin Skin Test
USG	—	U.S. Government
VARHS	—	Variant, Atypical and Resistant HIV Surveillance
WHO	—	World Health Organization
XDR-TB	—	Extensively Drug-Resistant TB

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**ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
July 10-11, 2007
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 July 10-11, 2007 at CDC's Corporate Square Offices, Conference Room A/B/C in Atlanta, Georgia.

Opening Session

Dr. Michael Fleenor, Chair of ACET, called the meeting to order at 8:30 a.m. on July 10, 2007. He welcomed the attendees to the proceedings and opened the floor for introductions. The list of participants is appended to the minutes as [Attachment 1](#).

Dr. Kenneth Castro, Director of DTBE and Acting Executive Secretary of ACET, 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 or voting on these discussions.

Update on NCHHSTP Activities

Ms. Susan DeLisle, of NCHHSTP, reported on NCHHSTP's activities in the temporary absence of Dr. Kevin Fenton, Director of NCHHSTP. Dr. Julie Gerberding, Director of CDC, testified before two Congressional committees on June 6, 2007 on extensively drug-

resistant tuberculosis (XDR-TB). Dr. Gerberding's testimony is in the public domain and can be viewed on the CDC web site.

The President's FY'08 budget request for TB is \$136.6 million. However, the Senate Appropriations Committee's mark up of \$147 million reflects an increase of \$10 million over the FY'07 TB level.

The Coordinating Center for Infectious Diseases (CCID) Board of Scientific Counselors (BSC) met with NCHHSTP staff in March 2007 to discuss antimicrobial resistance. Representatives from all NCHHSTP divisions presented overviews of surveillance, laboratory and other activities to address drug resistance in HIV, STDs, TB, and viral hepatitis.

The BSC made several recommendations for NCHHSTP to strengthen its antimicrobial resistance activities. For drug resistance in international settings, surveillance for XDR-TB and HIV drug resistance should be categorized as "high priority," especially among pregnant women <25 years of age and children. Blood spot methods should be developed for infants and adults for medication monitoring and general laboratory capacity. For XDR-TB, the development of laboratory capacity for TB culture should be categorized as "high priority," particularly for situations in which HIV testing institutions are receiving support. Rapid drug suspect tests should be developed for screening use at a minimum.

The development of more formal laboratory networks for monitoring gonorrhea antibiotic resistance and herpes simplex virus 2 (HSV-2) resistance should be categorized as "medium priority." Existing international collaborations should be maximized for emerging infectious diseases, such as H5N1 influenza and severe respiratory acute syndrome, particularly in the Western Pacific Region. Lessons learned from international HIV-related trials should be reviewed and applied to monitor HSV-2 resistance. The BSC gave HSV-2 resistance monitoring a much lower priority than the development of basic HIV and XDR-TB monitoring capacity.

For drug resistance in domestic settings, the BSC categorized several recommendations as "high priority."

- Surveillance should be performed for XDR-TB and HIV drug resistance among persons with new HIV infection.
- The proposal for variant, atypical, and resistant HIV surveillance (VARHS) should be strongly endorsed. VARHS surveillance should be population-based if possible and special interview questions should be asked in nested case-control comparison studies.
- The collection of specimens for sequencing of HIV resistance should be categorized as "surveillance" rather than "research."
- The possibility of conducting surveillance for resistant HIV strains should be investigated.

- CDC should explore the feasibility of conducting HIV resistance testing for low prevalence mutations.
- Collaborative efforts should be undertaken with states to increase real time XDR-TB reporting and multidrug-resistant TB (MDR-TB) reporting if possible.
- Collaborative efforts should be undertaken with states to enhance outbreak detection by assuring the completion of contact investigations through onsite or telephone-based Epi-AIDS or other types of mechanisms.
- Rapid molecular methods should be developed and made available for screening of drug resistance.
- Results of all HIV and TB drug resistance should be readily available and easy to interpret.

NCHHSTP has had three key changes in its senior leadership following the previous ACET meeting with staff being appointed in the following positions: Acting Associate Director for Program Integration, Acting Associate Director for Laboratory Sciences, and Acting Associate Director for Health Disparities.

NCHHSTP formed cross-center workgroups to specifically focus on eight high priority activities: drug users, corrections, health disparities, men who have sex with men (MSM) health, global antenatal health, surveillance and strategic information, program integration, and modeling and health results measures.

Dr. Castro added that DTBE expects to have the strongest relationships with NCHHSTP's health disparities, corrections, surveillance and program integration cross-center workgroups.

DTBE Director's Report

Dr. Castro covered the following areas in his report. DTBE has had four key changes in its senior leadership following the previous ACET meeting. Positions were filled for DTBE's Field Services and Evaluation Branch Chief and International Research and Programs Branch Chief. The team leader for the genotyping component of the Mycobacteriology Laboratory has retired. A key DTBE staff member accepted a position with Otsuka Pharmaceuticals. Other staff changes can be viewed on the DTBE web site.

DTBE initiated the second part of its budget redistribution plan to respond to the changing TB epidemiology in FY'05. Of all TB cooperative agreement resources, 35% were redistributed based on the formula. If \$10-\$14 million in new funding is approved based on the Senate Appropriations Committee's mark or new Congressional language, DTBE could avoid diverting funds from existing TB activities. The new resources would be used to supplement areas with a history of inadequate funding, strengthen research capacity, and enhance other TB activities.

CDC's assessment of the National Electronic Disease Surveillance System showed that the TB Program Area Module (PAM) was deficient. DTBE will assist in developing a new TB PAM based on the revised Reported Verified Case of TB (RVCT) and previous guidance from ACET on the definition of binational cases and other issues. DTBE will provide technical assistance to reporting areas that are developing TB surveillance systems. The guidance primarily will focus on the design of enhanced Public Health Information Network compliant messages for RVCT data reported to DTBE.

DTBE participated in a number of TB, XDR-TB, and MDR-TB investigations from July 2006-July 2007 in response to requests for epidemiologic assistance from South Africa and several states and large cities in the United States. The settings of these outbreaks and clusters included a prison/community, Navy aircraft carrier, casino, passenger cruise ship and overseas travel.

DTBE launched six new TB Epidemiologic Studies Consortium (TBESC) studies in FY'07 focusing on the following areas: (1) TB in African Americans; (2) use QuantiFERON (QFT) Gold in contact tracing; (3) use of QFT as an initial screening tool for U.S.-bound immigrants and the feasibility of follow-up in the United States; (4) treatment practices and outcomes for MDR-/XDR-TB; (5) evaluation of a new social network analysis tool; and (6) an ethnographic study of TB in the Karen-Burmese population.

DTBE is extensively engaged in several TB clinical trials and other studies: (1) the TB Trials Consortium (TBTC) Study 29 to evaluate the possibility of using moxifloxacin and rifapentine as a first-line drug regimen; (2) a meeting with the AIDS Clinical Trials Group in late summer 2007 to expand clinical trial capacity; (3) enhancement of trial capacity in Durban for MDR-TB using one-year funding from the CCID Emerging Infectious Diseases Program; (4) cost studies for MDR-/XDR-TB; (5) the analytic phase of Task Order 2 contact studies; and (6) HIV diagnostic testing of TB patients using CDC's recent opt-out guidance to minimize potential obstacles for HIV testing of TB patients.

DTBE is conducting a number of activities to translate science to policy. Discussions are underway to develop guidelines for the QFT-Gold in-tube assay and potentially the T-spot TB blood test. Ethnographic guides are being printed in several languages to target populations with a high TB burden, including Lao Hmong, Mexican, Somali, Vietnamese, Chinese and Burmese immigrants and refugees.

DTBE's recently completed and upcoming communications and education activities include (1) serving as a subject matter expert for an individual who traveled with XDR-TB; (2) performing a usability study to redesign the DTBE web site; (3) developing new education and training materials, such as *Forging Partnerships to Eliminate TB: Guide and Toolkit*; (4) releasing revisions in 2007-2008 on the TB core curriculum and self-study modules; (5) convening the TB Education and Training Network conference in August 2007; and (6) holding the TB Program Manager's Course in October 2007.

DTBE's Mycobacteriology Laboratory has conducted several activities to support its strategic planning process. The mission statement was updated with a stronger focus on research, the reference laboratory, and both domestic and international technical assistance. DTBE is exploring the possibility of restructuring the laboratory to better identify and establish priorities for various projects.

DTBE is continuing its international activities by (1) providing technical assistance to the Global AIDS Program, President's Emergency Plan for AIDS Relief, and other technical advisory groups; (2) conducting activities related to MDR-/XDR-TB, the global plan, Green Light Committee and TB along the U.S.-Mexico Border; (3) enhancing awareness of travel and quarantine needs; (4) strengthening global disease detection capacity in Thailand; and (5) assessing liquid-based media for culture and drug susceptibility testing (DST) in Thailand.

Update by the ACET Foreign-Born Workgroup (FBWG)

Dr. Dolly Katz, of DTBE, reported on FBWG's progress in updating the 1998 "Recommendations for Prevention and Control of Tuberculosis Among Foreign-Born Persons" (FBPs). FBWG's revised document will contain recommendations in nine major areas: new screening guidance, critical program elements, special issues for health departments, laboratory issues, special FBPs, critical partners, education and training resources, policy recommendations, and future research needs.

In developing the new screening guidance, FBWG discussed FBPs in the United States that should be targeted for screening and reviewed data on TB rates per 100,000 by world region of origin and time spent in the United States. With the exception of Western Europe, Canada, and a few other countries, FBWG acknowledged that TB rates by world region of origin are well above the rate of 2.5 for U.S.-born persons. FBWG also recognized that TB rates among FBPs typically decline after the first two years in the United States, but remain elevated. For example, TB rates in the sub-Saharan population are >20 times higher than U.S.-born persons. These data show that most FBPs are at a relatively high risk of developing TB.

FBWG considered several key issues in its ongoing efforts to update the 1998 foreign-born guidelines. The risk of TB disease is high among nearly all FBPs regardless of duration of residence in the United States. Screening recommendations for individuals need to be simple. Health departments and other institutions have limited resources for screening. FBWG's preliminary recommendations for these two groups of providers are outlined below.

For individual physicians and institutions, all FBPs should be screened, tested and counseled with the exception of FBPs from Canada, Australia, New Zealand, Western

Europe, Japan, and Cuba. The highest priority for TB treatment should be persons with latent TB infection (LTBI), co-morbidities that increase the risk of disease, medical risk factors, abnormal x-rays, or recent entry to the United States (within the past two years). The benefits of LTBI treatment might still outweigh risks, but the provider and patient should jointly make this decision. TB treatment should be administered to patients who develop a risk factor at a later time. Providers should “focus” on TB if the patient develops symptoms.

For health departments, academic institutions, workplaces, congregate living facilities, and other institutions, solid guidance should be provided on outreach activities. Risk groups should be determined for each respective area. Interventions should be targeted beginning with highest risk to lowest risk FBPs based on available resources. Academic institutions, workplaces, and other congregate settings should be considered as ideal locations to begin conducting outreach activities.

Special outreach efforts should be considered for FBPs at extremely high risk of TB in which the risk of disease parallels contacts. For example, published and unpublished data show that recently arrived Ethiopians have extremely high rates of TB with a two-year risk close to 1.5%. This risk compares to a two-year risk for contacts ranging from 0.5%-2%. Special programs should be considered for these groups to enhance the possibility of treatment completion.

Dr. Fleenor advised CDC to consider strengthening its collaborations with the Department of Defense (DOD) due to the large number of FBPs involved in military training. Dr. Castro raised the possibility of extending an invitation for a DOD staff member to serve as a new ACET *ex-officio* member.

Due to the time constraints in discussing the updated foreign-born guidelines in detail, Dr. Katz asked ACET to submit comments to her by e-mail to assist FBWG in further revising and strengthening the document.

Overview of NCHHSTP’s Program Collaboration and Service Collaboration (PCSI) Initiative

Ms. DeLisle explained that NCHHSTP launched the PCSI initiative due to four key determinants of epidemics. First, at-risk populations are similar or overlap in all four epidemics of HIV, viral hepatitis, STD and TB. Second, disease interactions have common transmission and sexual risk behaviors for HIV, hepatitis and STDs. STDs increase the risk of HIV infection. Concurrent disease influences the clinical course of disease and outcomes. Third, social determinants are common among the epidemics, including poor access to and quality of health care; stigma, discrimination, and homophobia; and poverty and other socioeconomic factors. Fourth, prevention and control can be maximized in all four epidemics because effective interventions exist to reduce the burden of TB, viral

hepatitis, HIV and most STDs. However, challenges must be overcome in funding, delivery and monitoring of services, and the quality of prevention services.

NCHHSTP identified a number of common purposes and strategies for the PCSI initiative. Health disparities should be eliminated, particularly in sub-populations with a disproportionate burden of disease. Stigma and associated mistrust should be managed and reduced. Access to high-quality and culturally competent services should be increased for marginalized, under-insured, and uninsured populations. Similar methods of contact tracing should be used to interrupt transmission of disease. Disease should be diagnosed, and treatment or referral to care should be provided expeditiously. Confidentiality systems should be maintained.

NCHHSTP identified a number of common purposes and strategies that bind, HIV, Viral Hepatitis, STD and TB programs; these are eliminating health disparities, particularly in sub-populations with a disproportionate burden of disease; managing stigma and associated mistrust; increasing access to high-quality and culturally competent services for marginalized, under-insured and uninsured populations; employing similar methods of contact tracing to interrupt transmission of disease; expeditious diagnoses and treatment or referral to care; maintaining confidential systems.

The “PCSI vision” is to remove barriers to facilitating adoption of service delivery integration at the client level by aligning NCHHSTP’s activities, systems, and policies within this goal. Reports, briefs, and the literature show that barriers to service delivery integration include (1) restrictive and inflexible use of categorical funds; (2) prescriptive program announcements and discordant reporting requirements; (3) burdensome and inefficient administrative structures; (4) lack of harmony, consistency, synchronization of data collection, and surveillance; (5) minimal guidelines on integrated prevention; (6) insufficient translation and integration of science and programs; and (7) inadequate financial and technical support for cross-training, evaluation, and dissemination of best practices. NCHHSTP plans to develop and distribute a green paper with citations on these barriers to stimulate dialogue and debate on the PCSI initiative.

In addition to conducting a literature review, senior leadership from the four NCHHSTP divisions also made site visits to programs throughout the country. NCHHSTP grantees made a series of recommendations on surveillance and data collection, guidance, training, coordination, and grants and cooperative agreements. NCHHSTP’s site visit reports are available on the CDC web site.

For “surveillance and data collection,” NCHHSTP grantees advised CDC to harmonize data collection instruments and surveillance systems, standardize variables, and develop a standard case report form. For “guidance,” the NCHHSTP grantees advised CDC to develop integrated screening, treatment, and program guidelines on MSM, adolescents, correctional settings, and primary care. Standards should be created for a minimum set of integration activities. Guidance should be developed on service delivery integration.

Elements of plans that enhance collaboration between public health and community-based organizations (CBOs) should be better defined.

For “training,” NCHHSTP grantees advised CDC to structure training that reflects collaboration across NCHHSTP activities. Staff should be trained on service delivery integration. A training module should be developed that allows participants to operate from a common knowledge base. Training should be programmatic rather than clinical in nature. National models should be designed to cross-train public health workers to provide services in all four diseases.

For “grants and cooperative agreements,” NCHHSTP grantees advised CDC to structure grant announcements to facilitate integration and collaboration across CDC centers and within NCHHSTP. Language should be included that requires integration plans with measurable objectives. Objectives for partnership and collaboration should be incorporated. Flexibility should be promoted to ensure local decision-making on the expenditure of funds. Administrative inefficiencies that inhibit the development of integrated programs should be modified.

For “coordination,” NCHHSTP grantees advised CDC to develop a catalog of effective integration strategies to share with other federal agencies and CBOs. Integration should be supported through the development and dissemination of supporting policies, standards of care, guidelines, and an assessment of cost-effectiveness of integrated interventions. Integration of research, translation, and dissemination should be systemized and coordinated. Integration efforts should be coordinated among relevant federal agencies.

NCHHSTP will convene an external consultation on August 21-22, 2007, in Atlanta, Georgia, to provide a forum for ~100 key stakeholders to give advice on establishing PCSI priorities over the next five years. The participants will include funded programs and CBOs, national organizations, state surveillance coordinators, correctional settings, members of ACET and the CDC/HRSA Advisory Committee on HIV and STD Prevention and Treatment, other federal agencies, and staff from each NCHHSTP division. NCHHSTP formed a diverse planning committee with several national organizations to assist in planning the consultation.

Participants at the external consultation will be asked to provide CDC with guidance in six key domains: the PCSI vision and level of integration; implementation and program policy; performance indicators, strategic information, and evaluation; surveillance and data; workforce development, training and education; and guidance and guidelines.

From the summer of 2007 to the spring of 2008, NCHHSTP will prepare and submit the PCSI green paper for internal clearance. However, the green paper will be distributed to stakeholders for review and comment prior to the clearance process. After the external consultation, the green paper will be reconciled and finalized as a PCSI white paper on policy. A PCSI action plan will be published.

The ACET members made two recommendations for NCHHSTP to consider during its ongoing efforts to refine and launch the PCSI initiative. First, PSCI performance indicators on strategic information, evaluation, surveillance, and data should be developed and distributed to stakeholders for review and comment prior to the external consultation. Second, the PSCI initiative should be designed with a strong focus and understanding of significant disparities among the four disease areas in addition to common trends and links.

Overview of the Development of Applied Epidemiology Competencies (AECs)

Dr. Denise Koo, of the CDC Office of Workforce and Career Development, explained that CDC, together with the Council of State and Territorial Epidemiologists (CSTE) developed the AECs in part due to the insufficient number of public health epidemiologists. Moreover, some “epidemiologists” are not adequately trained and lack clear career ladders. Efforts to define the field have been independent, uncoordinated, and largely focused on academic epidemiology.

CDC targeted the AECs to epidemiologists practicing in governmental public health agencies, with a legal mandate to conduct public health activities at local, state, or federal levels. Epidemiologic and non-epidemiologic competencies with multiple tiers of practice were created for epidemiologists. The AECs should be useful for defining necessary skills for hiring epidemiologists. They should also be useful for developing methods to evaluate, reward and promote workers; they provide a road map for training the existing workforce and guidelines for academia. CDC expects the AECs to improve capacity to define the field and also to serve as a valuable resource in any certification process.

CDC took several actions in its methodology to develop the AECs. Existing frameworks and competencies for epidemiology and public health were reviewed. An expert panel with cross-cutting representation was convened and divided into a leadership group, a review panel, along with a consultant/editor. Additional feedback on informatics competencies for epidemiologists was solicited as well.

Dr. Koo explained that the definition of “epidemiologist” developed by the Council of State and Territorial Epidemiologists (CSTE) was adapted by the expert panel; and that the AECs built upon the competency framework for public health professionals developed by the Council on Linkages Between Academia and Public Health Practice. Language was crafted to reflect the unique aspects of epidemiologic practice and also to acknowledge differences in proficiency depending on the level of experience and job expectations.

The proposed AECs were presented at meetings of professional associations. Web-based validation surveys were administered to the practice and academic communities to obtain quantitative and qualitative input from a diverse range of partner organizations.

Respondents to the survey strongly supported the proposed AECs, with none of the competencies receiving <50% approval. Support for the AECs increased as the tier level increased. Responses were consistent with general definitions for each tier level with respect to the highest achieved degree and job title. However, CDC recognized limitations in the validation process such as the fact that the survey was not systematic, with a potential bias due to self-reports, and that the survey asked questions about the AECs at the general level only.

Dr. Koo pointed out that more details on the skill domains and tiers of the AECs were distributed to ACET for review. She noted that additional information also could be obtained from the CDC and CSTE web sites. CDC and CSTE hope the AECs will be useful for practitioners, employers, and educators.

Overview of the National Tuberculosis Curriculum Consortium (NTCC)

Dr. Antonino Catanzaro, of the University of California-San Diego, explained that NTCC is supported by a five-year contract from the National Institutes of Health (NIH) to strengthen capacity to teach TB to undergraduate medical, nursing, and allied health students. NTCC courses are targeted to students pursuing careers as medical doctors, doctors of osteopathy, baccalaureate nurses, nurse practitioners, physician assistants, pharmacists, respiratory therapists, public health professionals, medical technologists, and clinical laboratory scientists.

NTCC is organized with a project director, curriculum unit director, educational computing unit director, and administrative unit director at five regional coordinating centers in New York City, Arkansas, Detroit, Southern California, and Texas. NTCC has national consortium partners at 24 schools with expertise in TB and curriculum development. The remaining partners serve as program directors or department heads. NTCC also has 30 partner organizations that focus on curriculum development, accreditation and certification, and life-long learning.

NTCC's Educational Products Center (EPC) includes computerized cases, resource banks, multimedia images, clinical case descriptions, PowerPoint lectures, games, and a question bank. Standardized patient cases are currently being developed for inclusion in the EPC. The products are designed to augment existing curricula. From July 2006-July 2007, the EPC had 669 registered users representing 289 organizations and 21 countries. EPC products were used or downloaded >5,500 times, with multimedia images being the most popular product among users. Dr. Catanzaro presented a virtual demonstration of the EPC.

Dr. Catanzaro announced that NTCC's five-year contract ends in October 2008. Additional funding is being sought from consortium schools, foundations, and NIH. The possibility of expanding NTCC to additional countries and partners is being explored as well. Efforts also

are being made to retain the NTCC web site to keep products up-to-date, maintain public access, and ensure continued impact on TB education.

Dr. Fleenor announced that ACET would have an opportunity during its business session to formulate guidance on TB professional training and education initiatives. In the interim, ACET advised NTCC to use virtual TB experiences or create a separate approach to specifically increase TB competency of infectious disease and pulmonary fellows.

Update on Technical Instructions for Overseas Screening and Treatment of TB

Dr. Drew Posey, of the CDC Division of Global Migration and Quarantine, reported that the technical instructions (TIs) for TB screening and treatment require medical evaluations for applicants ≥ 6 months of age, a tuberculin skin test (TST) in children six months to five years of age, sputum cultures for applicants with abnormal chest radiographs, DST on positive cultures, and directly observed therapy (DOT) for smear- or culture-positive applicants. The validity period for medical examinations was reduced to six months for applicants with no TB classification and three months for applicants with a Class B1 TB classification.

The HHS Office of General Council determined that the requirement for chest radiographs in applicants < 15 years of age would conflict with regulatory language. As a result, CDC made an interim modification to the TIs and distributed the revision to the Department of State (DOS) in April 2007. CDC is revising the 2007 TIs based on TB incidence of $\geq 20/100,000$ established by the World Health Organization (WHO). In the revised TIs, CDC will incorporate the interim guidance, lessons learned from the Thailand evaluation, and comments submitted by ACET and the National Tuberculosis Controllers Association (NTCA). The new document will be distributed to DOS by the end of FY'07 before other countries begin using the new TIs.

CDC also formed the TB TI Workgroup to discuss the implementation of the TIs, facilitate streamlined communication among stakeholders, and obtain input on the revised TIs. ACET, NTCA, CDC, and the National Coalition for the Elimination of Tuberculosis serve on the workgroup and met by conference call and a face-to-face meeting. In FY'07, the TIs will be implemented in Mexico, Philippines, Thailand, and Vietnam. CDC and external experts made site visits to all four countries to evaluate TB laboratory capacity and DOT programs in preparation for the implementation of the 2007 TIs.

CDC is also focusing on a new Bhutanese refugee group that is scheduled to begin resettlement in FY'08. DOS plans to resettle 7,000-8,000 refugees, with screening to begin in November 2007. The remainder of the 105,000 refugees will be resettled at a rate of 12,000-15,000 persons per year thereafter.

In preparation for the resettlement, CDC will implement the 2007 TIs for Bhutanese refugees and meet with Nepal's national TB program, laboratory and the International Organization for Migration (IOM). Nepal has a very high TB rate of 180/100,000 and an MDR-TB rate of 1.3% of TB cases. CDC has made two site visits to Nepal to review the Katmandu panel site evaluation and refugee evaluation. IOM will perform medical screening near the Bhutanese refugee camps and deliver DOT. A TB laboratory also will be developed near the refugee camps.

Onsite Evaluation of the TB Screening Program for U.S.-Bound Burmese Refugees in Thailand

Dr. Charles Nolan, of the Seattle-King County Department of Public Health, reported on an evaluation that CDC conducted in Thailand in collaboration with a team of external experts. The evaluation team was charged with conducting three major activities: (1) assess IOM's operation within Thailand in relation to CDC's new TIs for TB screening of refugees; (2) provide recommendations to IOM for TB screening and treatment of refugees; and (3) formulate guidance to CDC to improve the effectiveness and practicality of the new TB TIs.

The evaluation team undertook these efforts in response to ACET's recommendation in February 2006 to assess the Hmong TB control program, evaluate the impact of changes in screening, and inform the new screening requirements. Because the Hmong resettlement was nearly complete, however, a decision was made to evaluate IOM's new screening program of 140,000 Burmese refugees living in Thailand who were approved for resettlement in the United States. The IOM program used the Hmong screening algorithm.

From December 2006 to May 2007, the evaluation team held conference calls, met in Bangkok, made a visit to the Mae La refugee camp, and drafted a trip report. The evaluation team took several actions during the site visit to the Mae La refugee camp in April 2007. Tours were conducted of the camp, medical and laboratory facilities, and the "TB Village." The TB case detection process was assessed. Sputum collection, DOT administration, and training and education sessions were observed. Patients, DOT workers, panel physicians, nurses, and other IOM staff were interviewed. The evaluation team also made a site visit to the IOM facility at Pha Wo Hospital in Mae Sot.

Key informant interviews revealed that the most important needs for the IOM TB screening program in Thailand were timely laboratory support services, enhanced data management, access to expert clinical and radiographic consultation, formal training for staff members, and clarification of new TIs for refugee screenings.

The evaluation team's key findings based on the onsite visit to the Mae La refugee camp and a review of data collected from the Tham Hin camp are summarized as follows. The IOM screening program was impressive. TB was over-diagnosed based on abnormal x-

rays with negative smears and cultures. Professional radiology consultation was problematic. The addition of culture and DST to the screening algorithm presented technical challenges but yielded invaluable information. Contamination rates in mycobacteria growth indicator tubes (MGIT) were high. The prevalence of TB among Burmese refugees was not higher than expected, and the MDR-TB rate was lower than in Hmong refugees.

Based on its findings and data review, the evaluation team made recommendations to IOM in four major areas: (1) reducing MGIT contamination rates; (2) standardizing the TST program; (3) enhancing training to interpret and implement the new TIs; and (4) enhancing training for panel physicians to interpret chest X-rays and use the American Thoracic Society (ATS)/CDC/Infectious Disease Society of America (IDSA) guidelines for diagnosis and treatment of TB, including culture-negative and extrapulmonary disease and contacts.

The evaluation team's recommendations to CDC are summarized as follows. Indicators should be developed for monitoring programs that use culture and DST for refugee screening according to the new TIs. The evaluation team proposed a number of indicators to support this recommendation. Minimum levels of training should be specified and accessible to panel radiologists and physicians. A network of clinical consultants should be established in the United States to assist panel radiologists and physicians in treating difficult TB cases. A surveillance system should be developed for reporting smear-positive TB cases in refugees shortly after arrival in the United States.

Overall, the evaluation team was highly impressed by the IOM program for screening U.S.-bound refugees and offered several suggestions to improve this excellent program. Despite technical challenges, the evaluation team strongly believed that cultures and DST add immense value to a refugee screening program. CDC was commended for adding an interim requirement that ended years of debate about the value of culture and DST in this setting. IOM was commended for adding value to refugee screening. The evaluation team concluded that the TB screening program for U.S.-bound refugees and immigrants should be evaluated and aggressively expanded if possible. The evaluation team's full report was distributed to ACET for review.

ACET commended the evaluation team on conducting a solid assessment of the TB screening program for U.S.-bound Burmese refugees in Thailand. The members advised CDC to compile and publish the valuable experiences, lessons learned, and successful outcomes of the evaluation as demonstration projects. The ACET members pointed out that the publication could serve as a tremendous resource as culture is expanded to other areas of the world.

Dr. Fleenor confirmed that ACET would revisit this suggestion during its business session to determine whether a formal recommendation should be made to CDC on the TB screening program for U.S.-bound refugees and immigrants.

Update by the TB in African American Workgroup (AAWG)

Mr. Shannon Jones III is an ACET member and chair of the AAWG. He covered the following areas in his report. AAs have a disproportionate burden of TB in the United States. The 2005 TB rate of 10.8/100,000 in AAs was eight times higher than the TB rate in whites of 1.3/100,000. Of U.S.-born persons reported with TB in 2005, 45% were AAs.

To address and prioritize the important issue of the TB disparity among AAs and other U.S.-born racial/ethnic groups, ACET voted to establish AAWG, appoint a representative from the National Medical Association to serve as a new liaison member, and assign CDC staff to coordinate AAWG's activities. AAWG convened its first conference call in May 2007 and will hold meetings twice a month for the first two months. AAWG established a goal of developing a solid strategic plan to address the TB disparity in AAs within six months, but the members are considering the possibility of extending this timeline. AAWG is also discussing the need to form subgroups to focus on specific components of the strategic plan.

To date, AAWG has formulated three key recommendations for ACET to consider. First, funding algorithms should be reconfigured to target resources to areas with the highest TB burden among AAs in proportion to population-based TB case rates. Second, initiatives and strategies should be developed to foster ongoing communications. Linkages with external partners should be established and supported to further address the TB disparity in AAs. Third, CDC should develop guidelines that govern practices of TB services for AA populations.

Mr. Jones confirmed that during the next ACET meeting, AAWG would present a more substantive update on the development of the strategic plan and implementation guidelines to address the TB disparity in AAs.

Update by NTCA

Ms. Carol Pozsik, Executive Director of NTCA, explained that the purpose of NTCA is to provide a collective voice for TB controllers to advance and advocate for TB control and elimination in the United States. NTCA also counsels and collaborates with organizations and individuals on issues and actions that impact TB control and elimination. NTCA partners with several agencies and organizations to fulfill its mission.

NTCA is interested in a number of ACET's key focus areas, including TB in U.S.-born AAs in the Southeast, CDC's new TIs for overseas panel physicians, new tools to replace TST, Medicaid funding to TB programs, overseas examinations of refugees, electronic notification

of overseas examinations, implications of XDR-TB on TB control programs, funding issues at local, state and federal levels, and new TB drugs, laboratory tests and vaccines.

NTCA renewed its call to action due to DTBE's budget cuts, the decline in TB program funds, and the insignificant amount of new resources for TB research on drugs and vaccine development. NTCA's primary concerns are capacity to address these problems at state and local levels, limited funding to provide services and continue to support programmatic activities, the ability of programs to achieve and sustain cutting edge technologies, and political will to achieve TB elimination in the United States. The Institute of Medicine report states that \$528 million would be needed each year to eliminate TB in the United States and \$250 million would be needed at this time to absolutely control TB.

To support these efforts, NTCA educates Congressional members. Although NTCA is prohibited from lobbying for increased funding due to its receipt of federal dollars, NTCA collaborates with a number of partners to conduct these activities. The NTCA Advocacy Committee has held numerous conference calls since March 2007 to educate Congressional members about TB. NTCA participated in ATS's briefing that was convened in June 2007 with ~50 Senate staffers. NTCA also gave a press conference to inform the media about TB and MDR-/XDR-TB.

Update on the Federal TB Task Force (FTBTF)

Dr. Phillip LoBue, of DTBE, reported on progress FTBTF has made in responding to XDR-TB following the March 2007 ACET meeting. FTBTF formed workgroups to develop respective sections of an XDR-TB action plan. The workgroups were charged with (1) using the 1992 *National Action Plan to Combat MDR-TB* as a model in developing the action plan; (2) covering domestic and international aspects of the U.S. government (USG) response in the action plan; and (3) formatting the action plan with problems, objectives, action steps, and lead USG agencies and partners.

The first draft of the action plan was distributed to ACET and other non-federal partners for review and comment in April 2007. In June 2007, the workgroups revised the following sections based on internal and external feedback: laboratory issues, infection control, research, surveillance, epidemiology and outbreak investigations, partnerships, clinical and programmatic issues, communication and education, and cost analysis. The workgroups also developed a new section on ethical and legal issues.

FTBTF and a contractor are assimilating the sections into a uniform second draft and expect to complete this version in August 2007. The multi-federal agency clearance process is expected to be completed in December 2007. The action plan is expected to be published in the *Morbidity and Mortality Weekly Report (MMWR)* by the end of December 2007. The cost of implementing the action plan is expected to be assessed after the

document is finalized. NIH will co-chair a task force with new representation by the Department of Homeland Security and the Department of Defense.

ACET pointed out that the action plan should highlight the need to evaluate new TB drugs in children, develop specific formulations for the pediatric population, and emphasize the importance of funding for this effort.

Overview of the TB Outbreak Response Plan (ORP) and Epi-AIDs

Dr. John Jereb, of DTBE, explained that DTBE's ORP serves as internal administrative policy and guidance. The ORP is updated each year, posted on the DTBE Intranet, and available to other groups and individuals upon request. DTBE designed the ORP to achieve internal consensus, establish a consistent communication process, coordinate agendas, clarify DTBE's responses, track situations and responses, ensure accountability, and provide training.

The five sections of the ORP address receipt of notifications, reporting of TB transmission, the Outbreak Evaluation Unit (OEU), outbreak responses, and outbreak reporting. DTBE receives information to include in the ORP from a variety of resources, such as health department and news media reports and genotyping databases. DTBE identifies information to include in the online report of TB transmission, shares the data with OEU, and then reviews recommendations developed by OEU.

DTBE identified several "red flags" to share information with OEU and generate a report, such as drug resistance, highly contagious patients, extremely susceptible contacts, children ≤ 5 years of age with TB and no source, a cluster of cases in place and time, genotype clusters, extensive TB transmission, transmission and contacts in several states, and suspected false-positive microbiology results. DTBE has several mechanisms to respond to a report, including Epi-AIDs, financial assistance, and onsite or telephone-based technical assistance from a public health advisor or staff epidemiologist.

Dr. Kashef Ijaz, of DTBE, explained that an Epi-AID is a formal request from a state epidemiologist for CDC to conduct an onsite epidemiologic investigation. CDC dispatches an Epidemic Intelligence Service officer to the outbreak site for two to three weeks to assist the local investigative team, prepare a trip report and recommendations, and evaluate the outbreak data to prevent further transmission.

From 2002-2005, DTBE was involved in 27 TB investigations and categorized 24 of these as TB outbreaks. The number of cases in the 24 TB outbreaks ranged from 2-44; the number of exposed contacts ranged from 94-1,722; and the proportion of persons with LTBI ranged from 4.5%-54.1%. Of the 24 TB outbreaks, seven involved FBPs, 14 involved U.S.-born minorities, nine involved homeless populations, and 13 involved drug users. The four

types of populations were not mutually exclusive. The settings of the outbreaks widely varied and included worksites, healthcare facilities, extended families and social circles, correctional facilities, homeless shelters, drug sharing environments, and a high school.

Contributing factors to the 24 TB outbreaks included delays in seeking treatment, delayed diagnoses, HIV co-infection, concomitant substance abuse, lack of personal and social support and resources to foster treatment and adherence, and protracted exposure periods with advanced disease at the time of diagnosis. The challenges of the 24 TB outbreaks included language and cultural differences, MDR-TB, stigma, distrust of health departments, unwillingness to receive LTBI treatment, and difficulties in identifying, locating and medically evaluating contacts.

A number of public health interventions were made in response to the 24 TB outbreaks. Interpreters and outreach workers were hired from the same community. Access to care was assured. Culturally appropriate educational and outreach efforts were targeted. Treatment incentives and enablers were provided. Collaborations among health departments, correctional facilities and homeless service providers were improved. TB screening procedures at homeless shelters were enhanced. Key health department staff members were dedicated to the outbreaks to establish trust in the community. Access to other services was facilitated, such as completion of high school education.

As of July 10, 2007, DTBE was involved in eight TB investigations throughout the country at the invitation of state and local TB controllers and categorized three of these as TB outbreaks. Populations involved in the 2006-July 10, 2007 TB outbreaks included drug users, FBPs, sailors and civilians aboard a ship, and an airline passenger traveling with MDR-/XDR-TB.

DTBE developed and launched an XDR-TB ORP in collaboration with the CDC Director's Emergency Operation Center. Diverse subject matter experts were convened to assist in preparing a two-tiered list of responders. To date, required paperwork, formalities, and medical and fit-testing requirements were completed. A plan for XDR-TB response deployments was formulated. Capacity to detect XDR-TB genotyping clusters is being enhanced by linking genotyping and surveillance data, including drug susceptibility data. DTBE developed the ORP for XDR-TB with both national and international components.

ACET advised CDC to make outbreak data in Epi-X reports available to each state regardless of its involvement in a TB outbreak. The members noted that results and lessons learned from Epi-X reports would be extremely valuable to TB programs throughout the country. ACET also suggested that CDC update its data repository on TB outbreaks to analyze the effectiveness of sociocultural issues in overcoming challenges associated with outbreaks in high-risk populations.

Update on Recommendations for the Use of BCG Vaccine

Dr. Elsa Villarino, of DTBE, reported that ACET and the Advisory Committee on Immunization Practices (ACIP) published a joint statement in the *MMWR* in 1996 regarding the use of BCG vaccine in the prevention and control of TB in the United States. CDC is now exploring the possibility of updating the recommendations due to a number of key factors. XDR-TB has elicited concerns similar to those raised during the 1985-1992 resurgence of TB and MDR-TB. No new data on BCG efficacy have been generated since the guidelines were published in 1996. Limited data have been produced on the duration of vaccine protection and new vaccine candidates. The recently available interferon gamma release assay (IGRA) might improve the current level of diagnostic accuracy for LTBI.

BCG vaccination is recommended at birth in areas with a high prevalence of TB for protection against serious or fatal forms of childhood TB. BCG vaccination does not prevent transmission of infection, but has been recommended worldwide as a primary mean of healthcare worker (HCW) protection. BCG vaccination is not recommended in TB control or immunization programs in the United States due to the low risk of TB in most of the U.S. population and low vaccine efficacy against infectious pulmonary TB. Moreover, exposure to other non-tuberculous mycobacteria (NTM) interferes with BCG. The future interpretation of post-exposure TST is imprecise in previously vaccinated persons.

The ACET/ACIP joint statement recommended that BCG vaccination be considered in three situations: (1) a high proportion of TB patients infected with *Mycobacterium tuberculosis* (*M.tb*) strains resistant to both isoniazid (INH) and rifampin (RIF); (2) transmission of drug-resistant strains to HCWs and the likelihood of subsequent infection; and (3) unsuccessful implementation of comprehensive TB infection control precautions. ACET and ACIP did not conclude that BCG vaccination was compulsory for employment or assignments into specific work areas.

In controlled trials, the effectiveness of BCG vaccine ranged from 80%-0%. A study published in 2004 showed 52% protection of BCG vaccine against pulmonary TB. The vaccine might cause BCG disease, particularly in immunocompromised persons. The position of some experts is that even with only 50% efficacy, BCG vaccine would be better than treatment of drug-resistant LTBI or TB.

Characteristics of diagnostic methods for LTBI are summarized as follows. Purified protein derivative (PPD) contains numerous *M.tb* antigens that are nearly identical to BCG or NTM antigens. TST might produce positive results in BCG-vaccinated persons or NTM-infected persons without LTBI. QFT-G uses the ESAT-6 and CPF-10 proteins to stimulate whole blood and diagnose LTBI based on the production of interferon gamma. ESAT-6 and CPF-10 are excreted by members of the tuberculosis complex, but are not excreted by any *Mycobacterium bovis* BCG substrain, PPD or most NTM. Although a number of current TB vaccine candidates show promise, none could be considered for inclusion in updated recommendations at this time.

Dr. Villarino asked ACET to consider and provide guidance on several questions to assist CDC in determining whether the 1996 BCG recommendations should be updated. (1) Does the IGRA measure the same protective immunity that would be expected from a positive TST? (2) What test should be used to test vaccinated individuals after BCG administration? (3) For post-vaccination of HCWs with TST ≥ 5 mm, should consideration be given to switching to IGRA-based testing as part of periodic LTBI screening in the future? (4) Would the IGRA be useful for post-vaccination surveillance programs?

Dr. Villarino concluded that the overall risk of transmission of infection to HCWs is small in U.S. healthcare facilities. The majority of risk is associated with the lack of infection control precautions when exposed to an undiagnosed patient with TB or through procedures that could potentially generate high concentrations of infectious particles. The use of BCG may be carefully considered according to individual circumstances, such as HCWs who are assigned to work in areas outside the United States with known MDR problems. In theory, improved specificity of IGRAs should make these tests more useful for post-vaccination follow-up compared to the TST.

ACET made several suggestions for CDC to consider while deciding whether to update the 1996 BCG guidelines.

- Fit-testing methods should be improved with elastomeric face masks. However, solid guidance should be given to clarify that elastomeric face masks do not provide 100% protection and would still be associated with some risk.
- Consideration should be given to boosting HCWs in areas with a high incidence of TB at the time of employment.
- Unrecognized risks of BCG vaccination for persons traveling overseas should be described.
- Data should be collected on the high number of HCWs in South Africa who have had TB in association with the XDR-TB outbreak.

Dr. Castro advised ACET to consider the possibility of forming a workgroup to specifically focus on updating the 1996 BCG recommendations. Dr. Fleenor confirmed that ACET would discuss the need to establish a new BCG workgroup during its business session.

Overview of Public Health Laws of Importance to TB Control

Dr. Richard Goodman, of the CDC Public Health Law Program, explained that CDC is considering options to improve understanding of the status and sufficiency of state laws for TB control and prevention in the setting of progressively emerging drug-resistant TB. At the federal level, the U.S. Constitution guides public health activities with clear language and definitions on federalism, police powers, the commerce clause, and tax and spend clause. At the state level, for example, Colorado revised its TB control statutes to specifically focus on MDR-TB and declared TB as an infectious and communicable disease.

Severe acute respiratory syndrome (SARS), novel and virulent influenza strains, drug-resistant TB, and other well-established and newly emergent problems have generated widespread interest over the past few years in improving understanding of state laws to better address prevention and control of communicable diseases. A number of issues have implications for public health laws and TB control in the United States: (1) the sufficiency of state TB laws in light of drug resistance; (2) potential legal impediments and issues for multi-jurisdictional coordination of TB control activities; (3) understanding and effective application of existing legal authorities; and (4) the relationship between state laws and principles of public health ethics for TB patients in the 21st century.

In coordinating multi-jurisdictional efforts, case management is further complicated when a TB patient travels to another jurisdiction. However, coordination can be achieved by enacting uniform laws. Moreover, memoranda of agreement can be negotiated and executed to cover issues related to screening for the level of infectiousness prior to travel, infection control during travel, responsibility for continuity and completion of treatment and management, and costs after travel.

A legal case in 2002 emphasized the need for public health officials to have knowledge of and understand relevant laws for TB control and other communicable diseases. A patient of Laotian ethnicity who spoke little English was diagnosed with MDR-TB and confined to a county jail for more than nine months while being treated. Public health officials can take a number of approaches to assess their legal preparedness for TB and other communicable threats. A comprehensive legal analysis can be conducted of state laws in a given jurisdiction. Laws can be assessed through a tailored tabletop exercise. State laws can be identified operationally

In 1993, ACET published recommendations on TB control laws in the United States in the *MMWR*. In developing the guidance, CDC asked TB control officers in all states to provide copies of TB control laws and regulations. Based on findings from the review of these laws and regulations, ACET formulated guidance on reporting requirements, additional reporting recommendations, and management of TB cases.

Dr. Goodman described several options for ACET to consider in expanding its 1993 guidance on TB laws. A comprehensive review and characterization can be conducted of all state laws for TB control. A focused assessment can be performed of state TB control laws to address the management and completion of treatment of patients with MDR-/XDR-TB. A focused assessment can be conducted of state procedure due process requirements for TB management. TB control laws can be examined following the dissemination of ACET's 1993 recommendations. Dr. Goodman encouraged ACET to access the CDC web site to obtain additional information on public health law and also to subscribe to CDC's weekly *Public Health Law News*.

- Strong and clear oversight from the federal level should be provided to states in applying public health laws for TB control, particularly in light of stigma associated with TB.
- CDC should collaborate with the Transnational TB Continuity of Care Workgroup. The workgroup made a recommendation to host a legal forum to address multi-jurisdictional issues across states and countries, differences between federal and state laws, and state resources to provide TB care to non-residents.
- ACET's 1993 guidance should be revised to clearly distinguish between the patient, disease and etiologic agent.
- The World Health Assembly's recent enactment of health regulations should be mentioned if ACET decides to update its recommendations on TB control laws.

Dr. Fleenor confirmed that ACET would further explore the possibility of updating its 1993 guidelines on TB control laws during the business session.

ACET Business Session 1

Dr. Fleenor announced that ACET would hold its business session on both days of the meeting because several CDC presenters were unable to attend day 1 of the meeting. For business session 1, Dr. Fleenor entertained a motion for ACET to approve the previous meeting minutes. In response to an issue raised by Dr. Flood, DTBE agreed to contact Dr. Kathleen Moser to ensure that her comment was accurately captured on page 35 of the minutes: "Funds should be diverted from San Diego County cooperative agreement dollars to a stand-alone funding source if the country truly values CureTB."

A motion was properly placed on the floor and seconded by Ms. Taylor and Dr. Fluck, respectively, for ACET to accept the previous minutes pending Dr. Moser's clarification of her comment. ACET **unanimously approved** the March 20-21, 2007 Draft Meeting Minutes with no further changes or discussion.

Dr. Fleenor noted that each ACET member received an "Information Security Awareness Training" CD-ROM. He pointed out that as special government employees, each ACET member would be required to take the online training course.

Dr. Fleenor announced that he would solicit volunteers for a few ACET members to attend NCHHSTP's external consultation on August 21-22, 2007 in Atlanta, Georgia, to provide CDC with input on establishing PCSI priorities. ACET members who attended the external consultation would be asked to report on the outcomes of this event to the full membership at a future meeting.

Dr. Fleenor asked ACET to take formal action on three proposed motions.

1. DTBE should extend an invitation for a DOD staff member to serve as a new ACET *ex-officio* member.
2. CDC and the Thailand evaluation team should publish findings of the onsite assessment of the TB screening program for U.S.-bound Burmese refugees for use in other international settings.
3. ACET should write a letter of support to the Office of Management and Budget (OMB) to facilitate implementation of the revised RVCT document to enhance understanding of the changing TB epidemiology in the United States. The motion was properly placed on the floor and seconded by Drs. Narita and Flood, respectively.

Resolution: ACET **unanimously approved** motions 1 and 2. ACET agreed to table motion 3 until the following day to provide the members with an opportunity to review the revised RVCT document.

Dr. Fleenor reviewed three additional issues that would need ACET's formal action during business session 2 on the following day: (1) development of new recommendations on the use of BCG in HCWs in areas with high TB incidence; (2) the need to form a new workgroup to update ACET's 1993 recommendations on TB control laws; and (3) guidance on the future of NTCC due to end of its five-year contract in October 2008.

Several ACET members made interim suggestions on these issues in preparation for the discussion on the following day.

- The CDC Public Health Law Program should be commissioned to update ACET's 1993 guidance on TB control laws and present findings to ACET for review and comment. This approach would eliminate the need for ACET to form a new workgroup, but implementation of the project would depend on CDC's resources to support this effort.

- ACET should collaborate with ACIP in updating the 1996 BCG guidelines if a decision is made to undertake this effort.
- The updated BCG recommendations should be limited to providing guidance on evaluating, monitoring and following HCWs in high-risk areas due to the lack of new data. Ms. Stricof offered to serve on this new workgroup if ACET voted to undertake this effort.
- The CDC Office of Workforce and Career Development should be encouraged to closely collaborate with NTCC and other professional associations on professional training and education initiatives and the implementation of its epidemiologic competencies.

With no further discussion or business brought before ACET, Dr. Fleenor recessed the meeting at 5:15 p.m. on July 10, 2007.

Overview of the Multinational Investigation of a Traveler with MDR-TB

Dr. Fleenor reconvened the ACET meeting at 8:40 a.m. on July 11, 2007, and yielded the floor to the first presenter.

Dr. Ann Buff, of DTBE, reviewed the timeline of events from January-May 2007 that led up to a patient with MDR-TB who traveled by air from the United States to other countries. On January 4, a white male 31 years of age was evaluated for left-sided chest pain and was otherwise asymptomatic. The working differential diagnosis at the initial visit was TB versus histoplasmosis. On January 12, the patient's primary care physician read the TST as negative. On January 18, the patient's chest CT scan showed a reticulonodular infiltrate in the apical and posterior segments of the right upper lobe with one 9 mm cavity noted.

On January 31, a pulmonologist prescribed a ten-day regimen of a macrolide antibiotic to the patient. On February 14, the patient's chest x-ray slightly improved following completion of treatment. On March 2, the pulmonologist read a second TST as positive at 15 mm. On March 8, the patient's repeat chest CT scan showed no significant changes. Bronchoalveolar lavage (BAL) fluid and biopsy tissue were smear-negative for acid fast bacilli (AFB). On March 21, the pathology report showed focal non-necrotizing granulomatous inflammation based on biopsy tissue taken during the bronchoscopy. The pulmonologist recommended the standard four-drug TB regimen. The patient expressed an interest in obtaining a second opinion prior to beginning TB treatment.

On March 26, *M.tb* was isolated from the patient's BAL specimen. On April 5, the patient completed the initial laboratory tests and started self-administered TB treatment. On April 25, the patient presented to the TB program in Fulton County, Georgia. His induced sputum was AFB smear-negative at this visit. Plans were made to arrange DOT and conduct a

contact investigation. On May 1, the infectious disease physician notified the patient that his *M.tb* isolates showed resistance to both INH and RIF. Due to the patient's upcoming travel plans, CDC was asked to expedite the *M.tb* isolates for second-line DST. Plans were made for the patient to discontinue the standard TB regimen and await second-line DST results.

On May 7, an initial investigation of the patient's close contacts was completed and all six contacts had negative TST results. On May 9, the CDC laboratory confirmed that the patient's *M.tb* isolates were resistant to all four drugs in the standard TB regimen. On May 10, the patient, his family, infectious disease physician, and the Fulton County medical director met for two hours. At that time, the patient was advised not to travel to Europe and was informed that National Jewish Hospital in Denver would be consulted for transfer of care. However, the patient fully intended to travel against medical advice. The Fulton County medical director initiated the process of administrative and potential legal action to prevent the patient from traveling.

On May 12, the patient left for Paris, France, two days earlier than originally planned, with the duration of the flight being 8.25 hours. On May 22, the CDC laboratory released a preliminary report showing that the patient's BAL isolate taken on March 8 had extensive drug resistance, including resistance to fluoroquinolones and injectable drugs. CDC contacted the patient in Rome, Italy, and engaged in telephone negotiations to assure the patient's safe return to the United States. On May 24, the patient left Rome for Prague, Czech Republic, and boarded a flight for Montreal, Canada, with the duration of the flight being 8.25 hours.

On May 24-25, the patient entered the United States by automobile and established contact with CDC. The patient agreed to a voluntary evaluation at Bellevue Hospital in New York City. The patient was served with a provisional isolation order at that time. On May 26-28, the patient was asymptomatic, with four induced sputa that were all AFB smear-negative.

Dr. Buff summarized preliminary results of the patient's contact investigation that involved family, friends, coworkers, HCWs, and at least 34 airline passengers in the United States and abroad. Due to the magnitude of the contact investigation, numerous partners are engaged in this effort, including CDC, the Fulton County Health Department, Georgia TB Control Program, private providers, National Institute for Occupational Safety and Health, state TB controllers, local health departments, WHO, the European CDC, and Health Canada.

The contact investigation showed that the patient had no known contact to persons with TB disease. The patient's travel history was found to be unremarkable with the exception of two vacations in 2006 to the high-burden countries of Vietnam and Cambodia. The patient had no TB symptoms, no positive AFB sputum smears, and no evidence of cavitary disease on chest radiograph. Based on its *2005 Contact Investigation Guidelines*, CDC estimated

that the patient's infectious period began on December 7, 2006, or four weeks before the date of the suspected diagnosis on January 4, 2007.

For the close contact investigation, the first round of screening and evaluation was initiated in May 2007. The second round of screening and evaluation will be performed after July 28 for contacts with ongoing exposure to the patient until mid-May 2007. In the first round of screening, 10 family members and 16 friends and coworkers were identified as close contacts. All of these close contacts have had negative TST results to date, but evaluations have not been completed on two persons.

For the HCW investigation, emphasis was placed on HCWs with exposure to the patient during the administration of procedures. For the air travel contact investigation, the first round of screening and evaluation was initiated on May 30. The second round of screening will be performed after July 23. Both U.S. and non-U.S. citizens and residents are being investigated. Based on WHO's *2006 TB and Air Travel Guidelines*, the patient met the definition of "infectiousness."

Only passengers who traveled with the patient on flights with a duration >8 hours and who were within two rows of the patient would have been considered for inclusion in the investigation according to WHO guidelines. However, a decision was made to offer screening and evaluation to all U.S. citizens and residents who were passengers on these flights. WHO guidelines also recommend screening of flight crew members who may have been in contact with the patient.

Of 435 passengers, 43 were determined to be "high priority." Of 270 passengers identified as U.S. citizens or residents, 26 were seated in high-priority areas of the plane. All 26 of these passengers were directly contacted. The first round of screening and evaluation has been completed on 21 of these passengers to date. Of 244 "lower-priority" passengers, 236 were contacted. The first round of screening and evaluation has been completed on 117 of these passengers to date.

Of the 270 passengers identified as U.S. citizens or residents, seven had positive TST results and seven reported a prior history of positive TST results. Of the seven passengers with current positive TST results, five were born outside of the United States. For the high-priority passengers, 17 were identified on the Air France flight and 30 were identified on the Czech Air flight.

Dr. Buff highlighted several challenges to conducting the contact investigation. Legal jurisdiction for the air travel investigation was unclear. Based on old International Health Regulations, France and Canada had legal authority to conduct investigations associated with the two flights because the country of arrival rather than departure has authority to prevent importation of disease. Different privacy laws of foreign carriers increased the difficulty in obtaining passenger manifests and custom forms. These legal issues caused

delays of more than one week in CDC receiving flight manifests that contained only passengers' names, seat assignments but no additional contact information.

Other barriers to the contact investigation included heightened anxiety among passengers due to strong media attention. A passive surveillance approach relied on passengers to contact CDC. CDC and its partners delivered inconsistent messages to the public. Public understanding of TB was limited, with some passengers being placed on administrative or medical leave by their employers. Risk communication was not effective.

Passengers were informed that two rounds of TB evaluation would be required. However, media reports that "downgraded" the patient's status from XDR-TB to MDR-TB might discourage passengers from returning for the second round of testing. All contact investigations of close contacts, HCWs and passengers will be completed in July 2007. Results of the contact investigation will be disseminated after the data are analyzed.

The ACET members made three key suggestions for CDC to consider in the current and future contact investigations of patients with TB.

- Consideration should be given to performing only second-stage TST in large contact investigations. This approach would provide an opportunity to collect valuable skin test data and avoid the possibility of boosting.
- CDC should clarify to the public during contact investigations that MDR-/XDR-TB are surrogates of infectiousness and do not provide actual evidence of a patient spreading disease.
- CDC's responses to MDR-/XDR-TB and regular TB should be the same because the mode of transmission does not differ. This strategy would minimize overreaction to MDR-TB on the part of public health officials and decrease public fear and anxiety.

Dr. Castro pointed out that the patient who traveled with MDR-TB inadvertently caused some benefits. The old International Health Regulations (IHRs) were updated and enacted in July 2007 to explicitly address exportation of disease. CDC was involved in this effort. Moreover, the European community and Canada have expressed willingness to more rapidly share data with CDC.

Overview of Prescription Failures and Links to Drug Resistance

Dr. Peter Cegielski, of DTBE, explained that "prescription failure" can be interpreted at the individual level affecting patient care directly and also at the population level relating to public health policy. At the individual level, three studies were published from 1947-1955 on (1) the increase in streptomycin-resistant mutants (SRMs) during monotherapy over five

weeks of treatment; (2) the emergence of drug-resistant TB during streptomycin treatment; and (3) INH resistance after two months of monotherapy.

Study 1 showed that the frequency of SRMs rapidly increased as treatment progressed over five weeks of treatment. Study 2 showed that <1 month of streptomycin treatment was a poor indicator to determine drug resistance. Study 3 showed that 88% of patients with 3+ cavitory disease remained culture-positive at two months of treatment. Of these patients, 87% were resistant to INH after receiving INH alone for two months.

A study published in 1993 analyzed TB management errors associated with acquired drug resistance in 35 MDR-TB cases from 1989-1990. Of the 35 MDR-TB cases, 28 had errors in management decisions, with an average of 3.9 errors per patient. A retrospective analysis was published in 2007 of 6,622 culture-positive pulmonary TB patients in Shanghai to determine acquired resistance to first-line drugs over the time period of 1999-2004. Of 322 patients with follow-up DST results, results differed from the baseline in 100 patients. Of 38 patients who had isolates available for analysis, only five had identical genotypes and acquired resistance to one or two drugs over a median of ten months.

A study published in 2007 had a cohort of 416 patients enrolled in a WHO drug resistance survey. Of 382 patients who had baseline isolates available, 82 AFB-positive cases had repeat positive cultures. Of 62 isolate pairs with identical restriction fragment length polymorphism, 19 developed additional resistance to one to three drugs after two to five months of treatment.

Dr. Cegielski summarized data on the development of resistance to second-line drugs during treatment. The two studies were conducted in South Africa in 2004 and Peru in 2005. The South Africa study showed that *M.tb* developed additional drug-resistant mutations in four of 13 MDR-TB patients over a treatment period of 3-56 weeks with second-line drugs. The Peru study showed that *M.tb* acquired resistance to ≥ 1 drugs following failed empiric treatment in 19 of 23 MDR-TB patients. *M.tb* also acquired resistance to two or three drugs in five of 19 patients.

Surveillance data have been collected in the United States on drug susceptible, MDR-TB, and XDR-TB cases by initial drug regimen, provider type, and the extent of DOT. The data excluded rifabutin resistance and final drug resistance in MDR-/XDR-TB patients and were limited to patients who were alive at the time of diagnosis over the time period of 1993-2006.

At the population level, persistent adherence to WHO's standard Category II treatment regimen in the context of substantial population prevalence of drug-resistant TB is a policy failure on the part of leading public health organizations because it leads to the amplification of resistance. The published literature demonstrates problems regarding WHO's standard Category II treatment regimen. Three key studies have focused on (1) cases retreated with the standard category in six countries; (2) drug-resistant cases treated with the standard

category in a Russian prison; and (3) primary drug resistance treated with the standard category in new smear-positive TB cases in Vietnam.

Dr. Cegielski made several observations based on results of the studies of acquired drug resistance. At the individual level, prevention of drug resistance depends on treatment with an adequate number of effective drugs. Empiric regimens should have a sufficient number of effective drugs pending the outcome of DST results. Improved DST methods are an urgent need.

At the public health level in the United States, recent developments related to XDR-TB are playing a critical role in increasing Congressional concern about TB. XDR-TB also might have implications for appropriations in the future to TB control and basic research of TB drug development and DST. At the international level, more vigorous efforts are needed to make culture and DST available to low- and middle-income countries, especially to patients at high risk for drug resistance. This approach could assist in preventing progressive acquisition of drug resistance that ultimately leads to XDR-TB.

The ACET members made two key suggestions that should be considered in conducting future studies on acquired drug resistance. First, stronger emphasis should be placed on laboratory cross-contamination which could easily explain some results related to the frequency and high rates of re-infection. Recent data reviews have shown that laboratory cross-contamination accounted for 3%-5% of patients with positive cultures. Second, national data should be collected to analyze predictors of acquired drug resistance, particularly policy implications for cavitory disease.

Overview of the Regional Training Medical and Consultation Centers (RTMCCs)

Dr. LoBue reported that CDC established the RTMCCs in January 2005 with a vision to make expert medical consultation for TB available to all healthcare providers in the United States, using a regional framework. For purposes of the RTMCCs, CDC defined "medical consultation" as a response to request for advice from a licensed healthcare provider regarding the management of an individual TB patient. CDC launched a competitive process and selected four sites in San Francisco, Texas, Florida, and New Jersey to serve as RTMCCs.

CDC made two keys changes following the initiation of the RTMCCs. First, the original scope was modified for the four sites to provide regional rather than national or state consultation. Second, a needs assessment was performed with potential users of the RTMCCs throughout the country, including TB controllers, medical consultants, and non-health department healthcare providers. Data were gathered on the users' perceived needs and obstacles, preferred modes of information delivery, existing capacity for medical

consultation, opportunities to strengthen current capacity, and desired degree of involvement by state and local TB programs.

Key findings of the needs assessment are summarized as follows. Existing capacity widely varied among states from a high level of “internationally recognized experts” to a low level of “essentially no capacity.” Each region had substantial capacity outside of the RTMCCs and expressed willingness to collaborate with the program. The primary needs included assistance on providing consultation on complex cases involving HIV co-morbidity, the pediatric population, adverse effects, and drug resistance. Key barriers to providing consultation included part-time or volunteer consultants at state and local levels and limited access to chest radiographs and other primary medical information.

Telephone and e-mail consultations were the top two preferred methods for the RTMCCs to deliver information. Nearly all respondents to the needs assessment expressed an interest in serving as the primary medical consultant and noted that the RTMCCs should provide second-line support as a “consultant to the consultant.”

CDC used the needs assessment results to make recommendations and propose strategies to advance the RTMCCs. An individualized approach would be developed to the extent possible. State or local TB programs would serve as the primary medical consultant for most states. RTMCCs would act as the primary medical consultant for states with limited medical capacity. The needs assessment also emphasized the need for the RTMCCs to provide other support activities, such as mentoring new or inexperienced consultants, convening annual consultant meetings and case conferences, providing specialized training for medical consultants, and developing and disseminating resource materials.

The needs assessment results also played a role in CDC issuing specific guidance to the RTMCCs on relying information back to TB programs. First, RTMCCs should promptly contact the responsible TB program for consultations on patients with a significant public health consequence. Second, RTMCCs could use periodic aggregate reports to provide feedback to states on other consultations. Of 1,720 medical consultations the RTMCCs provided to physicians, nurses and other HCWs in 2006, 217 involved drug resistance or MDR-TB.

Dr. Reynard McDonald of the New Jersey RTMCC, Dr. David Ashkin of the Florida RTMCC, Dr. Barbara Seaworth of the Texas RTMCC and an ACET member, and Dr. Joseph Goldenson of the San Francisco RTMCC and an ACET liaison made additional observations on the RTMCC program. The grantees noted that the RTMCCs have served as a valuable tool in training communities and health departments. The RTMCCs are currently attempting to develop a web-based portal in which “frequently asked questions” and responses would be posted on, and available to, users on one site; virtual conference rooms would be available for users to easily share x-rays and other data; and information would be rapidly documented and submitted to the consultant and health department.

In addition to these efforts, the grantees also emphasized the importance of designing a system for RTMCCs to obtain solid data from states in order to provide better medical consultations. The grantees pointed out the critical need for these improvements because resources must be further regionalized due to upcoming budget cuts of the RTMCC infrastructure.

The ACET members made a number of suggestions for CDC to consider in enhancing capacity of the RTMCCs in providing TB training and medical consultations.

- The RTMCCs should strengthen collaborations with health centers and other programs funded by the Health Resources and Services Administration (HRSA). HRSA-funded programs serve refugees, homeless persons, and other patients at high risk for TB throughout the country.
- The RTMCCs should enhance follow-up of medical consultations. This approach should be taken to measure and evaluate improvements in the care and public health of patients.
- The RTMCCs should offer more services and training to non-clinicians, such as front-line workers and other providers in the community who are in a position to make referrals on MDR-TB.
- The RTMCCs should emphasize the critical need for state and local programs to maintain capacity and develop mechanisms to respond to out-of-state requests for input and also to report and follow-up outcomes as necessary.

Dr. Castro thanked ACET for providing valuable input to CDC to improve existing training and medical consultation activities conducted by the RTMCCs. However, he asked ACET to formulate guidance to CDC specifically on the future role of the RTMCCs in treating MDR-/XDR-TB cases.

To support this effort, Dr. Castro raised the possibility of ACET issuing a recommendation to the CDC Office of General Counsel to determine the legal aspects of providing inter-jurisdictional medical consultations. He noted that ACET also could recommend the involvement of the CDC Public Health Law Program in this effort.

Dr. Fleenor confirmed that during its second business session, ACET would revisit the issue of developing recommendations to CDC on the future direction of the RTMCCs in treating MDR-/XDR-TB cases.

Overview of CDC's Laboratory Response to XDR-TB

Dr. Thomas Shinnick, of the DTBE Mycobacteriology Laboratory Branch, reported that the DTBE laboratory developed a seven-point global action plan to combat XDR-TB. Surveys

will be administered to determine the burden of XDR-TB. TB laboratory capacity will be enhanced with an emphasis on rapid DST.

The capacity of health practitioners will be improved to effectively respond to XDR-TB outbreaks and manage patients. Infection control precautions will be implemented. Research for anti-TB drug development and rapid diagnostic tests will be increased. Universal access to antiretroviral drugs will be promoted under joint TB/HIV activities.

DTBE acknowledged that both the coordinated USG response to XDR-TB and FTBTF's XDR-TB National Action Plan contain comprehensive laboratory components. As a result, DTBE will conduct several activities in eight major categories for consistency with these two efforts:

- Increase awareness of the need for prompt laboratory services.
- Ensure the availability of laboratory services for XDR-TB.
- Use a systems approach to improve TB laboratories.
- Identify laboratory capacity to facilitate rapid XDR-TB surveys.
- Develop consensus-based guidelines on TB testing.
- Build U.S. and international TB laboratory capacity.
- Create new and rapid diagnostic tests.
- Mobilize resources and support for international efforts.

In addition to conducting activities in the eight major categories for the laboratory response to XDR-TB, DTBE also will focus on quality improvement planning, research needs, and the development and evaluation of rapid DST that would be suitable for use in resource-limited settings. DTBE plans to closely collaborate and leverage resources with numerous partners at private, local, state, federal and international levels in implementing its laboratory response to XDR-TB.

Moreover, DTBE recognized the important need to develop new Centers of Excellence (COEs) to support its laboratory response to XDR-TB. In the near future, DTBE plans to update and disseminate the 2000 laboratory guidelines to advise the new COEs on the use of nucleic acid amplification testing (NAAT).

Dr. Shinnick concluded his presentation by announcing that local and state public health laboratories have expressed a strong interest in participating in DTBE's laboratory response to XDR-TB so long as solid leadership and guidance is provided from the federal level.

Several ACET members made suggestions for DTBE to consider in further developing and refining its laboratory response to XDR-TB.

- CDC should urge participating laboratories to provide AFB smear test results to physicians in small hospitals and local laboratories within 30 minutes. This

approach would inform the clinical decision-making process in small healthcare facilities on isolating patients in potential XDR-TB cases.

- CDC should shift the focus of its XDR-TB laboratory response from detecting to ruling out TB due to the low incidence of TB in the United States. CDC should provide leadership in facilitating the availability of rapid NAAT capacity in all hospitals to achieve this goal. This strategy would be a much needed improvement over the current practice of obtaining three negative AFB smears from patients.
- CDC should design the new laboratory COEs to include consultations that specifically address laboratory issues and difficult drug-resistant cases.
- CDC should conduct research to determine the rationale for the lower sensitivity of NAAT in TB versus the higher sensitivity of NAAT in herpes, STD and other infectious diseases. Studies to fill these laboratory data gaps could greatly assist clinicians in treating TB.

Overview of CDC's Support of the XDR-TB Response

Capt. Ralph O'Connor, of the CDC Division of Emergency Operations (DEO), explained that DEO is extensively involved in supporting CDC's XDR-TB response along with other centers and divisions. DEO is housed in the CDC Coordinating Office of Terrorism Preparedness and Emergency Response and has a vision to be recognized as the premier national public health emergency operations center.

DEO is responsible for conducting activities in seven primary areas: (1) manage CDC's public health watch and call center 24 hours per day, seven days a week and 365 days per year and augment these activities as necessary; (2) maintain situational awareness and alert CDC leadership and HHS about high-profile incidents; (3) analyze, synthesize, and summarize all operationally relevant information; (4) coordinate Incident Management System (IMS) training and staffing; (5) establish and maintain effective communications and coordination with partners; (6) conduct planning and exercises; and (7) provide logistical support.

DEO has led CDC's responses to several public health events, including the 9/11 terrorist attacks, anthrax and SARS outbreaks, Hurricanes Katrina and Rita, avian influenza, and West Nile virus. DEO also oversees the Director's Emergency Operations Center (DEOC) that was established to monitor CDC's global involvement in major public health events.

DEOC serves as CDC's incident management center during an emergency and provides capacity for all CDC entities to respond to requests for assistance by state, federal, local or

private partners. CDC traditionally categorized its response to emergencies as a “watch,” “alert,” or “response” mode. Over the past year, however, CDC refined the three response phases as tiers 0-3 to specify the number of staff that would be needed for a particular event.

CDC has designed its emergency response activities to be consistent with other federal efforts. Most notably, the National Response Plan establishes guiding principles for domestic incidents. The National Incident Management System provides a consistent nationwide approach for incident management. The ICS simplifies the management and reporting structure of an event and also promotes stability, consistency, familiarity, daily operations, and transparent transition of an incident. CDC primarily follows the ICS principles in responding to an event.

In its rapid response to XDR-TB, DEOC held internal and international conference calls and convened a meeting from 9:30 a.m. to 1:00 p.m. on June 1, 2007. DEOC took these actions to identify suspected secondary cases, determine violations of a federal or state isolation order, notify the media of significant events, and report important changes in clinical status of the index patient.

Other efforts have been made to support CDC’s emergency response activities. Contractors make aircraft available to CDC to transport specimens and up to 14 passengers with a two-hour response time for domestic trips and a six-hour response time for international trips. On June 14, 2007, CDC and DOD signed a biological containment system interagency agreement to transport infectious or contagious patients on a CDC aircraft.

Capt. O’Connor concluded his presentation by acknowledging the need for CDC to improve its emergency response activities. For example, DEOC’s separate toll-free number that is available to stakeholders during high-profile events should be more widely publicized.

Overview of the Role of Genotyping in the XDR-TB Response

Dr. Patrick Moonan, of DTBE, conveyed that FTBTF’s XDR-TB action plan strongly focuses on laboratory capacity. FTBTF noted in its action plan that epidemiologic studies are needed to better understand XDR-TB due to limited understanding of the risk factors and transmission dynamics of XDR-TB at both domestic and international levels.

In response to this problem, CDC developed a course of action to clarify an epidemiologic profile, risk factors, and transmission dynamics of XDR-TB. CDC created its course of action with two key components to systematically analyze national genotyping data in relation to XDR-TB cases. The National MDR-/XDR-TB Registry was designed to collect

revised RVCT variables and additional information on fluoroquinolones, treatment and outcome data, serial culture, and DST results.

The TB Genotyping Information System (GiMS) was designed to provide a centralized solution to track isolate submission and genotype results; improve communication of results; and enhance efficiency of epidemiologic analyses by automating data collection and compilation and associating data to surveillance records. The project charter for the TB GiMS was completed in March 2007, and funding is expected to be allocated in August 2007. CDC expects to launch phase 1 of the TB GiMS in September-December 2007 and pilot the project in January-March 2008.

CDC will use TBESC Task Order 8 to respond to the problem outlined in FTBTF's XDR-TB action plan to understand transmission dynamics under different exposure settings, such as high-, medium- and low-incidence areas. The action step to address this issue will be to compare results of in-depth analysis of existing XDR-TB contact investigations and national genotyping data for different exposure settings. TBESC Task Order 8 was designed as a three-year cross-sectional study of the molecular epidemiology of MDR-TB in the United States. The objectives of the study are to determine factors related to the frequency, contribution, transmission, and prevention of MDR-TB in the United States. To date, 10 patients have been enrolled in TBESC Task Order 8.

Dr. Moonan described the role of genotyping in a multinational investigation of a patient with MDR-TB who traveled by air from the United States to other countries. Preliminary polymerase chain reaction (PCR) based genotyping results became available to CDC on May 31, 2007, and were shared with >100 international and domestic colleagues. In an effort to identify the origin of transmission, CDC questioned whether the strain had been previously identified in any surveillance activities or research studies.

CDC learned that the strain of the patient was in the Haarlem 3 family. The PCR genotype was found to be unique to the United States and in worldwide databases. The investigation of the XDR-TB case mobilized a large international network of experts, demonstrated the need for enhanced global molecular surveillance, and revealed gaps in the current domestic genotyping program.

Dr. Moonan announced that CDC is making progress in genotyping XDR-TB cases by increasing laboratory capacity, enhancing technologies, producing tools to manage and analyze data, and making preparations to conduct several epidemiologic studies.

The ACET members made two key suggestions for CDC to consider in its ongoing efforts to use genotyping in the XDR-TB response. First, CDC should take advantage of the unique opportunity to apply universal genotyping in XDR-TB preparedness. For the first time, this technology can be used to analyze a population of cases at the state or national level. Genotyping also can play a role in distinguishing between re-infection and acquired drug resistance by examining initial and final drug resistance patterns along with genotyping

data. This approach should be taken to quantify the problem of XDR-TB in the United States.

Second, CDC should pay for a system and shipping costs that bundle the components of rapid diagnosis and medical consultation of MDR-TB and real-time genotyping to detect transmission of outbreaks. For example, CDC could pay for the rapid RIF assay for resistance to any TB-positive isolate from any location in the United States. This approach should be taken to facilitate genotyping the isolate, directly sending the isolate to second-line laboratories, and encouraging early involvement of regional centers for RIF-resistant isolates.

ACET Business Session 2

Dr. Fleenor opened the floor for ACET to discuss and take action on its outstanding business items.

Dr. LoBue recalled that during the March 2007 meeting, ACET discussed the Office of Human Research Protection's (OHRP) proposed guidance to define certain activities as "research" and engage CDC scientists in these "research" activities. CDC and other groups expressed concern that OHRP's proposed guidance would have serious implications for program evaluation efforts, the use of surveillance data, and CDC's other public health functions. The public comment period has closed on the proposed guidance and OHRP has not yet informed CDC of its official decision to revise the document.

Resolution: CDC would provide an update to ACET at a future meeting on OHRP's final determination on revising its proposed guidance on research.

Dr. Castro advised ACET to engage in a discussion during its next meeting on the allocation of new TB funding of \$10 million that has been proposed. He encouraged ACET to focus its discussion on TB research, budget cuts to TBESC and TBTC, support for laboratory capacity, global TB activities, and TB training, education and consultation. However, he also urged ACET to discuss the second part of the TB budget redistribution plan in the event level funding is appropriated in FY'08.

Dr. Castro noted that although the next ACET meeting would be held after the new fiscal year on October 1, 2008, CDC most likely would still be operating under a continuing resolution. As a result, he assured the members that the November 2007 meeting would still allow sufficient time for ACET to provide input on the allocation of new TB resources in FY'08. Dr. Castro confirmed that DTBE would present different TB budget models to assist ACET in formulating guidance to CDC.

Resolution: ACET agreed to place a discussion of DTBE's TB budget on its next agenda.

Dr. Castro described two options for ACET to consider in providing further input on funding of the XDR-TB action plan. First, Dr. Gerberding could be invited to attend the next ACET meeting and provide a status report. Second, the ACET Chair and a few members could request a face-to-face meeting with Dr. Gerberding prior to the next meeting. Dr. Gerberding could then be invited to the following meeting to provide an update to the full membership.

Resolution: Drs. Castro and Fleenor would discuss the best approach for ACET to provide additional feedback on funding of the XDR-TB action plan and report their findings to ACET.

Dr. Fleenor noted that ACET tabled its motion on the revised RVCT document on the previous day. However, the document was not distributed for ACET's review and formal action on this issue.

Resolution: ACET would continue to table the motion on the revised RVCT document. Dr. Fleenor would consult with Dr. Castro to determine whether ACET could take formal action on the motion over the next two weeks outside of a public meeting. If ACET is allowed to vote on this issue via conference call, a letter of support would be written to OMB to facilitate implementation of the revised RVCT document. DTBE apologized for not providing ACET with the document overnight, but confirmed that the document would be distributed prior to the conference call.

Dr. John Bernardo, ACET's liaison representative to NTCA, announced that he drafted a letter to assist ACET in providing advice to NIH on the future of NTCC. He highlighted six major points that would potentially serve as the basis of ACET's recommendation.

- ACET expresses its formal support and continued funding of NTCC.
- ACET recommends an evaluation of NTCC's activities to determine both successful and ineffective efforts.
- ACET recommends that NTCC maintain its principal mission to educate medical and allied health students in the United States.
- ACET recommends an extension of NTCC's reach and scope to include training and education to pulmonary and infectious disease fellows.
- ACET recommends an extension of NTCC's scope to include international venues. WHO strategies, international TB standards developed by the Joint Commission and other available mechanisms should be considered to achieve this goal.
- ACET recommends that NTCC collaborate with Dr. Koo in CDC's Office of Workforce and Career Development.

On the one hand, some ACET members were in favor of providing more comprehensive guidance rather than sending a letter to NIH to specifically address NTCC. The members pointed out that ACET should emphasize the need for future funding of TB professional

training and education based on a review and evaluation of existing programs conducted by CDC and other groups.

In its broader recommendation, the members noted that ACET could ask CDC to convene a forum with federal partners and other organizations to explore the possibility of integrating various professional training and education initiatives. This opportunity also could be used to identify strategies to formally include TB in these ongoing efforts. For example, HRSA's AIDS Education and Training Centers and DEOC's dedicated funding for XDR-TB could serve as valuable resources in an integrated TB training and education initiative.

On the other hand, some ACET members were in favor of a parallel approach. For example, ACET would express its formal support for the continuation of NTCC, while recommending a comprehensive and integrated approach on TB professional training and education.

Resolution: ACET agreed to take a parallel approach in providing guidance on TB professional training and education.

For the first component, the following motion was properly placed on the floor and seconded by Dr. Seaworth and Mr. Kinney, respectively. "ACET supports NTCC's efforts and recommends continued funding of this program." ACET **unanimously approved** the motion. ACET agreed to revisit the issue of writing a letter to NIH to specifically address NTCC during the November 2007 meeting. Dr. Catanzaro would be invited to attend the meeting to ensure the accuracy of the content of the letter.

For the second component, ACET agreed that the following actions should be taken. Drs. Bernardo, Catanzaro and Seaworth would draft language on an integrated approach to TB professional training and education for ACET's discussion and formal action during the November 2007 meeting. Efforts would be made for various CDC divisions, NIH, HRSA, and other partners and stakeholders to make presentations and propose strategies to ACET on integrating, coordinating, evaluating, funding, and filling data gaps in existing education and training initiatives. A representative from the Francis J. Curry National Tuberculosis Center also would be invited to make a presentation during the next ACET meeting because this group previously developed a strategic plan for TB education.

Dr. Bernardo announced that he drafted a letter to express his concerns about the revised ATS/IDSA guidelines on community-acquired pneumonias (CAPs) because the statement has implications for TB control and antibiotic resistance. Several papers have documented that inappropriate use of fluoroquinolones in medical practice could lead to delays in diagnosis and drug resistance, particularly in patients with unsuspected TB. The revised ATS/IDSA guidelines give fluoroquinolones more prominence in recommendations for empiric treatment of CAPs and only mention TB in a cursory fashion.

Dr. Bernardo highlighted the major suggestions in his letter. One, ATS and IDSA should re-review the revised guidelines in the context of TB. Two, ATS and IDSA should consider publishing an editorial or modifying the revised guidelines to strongly advise physicians to consider TB. Three, ATS and IDSA should develop and distribute a table of TB risk factors and web links to other TB resources to assist physicians in the decision-making process. Four, physicians should be urged to use antibiotics other than fluoroquinolones in patients who are at risk for TB. Dr. Bernardo noted that his letter and the revised ATS/IDSA guidelines were distributed to ACET for review and potential action.

Resolution: The following motion was properly placed on the floor and seconded by Drs. Flood and Burman, respectively. “The authors of the revised ATS/IDSA guidelines on CAPs should reconsider the recommendations on fluoroquinolones; include risk factors related to TB diagnosis in the statement; and modify the guidelines to illustrate a major thrust and focus on TB.” Dr. Flood made the motion with the provision for CDC to confirm whether ACET is chartered to provide formal advice and recommendations to professional societies. ACET **unanimously approved** the motion with respect to Dr. Flood’s disclaimer.

Several ACET members noted that the Centers for Medicare and Medicaid Services is an HHS agency and has adopted rapid administration of fluoroquinolones and other antibiotics as a patient quality indicator in the treatment of CAPs. Dr. Diana Schneider, ACET’s *ex-officio* member for the Division of Immigration Health Services, suggested directing the recommendation to the HHS Secretary in addition to ATS and IDSA.

Dr. Fleenor reminded the members that on the previous day, ACET did not resolve the issue of whether to address BCG vaccination.

Resolution: The following motion was properly placed on the floor and seconded by Drs. Seaworth and Lopez-De Fede, respectively. “ACET should form a new BCG Workgroup with the following charge: (1) review the existing literature; (2) collect data on the potential efficacy or disadvantages of BCG vaccination; (3) draft guidance on BCG vaccination of HCWs and students traveling abroad to work in healthcare-related fields; and (4) present draft recommendations for ACET’s review and consideration during the November 2007 meeting.” ACET **unanimously approved** the motion.

Dr. Seaworth would chair the new BCG Workgroup and Dr. Nardell and Ms. Stricof would serve as members. Dr. Fleenor asked other ACET members and liaison representatives to inform him of their interest in serving on the workgroup.

Dr. Fleenor reminded the members that on the previous day, ACET did not resolve the issue of whether to update its 1993 guidelines on TB control laws.

Resolution: The following motion was properly placed on the floor and seconded by Drs. Burman and Flood, respectively. “ACET recommends that CDC and key stakeholders

review TB control laws with an emphasis on inter-jurisdictional issues and legal concerns related to RTMCC consultations.” ACET **unanimously approved** the motion.

Dr. Schneider was aware of the broad nature of the motion, but she was asked ACET to expand the language of the recommendation to specifically highlight certain areas: (1) cross-jurisdictional issues, (2) federal authorities related to persons leaving the United States, (3) clarification of the scope of the new International Health Regulations in the context of TB, and (4) coordination between ACET’s updated guidelines on TB control laws and ongoing activities conducted by the CDC Public Health Law Program and the Transnational TB Continuity of Care Workgroup. None of the voting members expressed opposition to the expanded language proposed by Dr. Schneider.

Several members made suggestions for the ACET Chair and Executive Secretary to consider in improving future meetings.

- Materials should be distributed to ACET well in advance of meetings to assist the members in making substantive recommendations to CDC during meetings.
- The number of presentations should be reduced.
- A list of items requiring formal action by ACET should be circulated to the voting members prior to meetings.
- Goals and objectives should be clearly identified for each agenda item.
- A glossary of acronyms should be developed and distributed to each ACET member.
- PowerPoint presentations should be compiled and distributed to ACET on CD-ROM.

In response to ACET’s suggestion to decrease the number of presentations, Dr. Fleenor explained that he and DTBE recently developed a new process for ACET to gather information and provide guidance to CDC over two meetings.

For example, the current meeting served as meeting 1 and was heavily weighted with presentations on XDR-TB strategic plans, action plans and other activities requiring ACET’s formal action. Following the meeting, ACET would review the PowerPoint slides, background materials and other information on XDR-TB presented by the speakers.

The November 2007 meeting would serve as meeting 2 with a significant reduction in the number of presentations and increased time for discussion to allow ACET to formulate solid recommendations to CDC on its XDR-TB activities. Dr. Fleenor encouraged ACET to provide him with feedback on the new process following the November 2007 meeting.

Due to time constraints, Dr. Fleenor asked the ACET members to contact him via e-mail or telephone to propose future agenda items.

Closing Session

The next ACET meeting was scheduled for November 27-28, 2007. DTBE would poll the members by e-mail to determine availability for convening the following meeting on March 4-5, 2008 or March 25-26, 2008.

With no further discussion or business brought before ACET, Dr. Fleenor adjourned the meeting at 2:50 p.m. on July 11, 2007.

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

Date

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